PTSD & Metabolic Syndrome: The Inflammation, Blood Sugar Regulation, Hormone, & Genomic Relationships with Nutrition Interventions

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BACKGROUND

Post Traumatic Stress Syndrome (PTSD) is highly associated with Metabolic Syndrome (MetS), and PTSD can mimic MetS in its presentation along with its own defining factors (Miranda et al, 2022; Llhua et al, 2020; Weiss et al, 2011). Comorbid conditions associated with PTSD may either cause PTSD or arise from PTSD due to the initial or series of trauma events that generate acute or chronic symptoms (Mellon et al, 2018). Those include cardiovascular disease, immune dysfunction, cancer, and other psychiatric diseases (Mellon et al, 2018). MetS includes diagnosis of a number of the following conditions: hypertension, abdominal obesity, elevated triglycerides, reduced HDL cholesterol, and glucose dysregulation (Abou Ziki and Mani, 2016). This literature review explores biomarkers, genes, and interventions in these connections and adds to previous research by one of the authors (Coomes, 2021).

RESEARCH OBJECTIVES

This purpose of this research is to explore to the inflammation, blood sugar regulation, hormone, and genomic relationships between PTSD and MetS. This will also include metabolic and neurotransmitter relationships as well to provide stronger evidence for nutrition interventions in the care of these conditions.

METHODS

For this literature review, significant exploratory assessment of previously published or nonpublished research was used to compile evidence and data on PTSD and MetS. To assess direct correlations, associations, and causal relationships, databases such as Google, Google Scholar, and PubMed were used with the following search terms: "PTSD," "Metabolic Syndrome," "research," "nutrition" along with specific names of biomarkers to find direct evidence on these topics along with reproducibility in research to establish accurate directions and evidence in the relationships.

RESULTS

The charts to the right and relationships shown below help to show the evidence that came out of this research, and it's important to realize the increasing strength of the metabolic presentation in PTSD in consideration of future treatment options and plans. Increased inflammation can both influence the risk and expression of PTSD. PTSD increases risk for autoimmune diseases and other comorbid diseases (Anderson, 2016) . While cortisol is often found to be decreased in chronic PTSD, the initial increases of cortisol that generates hypothalamus-pituitary-adrenal (HPA) axis dysfunction can lead to hippocampus (memory) issues that increases risk for PTSD and Alzheimer's Disease (AD), and it has been noted that this relationship is important for future treatments (Griffin et al, 2014). These relationships are shown below.

Pre-trauma inflammation → PTSD → Chronic Inflammation
PTSD ←→ Inflammation
PTSD & MetS → Increased risk of Cancer and Autoimmune Disease

