PSIG Research: Abstracts, Articles and Reviews

Every other month, the Pain Special Interest Group provides updates on new topics, new information and research related topics. Please feel free to submit a topic or research question to dana-dailey@uiowa.edu. If you would like to help in preparing the information, please let me know as well.

Special thanks to Megan Prybil, MPT for contributing articles to this month's research topic on Nutrition, Inflammation and Pain. Prior to becoming a PT, Megan earned a dual-degree in Nutrition and Exercise Sciences (B.S. Foods & Nutrition, B.S. Kinesiology) from Kansas State University. She integrates nutrition education into her physical therapy practice and is a professional trainer on this topic.

November 2018 Topic: Nutrition, Inflammation and Pain

Bibliography

1. Totsch SK, Quinn TL, Strath LJ, et al. The impact of the Standard American Diet in rats: Effects on behavior, physiology and recovery from inflammatory injury. Scand J Pain. 2017;17:316-24.

2. Totsch SK, Waite ME, Tomkovich A. Total Western Diet alters mechanical and thermal sensitivity and prolongs hypersensitivity following complete Freund's adjuvant in mice. J Pain. 2016;17(1):119-25.

3. Rea K, Dinan TG, Cryan JF. The microbiome: A key regulator of stress and neuroinflammation. Neurobiol Stress. 2016;4:23-33.

4. Lerner A, Neidhofer S, Torsteb M. The gut microbiome feelings of the brain: A perspective for non-microbiologists. Microorganisms. 2017;5(4):66

5. Toribio-Mateas M. Harnessing the power of microbiome assessment tools as part of neuroprotective nutrition and lifestyle medicine interventions. Microorganisms 2018;6(2)35.

The impact of the Standard American Diet in rats: Effects on behavior, physiology and recovery from inflammatory injury.
Totsch SK, Quinn TL, Strath LJ, et al. Scand J Pain.

Abstract
BACKGROUND AND AIMS:
Obesity is a significant health concern in the Western world and the presence of comorbid conditions suggests an interaction. The overlapping distributions of chronic pain populations and obesity suggests that an interaction may exist. Poor quality diet (high carbohydrates, saturated fats, omega-6 polyunsaturated fatty acids) can lead to increased adiposity which can activate immune cells independent of the

activating effect of the diet components themselves. This dual action can contribute to chronic inflammation that may alter susceptibility to chronic pain and prolong recovery from injury. However, traditional examinations of diet focus on high-fat diets that often contain a single source of fat, that is not reflective of an American diet. Thus, we examined the impact of a novel human-relevant (high-carbohydrate) American diet on measures of pain and inflammation in rats, as well as the effect on recovery and immune cell activation.

METHODS:
We developed a novel, human-relevant Standard American Diet (SAD) to better model the kilocalorie levels and nutrient sources in an American population. Male and female rats were fed the SAD over the course of 20 weeks prior to persistent inflammatory pain induction with Complete Freund's Adjuvant (CFA). Mechanical and thermal sensitivity were measured weekly. Spontaneous pain, open field locomotion and blood glucose levels were measured during diet consumption. Body composition was assessed at 20 weeks. Following full recovery from CFA-induced hypersensitivity, blood was analyzed for inflammatory mediators and spinal cords were immunohistochemically processed for microglial markers.

RESULTS:
Chronic consumption of the SAD increased fat mass, decreased lean mass and reduce bone mineral density. SAD-fed rats had increased leptin levels and pro-inflammatory cytokines in peripheral blood serum. Following CFA administration, mechanical sensitivity was assessed and recovery was delayed significantly in SAD-fed animals. Sex differences in the impact of the SAD were also observed. The SAD increased body weight and common T-cell related inflammatory mediators in female, but not male, animals. In males, the SAD had a greater effect on bone mineral density and body composition. Long-term consumption of the SAD resulted in elevated microglial staining in the dorsal horn of the spinal cord, but no sex differences were observed.

CONCLUSIONS:
We demonstrated the negative effects of an American diet on physiology, behavior and recovery from injury. SAD consumption elevated pro-inflammatory mediators and increased microglial activation in the spinal cord. While there were sex differences in weight gain and inflammation, both sexes showed prolonged recovery from injury.

IMPLICATIONS:
These data suggest that poor quality diet may increase susceptibility to chronic pain due to persistent peripheral and central immune system activation. Furthermore, consumption of a diet that is high in carbohydrates and omega-6 polyunsaturated fatty acid is likely to lead to protracted recovery following trauma or surgical procedures. These data suggest that recovery of a number of patients eating a poor quality diet may be expedited with a change in diet to one that is healthier.

