

## Orthomolecular Therapeutics to Support Resilience

I have been working with individuals who experience emotional overwhelm for many years. I have noticed that the system of mental health care in Ontario, Canada, tends to be very responsive to patients when they are acutely dysregulated. I define this as a mental state characterized by significant distress that includes but is not limited to the following: severe or unremitting anxiety; marked mood instability; violent and/or aggressive behaviour; unrelenting suicidality, suicidal intent, or suicide attempt; and/or unremitting (i.e., unmanageable) psychosis. Such patients are usually brought to the hospital (or end up in hospital) where they are promptly evaluated and treated until they have been sufficiently stabilized. Then they are released back into the community for ongoing treatment by a family physician, general practitioner, and/or a psychiatrist. Thus, in Ontario, and likely in Canada overall, there is a fairly responsive mental health system that manages acute crises rather well and helps patients to achieve some measure of stability before they are released into the general community once again.

The problem is that the mental health system has been more or less hijacked by the massive demands and resources that become mobilized to deal effectively with acute mental health crises. As a result, not enough resources have been allocated to prevent mental health crises, and/or to encourage resilience among vulnerable individuals. What would happen if orthomolecular medicine was used to build resilience among people struggling with persistent mental health issues? What would this orthomolecular programme look like?

Before delving more deeply, it is important to have some working definition of what resilience is. Resilience is a concept that speaks to an individual's ability to meet life's challenges. Even though no consensus or operational definition of resilience has been

universally accepted, it has been defined as the "positive adaptation, or the ability to maintain or regain mental health, despite experiencing adversity."<sup>1</sup> Resilience has also been conceptualized as having the capacity to thrive when faced with adversity, which equates to achieving a state of biopsychospiritual balance.<sup>2</sup>

When examining the sources of resilience in a person's life, it is imperative that various sources of resilience work in concert to ensure the presence of enough protective factors so that resilience is achieved. Herman et al<sup>1</sup> determined that the sources of resilience include the following: (1) Personal Factors that encompass protective personality traits (i.e., openness, extraversion, and agreeableness), other factors (i.e., an internal locus of control, self-efficacy, self-esteem, and cognitive appraisal), and optimism; (2) Biological Factors that involve beneficial physical changes in the brain (i.e., brain size, alterations in neural networks, receptor sensitivity, and/or neurotransmitter synthesis and reuptake) to lessen the vulnerability to psychopathology; and (3) Environmental-Systemic Factors that encompasses the microenvironment (i.e., relationships with family and peers) and the macrosystemic level (e.g., having access to good schools, adequate community resources, religion and spirituality, effective social policy, and very little exposure to violence). If too many stressors overwhelm an individual's resilience sources, it is likely that mental health issues will emerge that could result in chronic mental dysfunction. If, on the other hand, there are enough protective sources of resilience, it is conceivable that an individual will be able to maintain mental health despite the presence of ongoing stressors, or might even thrive amidst adversity.

Since orthomolecular medicine aims to provide for the optimal molecular environment of the brain and other tissues, it is conceivable that the use of specific vitamins (and their metabolites), minerals, and other naturally-occurring molecules would support the Personal and Biological Factors (as mentioned previously) involved in facilitat-

ing or furthering resilience.

I have compiled a list of orthomolecular therapeutics – based on empirical observation, safety (and their low potential for harm if unsupervised) and some published evidence – that could be offered to individuals as resilience-building therapeutics, or that could be safely taken without clinical supervision. The published evidence presented here is by no means exhaustive and the groups studied in many of the described intervention trials are vastly different from most individuals that would benefit from these treatments. Nonetheless, it seems reasonable that for individuals in need of resilience, a combination of several or many of the orthomolecular therapeutics described below might prove invaluable. If orthomolecular therapeutics were applied on a broad scale, the cost savings to the mental health system as a whole would potentially be significant. There would presumably be reductions in the incidence of psychiatric disorders, including fewer demands on the system by reducing acute mental health crises.

