A Transdiagnostic Approach to the Orthomolecular Treatment of Emotional Disorders: Preliminary Ideas for Intervention and Suggestions for Future Research

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Abstract *Most serious mental disorders are currently treated as though they are discrete diagnostic entities deserving of disorder-specific treatment. However, it is known that many commonalities exist across all emotional disorders (particularly early-stage or mild-to-moderate anxiety and mood disorders). Accordingly, a more parsimonious approach might offer substantive benefits with less cost and broader therapeutic efficacy. In the field of psychology, broad-spectrum transdiagnostic approaches are gaining traction because of their emphasis on psychological perturbations common to emotional disorders. The transdiagnostic approach suggests an array of possibilities when considering potential orthomolecular treatments for emotional disorders. If orthomolecular treatments could lessen or ameliorate psychological perturbations associated with mild to moderate emotional disorders, it should be possible to achieve favourable outcomes with fewer costs and without the need for extensive laboratory testing and time-consuming medical investigations. The innovative, comprehensive, and targeted therapeutic system proposed in this paper is based on the underlying pathology associated with emotional disorders, and aims to address negative affect (a.k.a., neuroticism), repetitive negative thinking, experiential avoidance, and dysfunctional decision-making and cognitive control. It is presumed that some of the orthomolecular interventions proposed in the Transdiagnostic Orthomolecular Approach Version 1.0 should be capable of ameliorating the shared psychological perturbations associated with mild to moderate emotional disorders. The limitations of this approach are also described, as are areas for potential research and future directions.*

Introduction

Magnitude of the Problem

A 2013 report by the Mental Health Commission of Canada highlighted that almost everyone in society is affected by the significant burden of mental illnesses.[1] It is worth citing some statistics from this report. For instance, more than 6.7 million people in Canada live with a mental health problem or a mental illness. This amounts to 19.8% of the population, or approximately one in five persons in Canada. Over the duration of a lifetime 43% of people in Canada will experience a mental health problem or illness, which amounts to four out of ten people. If these findings are extended to families and caregivers then almost every person in Canada is affected either directly or indirectly by mental health problems or illnesses. Mental health problems and illnesses also account

for the greatest total direct care costs compared to six other major health conditions. Some 21.4% of the working population has mental health problems or illnesses that adversely impact their work and productivity. In 2011, this cost more $6.4 billion in lost productivity and this loss is estimated to increase to $16 billion in 2041. Over the next thirty years, the cumulative costs for providing treatment, care, and support services for Canadians with mental health problems are projected to surpass $2.53 trillion current dollars.

Disappointing Long-term Outcomes from Psychotropic Medications

Analysis of the long-term data on the efficacy of psychotropic medications has regrettably not yielded the robust evidence of improvements in morbidity that seemed possible and likely when these medications were first discovered and used.[2-17] For a more thorough discussion of this perspective, please consider reviewing one of the author's prior publications in this journal.[18] Since the significance of this problem is so massive, it is essential that every possible treatment option be explored to limit the burden of mental health problems and illnesses upon society.

Novel Ideas Emerging From Transdiagnostic Psychological Treatment Approaches

Most serious mental disorders are currently treated as though they are discrete diagnostic entities deserving of disorder-specific treatment. However, it is known that many commonalities exist across all emotional disorders (particularly early-stage or mild-to-moderate anxiety and mood disorders). Accordingly, a more parsimonious approach might offer substantive benefits with less cost and broader therapeutic efficacy. In the field of psychology, broad-spectrum transdiagnostic approaches are gaining traction because of their treatment emphasis on common psychological perturbations that cross many emotional disorders. In a paper reviewing the conceptual background of the transdiagnostic treatment of emotional disorders, various citations were presented to demonstrate that: (1) a general neurotic syndrome more aptly explains many of the symptoms associated with anxiety and depression (i.e., these symptoms are mere phenotypic variations in the expression of this broader neurotic syndrome); (2) hyperexcitability of limbic structures accompanied by impaired or limited inhibitory control differentiates persons with anxiety and depression from those without these disorders; (3) two genetically-based core dimensions of temperament contribute to the etiology of anxiety and mood disorders (i.e., neuroticism/negative affectivity and extraversion/positive affectivity); and (4) generalized biological and psychological vulnerabilities associated with adverse early childhood experiences interfere with the development of effective coping strategies and self-efficacy.[19]

