Important Biomarkers and Nutrition Considerations in the Clinical Management of PTSD: The Role of Trauma Nutrition and Integrative Care

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INTRODUCTION

PTSD is considered a neuropsychiatric anxiety disorder based on the DSM-IV classification and includes symptoms associated with psychological and physical trauma and increased avoidance, detachment, dissociative, suicidal, irritability, and hypervigilance behaviors along with various physical symptoms (Aaseth et al, 2019; Gandubert et al, 2016; Glover et al, 2015; Levine et al, 2014; Kolassa et al, 2007). Standard of care approaches often include counseling and pharmaceutical interventions, which may offer only limited relief indicating that innovation in PTSD management is needed (Mellon et al, 2018). PTSD may affect those who have experienced psychological and physical trauma and can be acute and chronic in nature (Levine et al, 2014). PTSD may be more severe or reduced in nature due to genetic predisposition, pre-trauma factors, and the nature of care after the acute traumatic event (Gandeubert et al, 2016; Bryant et al, 2008).

In recent years, significant research has discovered the metabolic and neurological nature of PTSD beyond its psychological and psychiatric foundations along with its comorbid conditions (Ilchmann-Diounou and Menard, 2020; Aaseth et al, 2019; Blessing et al, 2017; Gradus et al, 2017; Michopoulous et al, 2016; Rosenbaum et al, 2015; Talbot et al, 2015; Fadgyas-Stanculete et al, 2014; Sueki et al, 2014; Pagoto et al, 2012; Weiss et al, 2011; Oglodek , 2011). PTSD has been shown to mimic Metabolic Syndrome (MetS) while significantly increasing the risk for diabetes and cardiovascular disease (Aeseth et al, 2019; Michopoulous et al, 2016; Rao et al, 2014). Functional and clinical nutrition approaches for PTSD can help to alleviate symptoms and attempt to reduce the risk for comorbid conditions while reducing impacts on healthcare systems, job forces, mortality, and relationships.

OBJECTIVES

The purpose of this research review is to tie together the multi-disciplinary research showing the psychological, metabolic, and neurological aspects of PTSD while also introducing evidence based functional clinical nutrition solutions for the many symptoms and comorbid conditions of PTSD. Important biomarkers and functional nutrition themeswill be considered in this introduction to a specialized trauma nutrition approach that would be especially suited for the practices of clinical nutritionists and integrative health practitioners.

METHODS

Literature review searches were conducted on the topic of PTSD in PubMed, Google Scholar, and with outside experts between 2020 and 2021. Search terms included, "PTSD, inflammation, nutrition, biomarkers, diet, thyroid, cardiovascular disease, vitamin, mineral, HPA axis, probiotics, urine pH, neurological, metabolic" and other related terms to find original and supportive research. Focus was maintained on randomized controlled trials, systematic reviews, meta-analysis, cohort studies, reviews, and support literature that would lead to original research. Research was analyzed for significant results where PTSD was the main focus and population or where research supported a key symptom or comorbidity associated with PTSD. Biomarker and nutritional considerations were categorized based on the significance in a study to PTSD, the population studied, and the ability to translate results to a human population. Human and animal studies were considered, but significant results with repeatability in a human population held precedence for making associations.

DISCUSSION & CONCLUSIONS

This review is extensive yet not complete in its full scope at looking at PTSD, its comorbid conditions, associated biomarkers, and best therapeutic intervention planning, but it does offer a significant starting point for assessing PTSD patients or those who are showing symptoms of PTSD and its psychological, metabolic, and neurological symptoms. This review is a major stepping stone in showing a fuller picture of the metabolic scope of PTSD, which has been downplayed so far in mainstream standard of care treatment planning. It is hopeful, with this foundational review, that future study with case reports, cohort studies, and randomized controlled treatment designs can be done to determine the levels of effectiveness of specific nutritional and integrative care protocols.

The most significant discovery in this research is the profound connection between PTSD and metabolic syndrome (MetS), where researchers have indicated that PTSD "mimics" many of the facets of MetS including increased insulin and leptin resistance, glucose dysregulation, metabolic acidosis concerns, mitochondrial dysfunction, chronic inflammation, sympathetic nervous system dysfunction, and HPA axis dysregulation (Michopoulos et al, 2016; Mellon et al, 2018). One of the core issues in MetS is chronic inflammation and dysregulation of blood and urine pH, which causes metabolic and urine acidosis states that can be improved to an extent with both multi mineral supplementation and the alkaline diet (König et al, 2009; Carnuba et al, 2017, Souto et al, 2011; Michopoulous et al, 2016). The tendency toward more acidic states for those with PTSD and metabolic syndrome can lead to chronic inflammation, significant increased risk for Type 2 Diabetes, and neuroinflammation, which can result in chronic disease and cognitive decline if not addressed early and appropriately (Wolf et al, 2016; Michopoulous et al, 2016; Mellon et al, 2018). It is even indicated that early treatment in the acute trauma stage can help prevent incidence of long term PTSD (Bryant et al, 2008).