### Resilience-Building Orthomolecular Therapeutics

In a study involving 120 healthy young adults (i.e., males and females in their mid-twenties) timed-release vitamin C (1,000 mg three times daily) was shown to improve the subjective response to acute psychological stress.<sup>3</sup> Vitamin C also moderated blood pressure and increased the salivary cortisol recovery. Basic animal research has shown that the adrenal cortex and the adrenal medulla both accumulate high levels of vitamin C and that vitamin functions as a crucial cofactor in catecholamine biosynthesis and adrenal steroidogenesis.<sup>4</sup>

A study involving healthy males assessed the impact of a supplement containing modest amounts of B-complex vitamins, 500 mg of vitamin C, and 100 mg of both calcium and magnesium.<sup>5</sup> The supplement was taken daily for 33 days and the results showed significant changes in the following parameters: increased vigour and decreased perceived levels of stress. A similar study

evaluating micronutrients and work-related stress used modest doses of B-complex vitamins with low doses of vitamins C and E, magnesium, calcium, other micronutrients, and herbal sedatives (i.e., *Avena sativa* and *Passiflora incarnata*).<sup>6</sup> The use of the supplement resulted in statistically significant reductions in psychological strain.

A study assessed oxidative status and magnesium balance among 35 male volunteers (age range: 18–38 years) exposed to chronic stress.<sup>7</sup> The results showed a negative correlation between magnesium homeostasis and oxidative stress as demonstrated by decreases in both free and total magnesium concentrations, and increases in oxidative damage. The cause of the altered magnesium status was believed to result from: (1) neuroendocrine factors that increased the urinary excretion of magnesium; and (2) complex hormonal alterations that impaired magnesium balance.

Other compelling research has demonstrated significant advantages upon mood and mental health from supplemental magnesium.<sup>8–10</sup> A deficiency of the mineral, coupled with excess calcium and stress, is related to numerous neuropsychiatric symptoms, including agitation, anxiety, irritability, confusion, asthenia, sleeplessness, headaches, delirium, hallucinations, and hyperexcitability.<sup>8</sup> Magnesium deficiency is related to major depression since deficiency can result in N-methyl-D-aspartate receptor dysfunction, neuronal injury and neuronal dysfunction.<sup>9,10</sup> Thus, it appears that it is critical to ensure optimal magnesium intakes (i.e., 125–300 mg in glycinate and taurinate forms with each meal and at bedtime<sup>8</sup>) to safeguard individuals from the negative psychobiological impacts that result from chronic stress.

Probiotic supplementation represents a novel approach to chronic stress management and promoting resilience. They are natural components of the intestinal microbiota and impact gut processes and physiology in a manner that confers better mental and physical health. Among their many functions, probiotics protect the intestinal barrier, reduce lipid peroxidation, increase

microbial-produced neurotransmitters (e.g., gamma-aminobutyric acid), enhance pathways between the gut and brain, improve nutritional status, and modulate neurotrophic chemicals (e.g., brain-derived neurotrophic factor).<sup>11</sup>

A study determined that a specific probiotic strain reduced symptoms of anxiety among patients having chronic fatigue syndrome (CFS). Thirty-nine patients with CFS were randomized to a daily supplementation with either a probiotic providing 24 billion colony forming units (that being, the *Lactobacillus casei* strain) or placebo for 8 weeks.<sup>12</sup> At the conclusion of the study, the CFS patients that took the probiotic supplement had increased levels of both *Lactobacillus* and *Bifidobacteria* in their stool samples, but also had significant reductions in their symptoms of anxiety. Since the probiotic treatment in this study was without any side effects, it certainly looks as though this intervention should be considered for all individuals with and without CFS for whom resilience would be an essential component to their recovery. It is not known just how probiotics influence anxiety (or other mental states), but they are likely capable of altering neurotransmitters, such as serotonin and dopamine. Probiotics might also influence how emotions (such as anxiety) are processed by directly communicating with specific areas of the brain through gut-brain interactions.