Based on these commonalities, transdiagnostic psychological treatments have been developed to assuage anxiety and depressive symptoms and the accompanying disorder-related comorbidities. Evolving evidence shows that several transdiagnostic psychological approaches have clinical evidence of efficacy for the treatment of emotional disorders.[20] For instance, the transdiagnostic Unified Protocol for the psychological treatment of emotional disorders addresses the common psychological perturbations of anxiety and depression by using psychotherapeutic targeted techniques to: (1) increase present-focused emotion awareness; (2) increase cognitive flexibility; (3) identify and prevent patterns of emotion avoidance and maladaptive emotion-driven behaviors; (4) increase awareness and tolerance of emotion-related physical sensations; and (5) improve interoceptive and situation-based emotion-focused exposure.[21]

Toward A Putative and Parsimonious Transdiagnostic Orthomolecular Approach to Emotional Disorders

The transdiagnostic psychological approach suggests an array of possibilities when considering potential orthomolecular treatments for emotional disorders. If

orthomolecular treatments could lessen or ameliorate shared psychological perturbations associated with early-stage and mild-to-moderate emotional disorders, it should be possible to achieve favourable outcomes with fewer costs and without the need for extensive laboratory testing and time-consuming medical investigations. To develop a transdiagnostic orthomolecular approach, it will be essential to identify shared psychological perturbations among individuals with emotional disorders, and then identify orthomolecular treatments that may moderate them. Only perturbations believed to be modifiable by orthomolecular interventions will be presented here.

Negative Affect/Neuroticism

A known psychological perturbation found among individuals with emotional disorders concerns high negative affect (NA; a.k.a., neuroticism).[22] NA "suggests subjective distress, and subsumes a range of negative mood states, including fear, anxiety, hostility, scorn, and disgust."[23] Put more succinctly, NA is considered a pervasive trait diathesis to experience negative emotions that influences cognition, self-concept, and worldview.[24] Research has shown that neuroticism or NA are genetically linked to emotional disorders and accounts for about 30% to 50% of the liability for individual emotional disorders.[22] High NA is a higher order factor that is closely related to all emotional disorders (e.g., see Figure 2 – "Structural Relations of Anxiety Disorders and Depression" from Barlow[22]). Put another way, all emotional disorders are significantly predicted by high NA or neuroticism (i.e., all p-values<0.001 in one study, for example[25]). High NA also results in autonomic arousal that leads to increased corticotrophin-releasing factor and hypothalamic-pituitary-adrenocortical axis overactivation.[22]

Positive Affect

In contrast to NA, positive affect (PA) "is a dimension reflecting pleasurable engagement with the environment."[23] Individuals high in this dimension have more enthusiasm, energy, mental alertness, joy and determination whereas those low in this dimension tend experience fatigue and lethargy.[23] Low PA is not associated with all emotional disorders however it does have strong associations to depression and social phobia.[24] Thus, low PA would not be considered a shared psychological perturbation found among individuals with emotional disorders.

Repetitive Negative Thinking

Repetitive negative thinking (RNT) encompasses rumination and worry. Since rumination and worry only differ in content (i.e., their temporal orientation), both are seen to arise from similar psychological processes and are found among all individuals with emotional disorders.[26] Individuals with rumination experience anxiety and depressive symptoms as their cognitions fluctuate between uncertainty and hopelessness.[27] Rumination is maladaptive because it negatively affects thinking and problem-solving capacity, and causes difficulties with the implementation of solutions, uncertainty, and less engagement in distracting, mood-elevating activities.[28] Research has shown that rumination predicts symptoms of both anxiety and depression, and that a ruminative response style is characteristic of individuals who have some combination of anxiety and depressive symptoms.[27] In a clinical sample of adults "baseline depression predicted increases in anxiety and baseline anxiety predicted increases in depression; rumination mediated both of these associations" (i.e., $p<0.001$, respectively).[28] In another clinical sample of adults, the results demonstrated that RNT is an important transdiagnostic factor in emotional disorders, and may be a suitable focus of treatment.[29]