↑ Cortisol → ↑ Hippocampus Dysfunction & Atrophy → PTSD & AD

	PTSD Biomarkers	MetS Biomarkers	Citations
Inflammation	**Homocysteine** INCREASED	**Homocysteine** INCREASED	Fu et al. 2019; De Vries et al. 2015
	CRP INCREASED	**CRP** INCREASED	Swart et al. 2021; Wang et al. 2017; O'Donovan et al. 2017; Anderson et al. 2016; Michopoulos et al. 2016
	IL-1β INCREASED **IL-4** BOTH **IL-6** INCREASED **IL-10** BOTH **IL-12** INCREASED **IL-17** INCREASED	**IL-1β** INCREASED **IL-4** INCREASED **IL-6** INCREASED **IL-10** INCREASED **IL-12** INCREASED **IL-17** INCREASED	Miranda et al 2022; Chair et al. 2021; Smith et al. 2021; Kim et al. 2020; Abdelazeem et al. 2021; de Oliveira et al. 2018; Wang et al. 2017; Neigh and Ali. 2016; Leclercq et al. 2016; Anderson et al. 2016; Michalke et al. 2015; Newton et al. 2014; Griffin et al. 2014; Gola et al. 2013
	TNF-α INCREASED **TNF-β** BOTH **INF-γ** INCREASED	**TNF-α** INCREASED **TNF-β** INCREASED **INFγ** INCREASED	Miranda et al 2022; Kim et al. 2020; Neigh and Ali. 2016; Anderson et al. 2016; Gola et al. 2013; Wang et al. 2017; Bennett and Rane. 2013
	WBCs INCREASED	**WBCs** INCREASED	Ajdacic-Gross et al. 2021; Kucukly et al. 2019; O'Donovan et al. 2017; Anderson et al. 2016
	Neutrophil Lymphocyte Ratio (NLR) INCREASED	**NLR INCREASED**	Miranda et al 2022; Sousa et al. 2022; Mohan et al. 2021
	Th1 BOTH **Th2** INCREASED **Th17** INCREASED **T-regs** DECREASED	**Th1** INCREASED **Th2** BOTH **Th17** INCREASED **T-regs** DECREASED	Smith et al. 2021; Wang et al. 2017; Anderson et al. 2016; Griffin et al. 2014
Blood Sugar Regulation & Metabolism	**Fasting Plasma Glucose (FPG)** INCREASED **HbA1c** INCREASED	**FPG** INCREASED **HbA1c** INCREASED	Miranda et al 2022; Kong and Cho. 2019; Arnsten Akuliar et al., 2019; Abou Ziki and Mani. 2016; Shpakov et al. 2015; Rosenbaum et al. 2015; Nowotny et al. 2010; Dadona et al., 2005
	Total Cholesterol INCREASED **LDL-C** INCREASED **HDL-C** DECREASED **Triglycerides** INCREASED	**Total Cholesterol** INCREASED **LDL-C** INCREASED **HDL-C** DECREASED **Triglycerides** INCREASED	Miranda et al 2022; Nemet et al. 2022; Fan et al. 2019; Paredes et al. 2019; Abou Ziki and Mani. 2016; Michopoulos et al. 2016; Kong and Cho. 2019; Anderson et al. 2016; Shpakov et al. 2015; Rosenbaum et al. 2015; Talbot et al. 2015; Dadona et al. 2005
	Blood pressure INCREASED **Heart Rate** INCREASED **Respiratory Rate** INCREASED **Heart Rate Variability (HRV)** DECREASED	**Blood pressure** INCREASED **Heart Rate** INCREASED **Respiratory Rate** INCREASED **HRV** DECREASED	Park and Khattar. 2023; DiNicolantonio and O'Keefe. 2021; Williamson et al. 2021; Abou Ziki and Mani. 2016; Edmondson et al. 2011; Chang et al. 2016; Yang et al. 2017; Chang et al. 2016; Michopoulos et al. 2016; Gandubert et al. 2016; Anderson et al. 2016; Rosenbaum et al. 2015; Farr et al. 2014; Rogowski et al. 2009; Shaker et al., 1998; Bryant et al., 2008; Blessing et al. 2017; Bedi and Arora. 2007; Shah et al. 2013
	BMI INCREASED **Waist circumference** INCREASED	**BMI** Normal to Obese **Waist circumference** INCREASED	Shi et al. 2020; Masoodkar et al., 2016; Gandubert et al. 2016; Farr et al. 2014; Abou Ziki and Mani. 2016
	Sodium UNCLEAR **Chloride** DECREASED **Potassium** INCREASED **Calcium** INCREASED **Anion Gap** INCREASED	**Sodium** BOTH **Chloride** BOTH **Potassium** DECREASED **Calcium** DECREASED **Anion Gap** INCREASED	Miranda et al 2022; DiNicolantonio and O'Keefe. 2021; Williamson et al. 2021; Arenson and Cohen. 2017
	Microbiome ↑ Dysbiosis	**Microbiome** ↑ Dysbiosis	Miranda et al 2022; Malan-Muller et al., 2022; Kao and Huang. 2021; Hemmings et al. 2018
Hormones & Neurotransmitters	**Leptin** INCREASED **Leptin Resistance** INCREASED	**Leptin** BOTH **Leptin Resistance** INCREASED	Aaseth et al. 2019; Abou Ziki and Mani. 2016; Michopoulos et al. 2016; Shpakov et al. 2015
	BDNF INCREASED	**BDNF** INCREASED	Blessing et al. 2017; Yang et al. 2018; Rana et al. 2019; Abou Ziki and Mani. 2016; Golden et al. 2010
	Insulin INCREASED **HOMA-IR** INCREASED	**Insulin** INCREASED in blood, DECREASED in brain **Insulin resistance** INCREASED **Insulin sensitivity** DECREASED	Shpakov et al. 2015; Nowotny et al. 2010; Rao et al. 2014; Aaseth et al. 2019; Blessing et al. 2017
	Cortisol DECREASED **CRH** INCREASED	**Cortisol** INCREASED	DiNicolantonio and O'Keefe. 2021; Pan et al. 2020; Michopoulos et al. 2017; Michopoulos et al. 2016; Gandubert et al. 2016; Anderson et al. 2016; Griffin et al. 2014; Jeong. 2012; de Rivett et al. 2008; Kolassa et al. 2007
	Norepinephrine INCREASED	**Norepinephrine** INCREASED	Michopoulos et al. 2016
	Dopamine DECREASED	**Dopamine** DECREASED	Pijl and Romijn. 2006
	Serotonin BOTH	**Serotonin** DECREASED	Seidemann et al. 2021; Muldoon et al. 2006; Miranda et al. 2022; Nisenzgeit et al. 2019
	Glutamate INCREASED	**Glutamate** INCREASED	Mallaiz-Payette et al. 2018; Averill et al. 2017
	GABA DECREASED	**GABA** DECREASED	Averill et al. 2017; Wan et al. 2014
	TSH INCREASED	**TSH** INCREASED	He et al. 2021; Teixeira et al. 2020; Jung et al. 2019;
	Estrogen DECREASED	**Estrogen** DECREASED	Paoli et al. 2021; Glover et al. 2015; Glover et al. 2012
	Testosterone DECREASED	**Testosterone** DECREASED	Deuter et al. 2021; Mulchahey et al. 2001; Josephs et al. 2017; Salam et al. 2012