Those with PTSD have disrupted and shorter sleep patterns, increased inflammation, more alcohol and drug use, unhealthy eating habits, and sedentary lifestyle (Aaseth et al, 2019; Michopoulos et al, 2016; Talbot et al, 2015). Along with this, risk for metabolic syndrome (MetS) is doubled for those with PTSD which is also complicated with increased sleep disturbances increasing metabolic dysfunction (Rosenbaum et al, 2015; Talbot et al, 2015). The risk for obesity for those with PTSD is 1.5 times the normal population (Aaseth et al, 2019; Pagoto et al, 2012). Low economic status also increases the association between PTSD and metabolic syndrome and deepens the obstacles for those with PTSD to fully recover (Aaseth et al, 2019; Talbot et al, 2015; Weiss et al, 2011).

The sympathetic nervous system response through the HPA axis is largely connected to cardiometabolic responses in PTSD (Aaseth et al, 2019). Increased norepinephrine responses will increase blood pressure whereas increased cortisol levels associated with early traumatic responses is associated with increased central obesity" (Aaseth et al, 2019). Cortisol, as a general rule, however, is often reduced in those with PTSD (Pan et al, 2020; Gandubert et al, 2016; Michopoulos et al, 2016; Wingenfeld et al, 2015; de Kloet et al, 2008; Kolassa et al, 2007).

Those with severe PTSD are also prone to increased emotional eating where PTSD has been established to create dysfunction among hunger hormones (Aaseth et al, 2019). This can lead to increased intake of inflammatory foods with sugar and saturated fat along with alcohol, which can all lead to increased insulin, leptin resistance, and ghrelin disturbances (Aaseth et al, 2019). This emphasizes the need to address inflammation in nutritional planning as a mechanism to reduce PTSD symptoms.

Physical therapy techniques can also play a role in modulating the sympathetic nervous system response and the patient response to chronic pain and fear (Sueki et al, 2014). By assisting the nervous system pathways in the brain and in the body while educating the patient on breath practices to calm critical musculature and fear response patterning, a patient can begin to replace old trauma memories with new repatterned functional awareness (Sueki et al, 2014).

It is critically important to bring together both functional nutrition assessments and planning with integrative care for the PTSD patient to personalize care based on the patient picture of medical conditions, symptoms, and deficiencies. There is a way out and through, and future research can help define these protocols more specifically for PTSD care management.

ACKNOWLEDGMENTS & CONFLICTS OF INTEREST

A major thank you goes out to Maryland University of Integrative Health (MUIH) for their support of this research and for the many health care providers, teachers, and professionals who have helped me sort out the answers for my personal case of PTSD to allow me to help others prevent the debilitating effects of this condition and live a full and thriving life. The author of this study has no conflict of interest concerns to report and has not received any payment to conduct this research review.

RESULTS

Table 1: PTSD & Associated Comorbid Conditions

PTSD Comorbid Conditions	Citation
IBS	Gradus et al, 2017; Iorio et al, 2014; Menon et al, 2013; The Gut Reaction to PTSD—Gallipoli, 2017; Fadgyas-Stanculete et al, 2014; Savas et al, 2009
Psoriasis	Pietzak et al, 2017; Oglodek, 2011
Autoimmune Diseases	Ilchmann-Diounou and Menard, 2020; Neigh and Ali, 2016
Metabolic Syndrome	Blessing et al, 2017; Michopoulos et al , 2016; Wolf et al, 2016; Rosenbaum et al, 2015; Weiss et al, 2011
Cardiovascular Disease	Michopoulos et al , 2016; Aaseth et al, 2019; Rosenbaum et al, 2015; von Kanel et al, 2010
Obesity	Michopoulos et al , 2016; Smith et al, 2015; Pagoto et al, 2012
Type 2 Diabetes	Rao et al, 2014; Aaseth et al, 2019
Dislipidemia	Talbot et al, 2015; Aaseth et al, 2019
Anxiety, Depression, HPA Axis dysfunction, Suicide	Michopoulos et al , 2016
Chronic Inflammation	Michopoulos et al , 2016
Substance Abuse	Michopoulos et al , 2016
Stomach ulcers	Gradus et al, 2017; The Gut Reaction to PTSD—Gallipoli, 2017
Intestinal Permeability	Ilchmann-Diounou and Menard, 2020
Dysbiosis of the Microbiome	Hemmings et al, 2017
Dyspepsia, indigestion, GERD, Abdominal pain	Menon et al, 2013; Savas et al, 2009
Hypothyroidism	Jung et al, 2019
Cognitive Decline	Wolf et al, 2016