Experiential Avoidance

Experiential avoidance (EA) is another transdiagnostic psychological perturbation believed to be associated with emotional disorders. It is characterized by an "unwillingness to remain in contact with aversive private experience (including bodily sensations,

emotions, thoughts, memories, and behavioral predispositions)" and "action taken to alter the aversive experiences or the events that elicit them."[30] EA mediates or influences the following mental health conditions: substance use relapse; the relationship between traumatic events and general psychological distress; symptom severity in generalized anxiety disorder and trichotillomania; and "the relationship between maladaptive coping and self-regulatory strategies, and psychological distress."[30] EA is not as strong a transdiagnostic factor as NA and RNT. The published data has not been able to delineate with certainty that EA is a broad transdiagnostic construct, or is instead a combination of related constructs (e.g., thought suppression, thought control, and avoidance coping). To confuse matters further, research has surprisingly described the aforementioned related constructs as classical examples of EA.[30] The preliminary and emerging evidence nonetheless suggests the EA plays a role in the psychopathology of emotional and other types of mental disorders.

Dysfunctional Decision-Making and Cognitive Control

Poor decision-making and difficulties exerting control over behaviors, thoughts, and emotions are common features shared by a variety of mental disorders, such as addiction, eating disorders, and emotional disorders. This dysfunction in decision-making and cognitive control are presumed to be transdiagnostic core mechanisms and diathesis factors for a variety of mental disorders.[31] It used to be presumed that top-down neural processes controlled goal-directed action (i.e., a central executive system), but in reality, a distributed network of interacting broad-scale brain systems control such actions.[32] Dysfunction in cognitive control networks results in such issues as (1) problems maintaining goals when faced with competing desires, (2) problems inhibiting routine or impulsive responses, (3) a proneness for drug-cues or threat-cues, (4) problems furnishing predictions and meta-cognitive control (e.g., poor planning when trying to avoid temptation as in addictions), (5) impaired ability to regulate negative emotions or stress, and (6) diminished cognitive flexibility.[31] The net effect of these issues is impulsivity in choices and difficulties suppressing or stopping the execution of habitual responses. These cognitive control deficits are found among individuals with emotional disorders, and involve disordered connectivity between various cognitive control networks that include the dorsolateral prefrontal cortex, parietal cortex, and anterior cingulate cortex.[31] Even though there are more questions than answers about dysfunctional decision-making and cognitive control, such as whether or not these problems arise from or cause mental disorders, these transdiagnostic mechanisms are implicated in numerous mental disorders, including emotional disorders.

A Putative Parsimonious Transdiagnostic Orthomolecular Approach To Emotional Disorders

Given the complexities involved with the above-noted psychological perturbations and how they interface with neural networks, physiological systems, and biochemical processes, the reader may question how orthomolecular interventions could help to moderate them. The reasoning for this perspective and approach is based on the fact that the brain is the most metabolically active organ and the "moment-to-moment functioning of the brain…requires an adequate supply of micronutrients that act as cofactors or as structural parts of enzymes."[33] Any alteration in micronutrient status will impact the brain because of the brain's marked sensitivity to its molecular environment. These changes are likely to impact psychological parameters long before biochemical assays or testing could establish that there is some abnormality (i.e., insufficiency, deficiency, and/or additional need) of a particular micronutrient or some combination thereof.[33]

Given the relationship between the brain's constant metabolic demands and micronutrient supply, psychological parameters would likely respond to improvements in

micronutrient supply, and therefore it makes sense to base orthomolecular recommendations on psychological parameters rather than measureable organic processes. The ultimate aim is to find empirical evidence which demonstrates the clinical efficacy of orthomolecular interventions to lessen the psychological morbidity associated with emotional disorders. The discussion presented below will highlight specific orthomolecules with evidence of clinical efficacy, then propose their hypothetical ability to interface with the psychological perturbations mentioned previously.