The use of omega-3 essential fatty acids confers a multitude of protective effects that support resilience, such as the prevention of suicide and full-blown psychosis, and stress moderation. In a study that evaluated 33 medication-free depressed subjects over a two-year period, seven of the subjects attempted suicide.<sup>13</sup> The results showed that low levels of docosahexaenoic acid (DHA) and higher omega-6-to-omega-3 ratios predicted suicide attempts among the depressed patients over the two-year study period. Thus, to moderate suicide attempts it would be important that clinicians work on dietary strategies to minimize the consumption of omega-6 fatty acids and maximize foods high in omega-3 essential fatty acids.

It would also be sensible to have individuals consume a daily omega-3 essential fatty acid supplement (i.e., providing ample amounts of DHA such as 500 mg or more).

Outside of suicidality, individuals can experience other distressing symptoms including psychosis. A trial investigated the impact of an omega-3 essential fatty acid supplement among subjects who were having psychotic symptoms (i.e. subthreshold psychosis), but had yet to progress to having a primary psychotic disorder (i.e., full-blown psychosis).<sup>14</sup> The subjects were randomized to receive a daily dose of 700 mg of eicosahexanoic acid (EPA), 480 mg of DHA, and 7.6 mg of mixed tocopherols for 12-weeks, and then monitored for 40-weeks. The total study period was 12 months. At the conclusion of the trial, 2 of 41 subjects in the treatment group transitioned to psychotic disorder compared to 11 of 40 subjects in the placebo group (4.9% versus 27.5% respectively;  $p=0.007$ ).

Other studies have shown that the consumption of omega-3 essential fatty acids can possibly lower levels of perceived stress,<sup>15</sup> and attenuate both the heart rate and muscle sympathetic nervous system responses to mental stress.<sup>16</sup> Given how important it is to prevent both suicidality and full-blown psychosis, and to moderate stress, it behooves clinicians to prescribe an omega-3 essential fatty acid with at least a two-to-one ratio of EPA to DHA (e.g., 1,000 mg of EPA and 500 mg of DHA) when augmenting resilience among individuals.

### **Resilience-Building Food-Derived Polyphenols**

Polyphenols are the most plentiful antioxidants in the human diet<sup>17</sup> largely found in fruits, vegetables, cereals, and beverages.<sup>18</sup> Diets that are rich in polyphenols offer protection against a broad range of diseases that include cancer, cardiovascular disease, diabetes, osteoporosis, and neurodegenerative disease.<sup>18</sup> Polyphenols influence cellular energy metabolism and alter signalling pathways of molecules (e.g., brain-derived neurotrophic factor) involved in the en-

hancement of brain function and synaptic plasticity.<sup>19</sup> They confer benefits upon mood and cognition, which help in the promotion of resilience. Thus, dietary manipulation (including therapeutic supplementation with polyphenol-rich sources like curcumin and green tea (contains epigallocatechingallate) represent an important pathway of supporting a more resilient brain.

### The Basic Resilience-Building Plan

Based on the information presented above, it appears that specific orthomolecular therapeutics and food-derived polyphenols support resilience by modulating the Personal and/or Biological Factors that help to maintain or regain mental health when faced with adversity. Here is the basic plan that individuals could follow, or that clinicians ought to consider when helping patients become more resilient.

- B-Complex Supplement: 1-3 pills/day depending on the specific product.
- Vitamin C: 500-3,000 mg/day.
- Magnesium: 125-300 mg in glycinate and taurinate forms with each meal and at bedtime.
- Multi-Strain Probiotic: 1-2 pills/day (providing 24 billion colony-forming units). It might be necessary to do several empiric trials of a couple of different probiotic products to assess which one works best.
- Omega-3 Essential Fatty Acids: The amounts of EPA and DHA should provide a minimum of 1,000 mg and 500 mg, respectively.
- Polyphenols: Consider supplementing with curcumin and green tea extracts. The labels vary depending on the type of curcumin and green tea extracts purchased. It is best to use a highly absorbable curcumin extract, and a green tea extract that contains high amounts of epigallocatechingallate so that several hundred milligrams per day can be obtained.