Table 2: Biomarkers associated with PTSD

Vitals/Biomarker	Action in PTSD	Citation
Blood Pressure	Increased	Edmondson et al, 2018; Farr et al, 2014; Gandubert et al, 2016; Rosenbaum et al, 2015
Heart Rate	Increased	Shalev et al, 1998; Bryant et al, 2008; Blessing et al, 2017; Bedi and Arora, 2007
Respiratory Rate	Increased	Bryant et al, 2008
Heart Rate Variability	Decreased	Shah et al, 2013
IL-1ß (pro-inflammatory cytokine)	Increased	Kim et al, 2020; Neigh and Ali, 2016; Gola et al, 2013
IL-4 (anti-inflammatory cytokine)	Increased	Kim et al, 2020; de Oliveira et al, 2018
IL-6 (pro-inflammatory cytokine)	Increased	Leclercq et al, 2016; Newton et al, 2014; de Oliveira et al, 2018; Kim et al, 2020; Neigh and Ali, 2016; Gola et al, 2013
IL-10 (anti-inflammatory cytokine) *IL-10 suppresses IL-1ß	Increased	de Oliveira et al, 2018; Kim et al, 2020
IL-12	Increased	Neigh and Ali, 2016
TNF-alpha (pro-inflammatory cytokine)	Increased	Kim et al, 2020; Neigh and Ali, 2016; Gola et al, 2013
INF-y (interferon gamma)	Increased	Kim et al, 2020
CRP	Increased	Kim et al, 2020; Neigh and Ali, 2016; Michopoulos et al, 2015; Aaseth et al, 2019
BMI	Increased	Gandubert et al, 2016; Farr et al, 2014
VAT (Visceral Adipose Tissue)	Increased	Aaseth et al, 2019; Rosenbaum et al, 2015
HbA1c	Increased	Gandubert et al, 2016
Glucose, Fasting Plasma Glucose	Increased	Rosenbaum et al, 2015; Nowotny et al, 2010
Insulin	Increased *affected also by increased fat, alcohol, and sugar consumption	Nowotny et al, 2010; Rao et al, 2014; Aaseth et al, 2019
HOMA-IR (Insulin Resistance)	Increased	Blessing et al, 2017
Total Cholesterol	Increased	Rosenbaum et al, 2015; Talbot et al, 2015
LDL	Increased	Talbot et al, 2015
HDL	Decreased	Rosenbaum et al, 2015
VLDL	Increased	Talbot et al, 2015
Triglycerides	Increased	Rosenbaum et al, 2015; Talbot et al, 2015
Cholesterol/HDL Ratio	Increased	Talbot et al, 2015
Fibrinogen	Increased	Aaseth et al, 2019; von Kanel et al, 2010
Leptin Resistance	Increased	Aaseth et al, 2019
Estrogen	Decreased levels increase fear signal activation while higher levels are more protective to reduce fear activation	Glover et al, 2015; Glover et al, 2012
Testosterone	Decreased	Deuter et al, 2021; Mulchahey et al, 2001; Josephs et al, 2017
Cortisol	Decreased	Gandubert et al, 2016; Michopoulos et al, 2017; Kolassa et al, 2007; de Kloet et al, 2008; Wingenfeld et al, 2015; Pan et al, 2020
Cortisol	Increased	Bedi and Arora, 2007
BDNF	Increased	Blessing et al, 2017
Norepinephrine	Increased	Bedi and Arora, 2007; Gandubert et al, 2016; Michopoulos et al, 2016; Geracioti et al, 2001; Pan et al, 2018; Wingenfeld et al, 2015
TSH	Increased *PTSD is significantly associated with hypothyroidism, ie. increased TSH	Jung et al, 2019
T3 (Free and Total)	Increased	Wang and Mason, 1999; Wang et al, 1995; Friedman et al, 2005; Toloza et al, 2020
Homocysteine	Increased	De Vries et al, 2015