Lessening Negative Affect (NA)/ Neuroticism

Certain orthomolecular interventions should have the capacity to moderate NA and reduce some of the morbidity associated with emotional disorders. To assist in the clinical management of NA, it would seem reasonable to offer patients orthomolecules that enhance mood (i.e., that possess antidepressant effects), such as omega-3 essential fatty acids (i.e., 1,000 mg/day of combined eicosapentaenoic acid/EPA and docosahexaenoic acid/DHA),[34] s-adenosylmethionine (1,600 mg/day),[34] 5-hydroxytryptophan (400 mg/day),[35] and magnesium glycinate (125-300 mg four times daily).[36]

Anxiety and/or stress are other aspects involved with NA, which can be moderated by a variety of orthomolecules, such as amino acids, magnesium, vitamin C, and omega-3 essential fatty acids. In a study that evaluated psychosocial stress in subjects with relatively high trait anxiety, the daily amounts of L-lysine and L-arginine shown to be beneficial were 3,000 mg of each.[37] Another study evaluated trait and stress-induced anxiety among healthy volunteers and found daily doses of 2,640 mg of each amino acid beneficial.[38] Gamma-aminobutyric acid (GABA) has been shown to lessen anxiety in a study (n=13) that evaluated its therapeutic effects.[39] Sixty minutes after ingesting 100 mg of PharmaGABA® (i.e., a form of GABA produced by a fermentation process that utilizes *Lactobacillus Hilgardii*[40]), the electroencephalographic readings showed statistically significant increases in alpha waves ($p<0.05$) and decreases in beta waves. The results showed PharmaGABA® to possess relaxation and anti-anxiety effects presumably by increasing the production of alpha waves. Similarly, L-theanine (200 mg/day) was shown to lessen baseline anxiety among healthy human subjects in a clinical trial, apparently by increasing alpha waves.[41]

Magnesium holds promise as a treatment to moderate anxiety and/or stress. Clinical trials that evaluated magnesium (100 mg/day) in combination with other micronutrients have shown benefits on perceived stress[42,43] and anxiety.[42] Magnesium (200 mg/day[44] or 250 mg/day[45]) in combination with vitamin B_6 improved anxiety-related premenstrual symptoms. Some data suggests that magnesium supplementation is warranted in situations involving chronic emotional stress (however defined), since excessive stress can disrupt magnesium homeostasis while also increasing oxidative stress.[46]

Vitamin C might lessen NA since preliminary human research has shown it to moderate stress both physiologically and psychologically. When 3,000 mg of timed-release vitamin C was given in divided doses throughout the day to 60 healthy adults for 14-days, blood pressure, cortisol, and subjective response to acute psychological stress were all palliated.[47] When 500 mg of vitamin C was included in a multiple vitamin/mineral preparation that contained modest amounts of B-complex vitamins, calcium and magnesium, and zinc, the results at the end of the trial demonstrated statistically-significant reductions in perceived stress.[42] Even though the latter study did not rely on vitamin C exclusively, basic animal research has shown that the adrenal cortex and the adrenal medulla both accumulate high levels of vitamin C and that the vitamin functions as a cofactor in catecholamine biosynthesis and adrenal steroidogenesis.[48]

Omega-3 essential fatty acids might also attenuate anxiety. In a three month clinical study, the daily use of 2,250 mg of EPA and 500 mg of DHA reduced anxiety among in-

dividuals who were substance abusers.[49] In another clinical study lasting three months, 2,085 mg of EPA and 348 mg of DHA reduced anxiety among medical students who did not have anxiety disorder diagnoses.[50]

Lessening Repetitive Negative Thinking (RNT)

As mentioned previously, rumination and worry reflect RNT, which is an overarching psychological process found among individuals with emotional disorders. Obsessive-compulsive disorder (OCD) is a related mental disorder even though it is considered distinct from the emotional disorders mentioned in this paper. Given the relationship between rumination and obsessional thinking,[51] clinical data demonstrating improvements in OCD after orthomolecular interventions might offer clinicians valuable therapeutic options when attempting to deintensify the psychological overwhelm that results from RNT among individuals with emotional disorders.