INTERVENTION	RESULTS	Citations
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. • **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. • **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 • **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	Alkaline Diet Carnuba et al., 2017; Souto et al. 2011; Michopoulos et al. 2016 Multi-mineral supplement Kong et al., 2009 Hydration Costa-Vieira et al. 2019 Vitamin B1 Ohir et al. 2019
Low FODMAP Diet and Digestion	• 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. • **Vitamin A:** Vitamin A helps to improve intestinal lining integrity while reducing CRP levels • **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. • **Zinc:** Zinc helps to restore gut mucosa and microbiome diversity • **Digestive Enzymes:** Digestive enzymes will help with macronutrient absorption while also reducing intestinal permeability to enable better vitamin and mineral absorption. • **Probiotics:** Increase of Bifidobacterium bacteria (spp, longus, animalis subsp Lactis) and Lactobacillus (spp, helveticus) probiotic species to help modulate PTSD symptoms and reduce dysbiosis.	Low FODMAP Diet Algera et al. 2019; Staudacher and Whelan. 2016 Digestive enzymes Resnick. 2010 Probiotics Lui. 2017 Vitamin A Farre et al. 2020 Vitamin D Khayyat and Attar. 2015; Farre et al. 2020 Zinc Skalny et al. 2021
Neuroinflammation and Detoxification	• **Reduce Glutamate containing foods due to increased neurotoxicity** • **Gluten Free Diet (also contains glutamate):** Gluten free diet helps to reduce symptoms of psoriasis and increased intestinal permeability associated with PTSD • **Vitamin B6:** Needed to help form GABA. GABA increases cortisol, which is helpful for those with low cortisol in PTSD • **Vitamin B12:** This nutrient supports a strong blood brain barrier and good 1 carbon metabolism. Vitamin B12 is a methyl donor nutrient. • **Vitamin C:** Vitamin C can help reduce neuroinflammation. • **Folate:** This nutrient supports a strong blood brain barrier and good 1 carbon metabolism. Folate is a methyl donor nutrient. • **Magnesium L Threonate:** Magnesium L Threonate (MgT) has enhanced ability to improve fear extinction in the brain. • **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. • **Omega 3 Fatty Acids:** Omega 3 fatty acids were attributed to reducing memory impairment in response to PTSD stressors in a rat model. • **Dietary Protein:** Helps to normalize cortisol levels, especially after exercise • **Cruciferous vegetables:** Cruciferous vegetables helps to repair detoxification pathways to help reduce neuroinflammation.	Gluten free diet Pietrzak et al. 2017 Neuroinflammation Coomes and McGarik. 2022 Magnesium L Threonate Hickey et al. 2013; Alhomaria et al. 2011 CoQ10 Acoma et al. 2018 Rezmer. 2019 Dludla et al. 2020 Vitamin B6 Stachowicz and Lebiedzińska, 2016 Protein Stachowicz and Lebiedzińska, 2016 Omega 3s Akpinar et al. 2019 Vitamin B12 McRae et al. 2018 Stover et al. 2017 Vitamin C Vasefi et al. 2019 Folate McRae et al. 2018 Stover et al. 2017 Nakamura et al. 2016 Higdon et al. 2007 Cruciferous vegetables Hodges and Minich. 2015; Nakamura et al. 2016; Alabdali et al. 2014; Higdon et al. 2007
Other Nutrients	• **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. • **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. • **Cannabis (THC):** The endocannabinoid system is activated in PTSD where THC, the psychoactive ingredient of cannabis, has been shown to help modulate PTSD symptoms.	Vitamin E Rusa. 2021; Calegari and Coser. 2012 Hibiscus Hudson. 2011 Cannabis Mayo et al. 2022
Therapies and Lifestyle	• **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. • **Exercise:** Helps to increase and normalize cortisol (helpful for those with PTSD with low cortisol)	Physical Therapy Scott et al. 2014 Exercise Stachowicz and Lebiedzińska, 2016 Hegberg et al., 2019