Table 3: Trauma Nutrition & Integrative Care Approaches

Dietary, Supplement, or Therapy Intervention	Results	Citation
Multi-mineral supplement with Potassium (600mg), Calcium (500mg), Magnesium (200mg), Sodium (200mg), Copper (1mg), Zinc (5mg), Iron (5 mg), Chromium (60 µg), Molybdenum (80 µg), Selenium (30 µg)	Significant improvements in both blood and urine pH resulted from intake of a full spectrum alkaline multimineral supplement twice a day with no major changes in diet. This would help improve metabolic and urine acidosis concerns with metabolic syndrome, diabetes, and PTSD.	König et al., 2009
Alkaline Diet	Eating a diet rich in acid producing foods produces a chronic low grade state of metabolic acidosis which shows up in blood and urine, increasing risk for metabolic disease such as T2D, which is a high risk factor of PTSD. PTSD mimics metabolic syndrome. Alkaline foods help to reduce this risk.	Carnuba et al, 2017; Souto et al, 2011; Michopoulos et al, 2016
Vitamin B1	Thiamine is a critical vitamin involved in glucose metabolism, brain and mitochondrial function, and psychological stability. Deficiency is related to both lactic acidosis and metabolic acidosis conditions associated with metabolic disorders and could be deficient in those with PTSD	Dhir et al, 2019
Magnesium L Threonate	Magnesium L Threonate (MgT) has enhanced ability to improve fear extinction in the brain.	Mickley et al, 2013; Albumaria et al, 2011
Omega 3 Fatty Acids	Omega 3 fatty acids were attributed to reducing memory impairment in response to PTSD stressors in a rat model.	Alquraan et al, 2019
Hydration	Increased mineral water intake was shown to have beneficial effects on blood pressure, triglycerides, glucose, and HDL cholesterol which can have a beneficial effect in reducing the acidic state produced in metabolic syndrome	Costa-Vieira et al, 2019
Physical Therapy	PTSD is associated with increased risk for chronic pain. Physical therapy techniques combined with Cognitive Behavior Therapy (CBT) can help patient unlearn pain cycles and rebuild nervous system responses to fear and pain.	Sueki et al, 2014
Gluten Free Diet	Gluten free diet helps to reduce symptoms of psoriasis and increased intestinal permeability associated with PTSD	Pietrzak et al, 2017
Vitamin B6	Needed to help form GABA. GABA increases cortisol, which is helpful for those with low cortisol in PTSD	Stachowicz and Lebiedzinska, 2016
Herb: Hibiscus	Hibiscus sabdariffa (sour tea) has had beneficial effects in reducing blood pressure and normalizing cholesterol and triglycerides with those diagnosed with diabetes and metabolic syndrome. Given that PTSD mimics metabolic syndrome, this herb would be beneficial for cardiovascular related symptoms.	Hudson, 2011
Low Carb Diet	High total and starchy carbohydrate intakes were associated with hyperlipidemia and metabolic syndrome (MetS) where a low carb diet could help reduce PTSD metabolic symptoms	Feng et al, 2015
Vitamin E, Tocotrienols	Vitamin E is protective against hypercholesterolemia and cardiovascular disease while also serving as an antioxidant. This vitamin can be helpful to reduce risk of comorbid conditions associated with PTSD.	Musa, 2021; Catagol and Ozer, 2012
CoQ10	CoQ10 is cardioprotective and can help reduce hyperlipidemia in diabetic patients. This can be helpful with PTSD patients since they are at a higher risk for both metabolic syndrome and diabetes.	Zozina et al, 2018 Raizner, 2019 Dludla et al, 2020
Adequate dietary protein	Helps to normalize cortisol levels, especially after exercise	Stachowicz and Lebiedzinska, 2016
Exercise	Helps to increase and normalize cortisol (helpful for those with PTSD with low cortisol)	Stachowicz and Lebiedzinska, 2016; Hegberg et al., 2019
Vitamin D	Vitamin D deficiency is found in those with IBS and supplementation is recommended based on levels from Serum Vitamin D testing. Vitamin D helps to improve intestinal lining integrity while reducing CRP levels. Vitamin D is recommended at 2000 IU/day/minimum.	Khayyat and Attar, 2015; Farre et al, 2020
Higher Fiber Diet	Higher fiber foods (2-3 servings daily) helps to reduce risk and incidence of PTSD.	Davison et al, 2021
Curcumin	Curcumin is helpful in reducing pro- inflammatory cytokine, IL-1ß, associated with IBS.	Khan et al, 2017
FODMAP Diet	Reduction of short chain fermentable carbohydrates through a low FODMAP diet helps to improve inflammatory symptoms in IBS. The low FODMAP diet REDUCES Bifidobacterium bacteria, so dosing of this probiotic species will need to be at a higher dose if this diet is prescribed for PTSD- IBS patients.	Algera et al, 2019; Staudacher and Whelan, 2016
Vitamin A	Vitamin A helps to improve intestinal lining integrity while reducing CRP levels.	Farre et al, 2020
Digestive Enzymes	Digestive enzymes will help with macronutrient absorption while also reducing intestinal permeability to enable better vitamin and mineral absorption.	Resnick, 2010
Probiotics	Increase of Bifidobacterium bacteria (spp, longus, animalis subsp Lactis) and Lactobacillus (spp, helveticus) probiotic species to help modulate PTSD symptoms and reduce dysbiosis.	Lui, 2017

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