One potential option is n-acetylcysteine (NAC), an amino acid that lowers symptoms of OCD by modulating glutamate.[52] A case report demonstrated improvements in symptoms of OCD when 3,000 mg/day of NAC was given to augment the effects of fluvoxamine.[53] A randomized controlled trial demonstrated that doses of NAC up to 2,400 mg/day in addition to standard treatment reduced symptoms in patients with refractory OCD.[54] However, a retrospective chart review of six treatment-resistant patients with refractory OCD disclosed that mean daily doses of NAC close to 3,000 mg/day over the course of six to twelve weeks failed to benefit the five patients that took NAC to augment standard treatment.[55] A recent randomized controlled trial did not show statistically significant and clinically meaningful effects when 3,000 mg of NAC was administered to adults patients with OCD.[56] Only four patients from this trial (20%) were considered responders to the NAC at sixteen weeks.

Glycine is another amino acid that can modulate glutamate activity in the brain and help to reduce symptoms of OCD.[57] In a randomized controlled trial, twenty-four adults were given either 60 grams/day of glycine or placebo for twelve weeks.[58] Patients who received glycine (n=5) experienced a mean decrease of 6.04 points in the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) compared with a 1.00 point decrease for those receiving placebo (n=9). The patients receiving glycine had an average 0.82 decrease in Y-BOCS score for each week they remained in the study, not quite reaching statistical significance (p=0.053). Two of the patients taking glycine were responders, whereas the placebo group had no responders . Despite the significant dropouts, two patients continued taking glycine under the care of their regular treating psychiatrist for over a year and continued to experience benefits. Poor palatability and nausea were the reasons for the high dropout rates in this trial. In a case involving a patient with refractory OCD, high daily doses of glycine that averaged around 40 g/day was able to significantly moderate symptoms over a five year duration.[59]

Lessening Experiential Avoidance (EA)

EA is often associated with addictive behaviors. One of the reasons why individuals seek out substances like alcohol or cannabis is because they feel emotionally overwhelmed from having aversive private experiences. They use substances to lessen the uncomfortable emotional intensity that arises from EA. Thus, it seems clinically plausible that orthomolecular interventions which have therapeutic efficacy in lessening addictive behaviors might also lessen EA among non-addicted individuals with emotional disorders.

NAC might lessen EA because it has been shown to help a range of impulsive-compulsive disorders (e.g., cannabis dependence, cocaine dependence, pathological gambling, pathological nail biting, pathological skin picking, smoking, and trichotillomania).[60,61] The daily doses used to lessen impulsive-compulsive behaviors varied in these studies, but ranged from 1,500 mg to 3,600 mg.

A case report demonstrated that a broad-spectrum micronutrient supplement containing mostly vitamins and minerals might lessen EA because it attenuated the use of alcohol and cigarettes.[62] When the patient was not taking the broad-spectrum micronutrient supplement, the use of alcohol and cigarettes increased, and then decreased again when the broad-spectrum micronutrient supplement was re-introduced.

These orthomolecular interventions do not only reduce the cravings (i.e., the behaviors) that drive impulsive-compulsive disorders. They likely also reduce some of the emotional overwhelm associated with EA, which helps to diminish avoidant behaviors.

Improving Cognitive Function to Assist with Decision-Making

It is conceivable that some orthomolecular interventions improve decision-making since they reduce impulsive-compulsive behaviors as noted above. It is also conceivable that some orthomolecular interventions support cognitive processes, which might have the added benefit of improving decision-making by exerting therapeutic effects upon cerebral cortical function. The literature pertaining to mild cognitive impairment (MCI) suggests that several orthomolecular interventions upregulate mental processes related to cerebral cortical function. This suggests that these interventions might improve cognitive performance and assist in beneficial decision-making among patients with emotional disorders.