PTSD Genes/SNPs	MetS Genes/SNPs
PARK2 (Nievergelt et al, 2019)	**PARK2** (Abou Ziki and Mani, 2016)
BDNF, rs6265, increases risk of PTSD in cancer (Chair et al, 2022)	**BDNF, rs6265,** increases risk of MetS (Rana et al, 2019; Abou Ziki and Mani, 2016)
COMT; rs4680 (Cornelis et al, 2012)	COMT, **rs4680**, associated with panic disorders and CVD (Mir et al, 2018; Zhao et al, 2021)
MTHFR C677T **rs1801133,** increases risk for MDD after childhood trauma and is also associated with reduce oxidative stress defense (Lok et al, 2013)	MTHFR C677T **rs1801133,** increases risk for obesity and high homocysteine levels (Fu et al, 2019)

CONCLUSION & LIMITATIONS

This research has produced extensive evidence for the association between PTSD and MetS along with evidence that both conditions are also associated with AD development. Critical genes associated with Parkinson's disease and one carbon metabolism helped to show the need to address biochemical and neurological dysfunctions in PTSD and MetS. Shifts in the Th1 to Th2 immunological response in PTSD also helped to show why PTSD can increase infections and risk for cancer/tumor development. Increased neuro-excitability as evidenced by increases in glutamate in both PTSD and MetS helped to show that addressing neuroinflammation is critical to the treatment in these conditions. Acid-base imbalances and obesity was noted in both PTSD and MetS whereas those in normal BMI categories with MetS have a higher risk of mortality likely because more medical attention is focused on those with MetS and obesity. Critical decreases in estrogen and testosterone were found in both PTSD which influences the ability to manage fear responses and MetS symptoms. The alkaline and low FODMAP diets along with critical micronutrients, physical therapy, and exercise were seen as positive interventions. Limitations to this research are present in the need to further establish more strength in these connections, more evaluation of the quality of research, and expanding on genomic connections. Future research is needed to continue validation of results.

REFERENCES & MORE INFORMATION

References and the full research paper is available by using your smart phone to scan the code to your right here.

If you have any further questions, please reach out to Dr. Jennifer Coomes at jcoomes@bastyr.edu or Jennifer@essencehealthandresearch.com.

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