### Conclusion

This editorial merely touches upon the concept of resilience and the possibility that specific orthomolecular therapeutics modu-

late some of the complex processes involved in maintaining and regaining mental health when faced with life stressors. It is important that we don't limit ourselves to the treatment of psychiatric disorders only, but that we consider building resilience when supporting individuals struggling with ongoing mental health issues.



–Jonathan E. Prousky, ND, MSc  
Editor

### References

1. Herrman H, Stewart DE, Diaz-Granados N, et al: What is resilience? *Can J Psychiatry*, 2011; 56: 258-265.
2. Connor KM, Davidson, JRT: Development of a new resilience scale: the Connor-Davidson Resilience Scale (CD-RISC). *Depress Anxiety*, 2003;18(2):76-82.
3. Brody S, Preut R, Schommer K, et al: A randomized controlled trial of high dose ascorbic acid for reduction of blood pressure, cortisol, and subjective responses to psychological stress. *Psychopharmacology (Berlin)*, 2002; 159: 319-324.
4. Patak P, Willenberg HS, Bornstein SR: Vitamin C is an important cofactor for both adrenal cortex and adrenal medulla. *Endocr Res*, 2004; 30: 871-875.
5. Kennedy DO, Veasey R, Watson A, et al: Effects of high-dose B vitamin complex with vitamin C and minerals on subjective mood and performance in healthy males. *Psychopharmacology (Berlin)*, 2010; 211: 55-68.
6. Stough C, Scholey A, Lloyd J, et al: The effect of 90 day administration of a high dose vitamin B-complex on work stress. *Hum Psychopharmacol*, 2011; 26: 470-476.
7. Cernak I, Savic V, Kotur J, et al: Alterations in magnesium and oxidative stress during chronic emotional stress. *Magnes Res*, 2000; 13: 29-36.
8. Eby GA, Eby KL: Rapid recovery from major depression using magnesium treatment. *Med Hypotheses*, 2006; 67: 362-370.
9. Eby GA, Eby KL: Magnesium for treatment-resistant depression: a review and hypothesis. *Med Hypotheses*, 2010; 74: 649-660.
10. Murck H: Ketamine, magnesium and major depression – from pharmacology to pathology and back. *J Psychiatr Res*, 2013; 47: 955-965.
11. Bested AC, Logan AC, Selhub EM: Intestinal microbiota, probiotics and mental health: from Metchnikoff to modern advances: Part II – contemporary contextual research. *Gut Pathog*, 2013; 5(1): 3.
12. Rao AV, Bested AC, Beaulne TM, et al: A random-

- ized, double-blind, placebo-controlled pilot study of a probiotic in emotional symptoms of chronic fatigue syndrome. *Gut Pathog*, 2009; 1(1): 6.
13. Sublette ME, Hibbein JR, Galfalvy H, et al: Omega-3 polyunsaturated essential fatty acid status as a predictor of future suicide risk. *Am J Psychiatry*, 2006; 163: 1100-1102.
  14. Amminger GP, Schäfer MR, Papageorgiou K, et al: Long-chain omega-3 fatty acids for indicated prevention of psychotic disorders: a randomized, placebo-controlled trial. *Arch Gen Psychiatry*, 2010; 67: 146-154.
  15. Bradbury J, Myers SP, Oliver C: An adaptogenic role for omega-3 fatty acids in stress: a randomized placebo controlled double blind intervention study (pilot). *Nutr J*, 2004; 3: 20.
  16. Carter JR, Schwartz CE, Yang H, et al: Fish oil and neurovascular reactivity to mental stress in humans. *Am J Physiol Regul Integr Comp Physiol*, 2013; 304: R523-R530.
  17. Scalbert A: Polyphenols: antioxidants and beyond. *Am J Clin Nutr*, 2005; 81(suppl): 215S-217S.
  18. Pandey KB, Rizvi SI: Plant polyphenols as dietary antioxidants in human health and disease. *Oxid Med Cell Longev*, 2009; 2: 270-278.
  19. Gomez-Pinilla F: Natural mood foods: the actions of polyphenols against psychiatric and cognitive disorders. *Nutr Neurosci*, 2012; 15: 127-133.
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