Omega-3 essential fatty acids are major components of neuronal cell membranes that impact various neurological pathways and processes. Evidence suggests that omega-3 essential fatty acids, particularly DHA, have the capacity to enhance cognitive performance in such areas as learning, memory, and speed of cognitive processing.[63] As for the optimal daily dose of both EPA and DHA that favourably impact cognitive function, that is difficult to determine since many different daily doses have been used in numerous clinical trials. In one trial, for example, daily doses of omega-3 essential fatty acids providing 1,320 mg of EPA and 880 mg of DHA resulted in improved executive function, as well as improved brain white matter structural integrity and grey matter volume in frontal, temporal, parietal, and limbic brain areas.[64] Thus, daily doses that approximate these amounts of EPA and DHA might be capable of augmenting cognitive function and performance.

The trace mineral chromium (1,000 mcg/day for 12 weeks) was evaluated in a randomized clinical trial involving 26 older adults.[65] The use of chromium resulted in reduced semantic interference on learning, recall, and recognition memory tasks compared to placebo. Among subjects taking chromium who were further evaluated with functional magnetic resonance imaging, the results showed increased activation in the right thalamic, right temporal, right posterior parietal, and bifrontal regions. The results showed that chromium can improve memory function in older adults at risk for neurodegeneration. While the sample size for this trial was small (n=15 for treatment group and n=11 for placebo), the effect sizes were moderate-to-large, suggesting that chromium might be capable of augmenting cognitive function and performance among individuals with emotional disorders.

Citicoline (cytidine 5'-diphosphocholine; CDP-choline) is an endogenous nutrient that functions as an essential precursor for the synthesis of phosphatidylcholine.[66] Citicoline protects cell membranes by accelerating the re-synthesis of phospholipids, and attenuates the progression of ischemic cell damage by abrogating the release of free fatty acids.[66] In a trial involving 20 patients with amnestic MCI (age range 50-90 years), 1,000 mg of citicoline twice daily for 90 days resulted in statistically significant improvements in cognitive function.[67] In a trial involving patients with mild vascular cognitive impairment, citicoline (500 mg twice daily) was deemed to be effective and shown to affect the following specific properties involved with cognitive function: (1) the biosynthesis of phospholipids in neuronal membranes; (2) brain metabolism; (3) norepinephrine and

dopamine levels in the central nervous system; and (4) neuroprotective effects during hypoxia and ischemia.[68] Similar to omega-3 essential fatty acids and chromium, citicoline might be able to improve cognitive function and performance, and therefore facilitate decision-making among individuals with emotional disorders.

Transdiagnostic Orthomolecular Approach to Emotional Disorders Version 1.0

Based on the assumptions presented in this paper, the therapeutic system described as Version 1.0 is aimed at lessening the morbidity associated with emotional disorders by lessening the emotional overwhelm associated with specific transdiagnostic psychological perturbations. This approach is compatible with the idea that psychological perturbations represent crucial and readily alterable psychological constructs that underlie the psychopathology of emotional disorders. This should interest clinicians since treatment is aimed at the moderation of psychological perturbations by optimizing biochemistry, physiology and metabolism. An important application of the therapeutic system is that it should also serve as a useful platform when psychiatric medications have not yielded favourable outcomes. This therapeutic approach could be safely combined with psychiatric medications, and may produce better clinical outcomes than monotherapeutics.

Table 1 (p. 125) summarizes the therapeutic system proposed in this paper, and the accompanying psychological perturbations that should be lessened when using multiple orthomolecular interventions to address the psychological morbidity associated with emotional disorders.

Limitations and Suggestions for Further Research

This paper proposes an untested approach. Various other orthomolecular substances could have also been included in the Transdiagnostic Orthomolecular Approach Version 1.0. The therapeutic system proposed is purely hypothetical since none of the orthomolecular interventions, either individually and/or in combination, have been specifically studied as substances capable of moderating the specific psychological perturbations mentioned in this paper.

This therapeutic approach might be limited in efficacy since it excludes the specific examination of biomarkers known to be associated with better outcomes in the treatment of emotional disorders, such as: (1) higher baseline plasma levels of vitamin B_{12} predict better outcomes from major depressive disorder;[69] and (2) elevations of plasma B-vitamin levels can lower homocysteine levels and have beneficial effects on mood.[70] Perhaps a more evolved (and expansive) Transdiagnostic Orthomolecular Approach than Version 1.0 will in the future include specific biomarkers known to be associated with emotional disorders.

Another limitation is that the Transdiagnostic Orthomolecular Approach Version 1.0 may not be capable of addressing all of the complexities associated with serious emotional disorders. Like any approach, its effectiveness could be enhanced if utilized as part of a comprehensive approach that might involve some combination of metabolic testing and differential diagnosing followed by pharmacotherapy, psychotherapy, mindfulness-based practice, regular exercise, and/or eating a more micronutrient-rich diet.

Nonetheless, this approach represents an attempt at identifying some well-known transdiagnostic psychological perturbations associated with emotional disorders and using specific orthomolecular treatments that might be capable of ameliorating them. The goal would be to offer struggling patients a combination of some of the aforementioned orthomolecular interventions to lessen the morbidity that often accompanies emotional disorders. It is presumed that an improvement in psychological functionality will likewise improve biomarkers associated with better outcomes in the treatment of emotional disorders without specifically testing for them. As was mentioned previously, any alteration in micronutrient status will impact the brain because of its marked sensitivity

Table 1. Transdiagnostic Orthomolecular Approach Version 1.0

Orthomolecular Intervention (in order of mention/ appearance)	Suggested Divided Daily Doses	Moderated Psychological Perturbation Associated with Emotional Disorders
Omega-3 Essential Fatty Acids (i.e., EPA and DHA)	1,000-2,250 mg EPA and 500-880 mg DHA	NA/Neuroticism; Dysfunctional decision-making and cognitive control
L-Lysine	2,640-3,000 mg	NA/Neuroticism
L-Arginine	2,640-3,000 mg	NA/Neuroticism
GABA (as PharmaGABA®)	100 mg	NA/Neuroticism
L-Theanine	200 mg	NA/Neuroticism
Vitamin C	500-3,000 mg	NA/Neuroticism
Magnesium	100-1,200 mg	NA/Neuroticism
NAC	1,500-3,000 mg	RNT; EA
Glycine	40-60 g	RNT
Broad-Spectrum Micronutrient[1]	8 pills	NA; EA
Chromium	1,000 mcg	Dysfunctional decision-making and cognitive control
Citicoline	1,000-2,000 mg	Dysfunctional decision-making and cognitive control

[1] Information pertaining to this specific broad-spectrum micronutrient product can be found at: http://www.truehope.com/ingredients.html

to its molecular environment. These changes could impact psychological parameters before biochemical assays or testing would be able to establish some evidence of metabolic abnormality.[33] Thus, addressing psychological perturbations with a transdiagnostic orthomolecular approach assumes that this approach would bring some normalcy to the psychopathological (and metabolic) processes implicated in emotional disorders even when biomarker testing might not be sensitive enough to identify metabolic derangements.

With respect to future research directions, many mental disorders share common transdiagnostic psychological perturbations. This approach could be extended to the treatment of schizophrenia spectrum and other psychotic disorders, obsessive-compulsive and related disorders, and possibly even trauma- and stressor-related disorders. Given that there are an increasing number of publications on transdiagnostic psychological approaches, the future of orthomolecular treatment could expand to offer transdiagnostic approaches to patients with a range of emotional disorders.

Conclusion

An innovative, comprehensive, and targeted therapeutic system is described that is based on the underlying pathology associated with emotional disorders. It is presumed that some combination of the orthomolecular interventions from the Transdiagnostic Orthomolecular Approach Version 1.0 should be capable of ameliorating the shared psychological perturbations associated with early-stage and mild-to-moderate emotional disorders.

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Competing Interests

The author declares that he has no competing interests.

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