Total Western Diet alters mechanical and thermal sensitivity and prolongs hypersensitivity following complete Freund’s adjuvant in mice.
Totsch SK, Waite ME, Tomkovich A.

Full text available free at Pub Med:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4817348/

Abstract
Obesity and chronic pain are often comorbid and their rates are increasing. It is unknown whether increased pain is caused by greater weight or poor diet quality or both. Therefore, we utilized a Total Western Diet (TWD) to investigate the functional and physiologic consequences of nutritionally poor diet in mice. For 13 weeks on the commercially available TWD, based on the National Health and Nutrition Examination Survey, thresholds of TWD-fed mice significantly increased in both thermal and mechanical tests. Quantitative magnetic resonance imaging revealed a significant increase in fat mass with a concomitant decrease in lean mass in the TWD-fed mice. In addition, there were significant increases in levels of serum leptin and inflammatory cytokines. After chronic pain induction using complete Freund's adjuvant, hypersensitivity was more pronounced and significantly prolonged in the TWD-fed mice. Therefore, prolonged exposure to poor diet quality resulted in altered acute nociceptive sensitivity, systemic inflammation, and persistent pain after inflammatory pain induction.

PERSPECTIVE:
These results highlight the negative effects of poor diet quality with respect to recovery from hypersensitivity and susceptibility to chronic pain. A complete understanding of the impact of diet can aid in treatment and recovery dynamics in human clinical patients.

The microbiome: A key regulator of stress and neuroinflammation.
Rea K, Dinan TG, Cryan JF. Neurobiol Stress. 2016;4:23-33
Full text available free at Pub Med:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5146205/

Abstract
There is a growing emphasis on the relationship between the complexity and diversity of the microorganisms that inhabit our gut (human gastrointestinal microbiota) and health/disease, including brain health and disorders of the central nervous system. The microbiota-gut-brain axis is a dynamic matrix of tissues and organs including the brain, glands, gut, immune cells and gastrointestinal microbiota that communicate in a complex multidirectional manner to maintain homeostasis. Changes in this environment can lead to a broad spectrum of physiological and behavioral effects including hypothalamic-pituitary-adrenal (HPA) axis activation and altered activity of neurotransmitter systems and immune function. While an appropriate, coordinated physiological response, such as an immune or stress response are necessary for survival, a dysfunctional response can be detrimental to the host contributing to the development of a number of CNS disorders. In this review, the involvement of the gastrointestinal microbiota in stress-mediated and immune-mediated modulation of neuroendocrine, immune and neurotransmitter systems and the consequential behavior is considered. We also focus on the mechanisms by which commensal gut microbiota can regulate neuroinflammation and further aim to exploit our understanding of their role in stress-related disorders as a consequence of neuroinflammatory processes.

The gut microbiome feelings of the brain: A perspective for non-microbiologists.
Lerner A, Neidhofer S, Torsteb M
Full text available free at Pub Med:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5748575/

Abstract
OBJECTIVES: To comprehensively review the scientific knowledge on the gut-brain axis.
Methods**:** Various publications on the gut-brain axis, until 31 July 2017, were screened using the Medline, Google, and Cochrane Library databases. The search was performed using the following keywords: "gut-brain axis", "gut-microbiota-brain axis", "nutrition microbiome/microbiota", "enteric nervous system", "enteric glial cells/network", "gut-brain pathways", "microbiome immune system", "microbiome neuroendocrine system" and "intestinal/gut/enteric neuropeptides". Relevant articles were selected and reviewed.

Results: Tremendous progress has been made in exploring the interactions between nutrients, the microbiome, and the intestinal, epithelium-enteric nervous, endocrine and immune systems and the brain. The basis of the gut-brain axis comprises of an array of multichannel sensing and trafficking pathways that are suggested to convey the enteric signals to the brain. These are mediated by neuroanatomy (represented by the vagal and spinal afferent neurons), the neuroendocrine-hypothalamic-pituitary-adrenal (HPA) axis (represented by the gut hormones), immune routes (represented by multiple cytokines), microbially-derived neurotransmitters, and finally the gate keepers of the intestinal and brain barriers. Their mutual and harmonious but intricate interaction is essential for human life and brain performance. However, a failure in the interaction leads to a number of inflammatory-, autoimmune-, neurodegenerative-, metabolic-, mood-, behavioral-, cognitive-, autism-spectrum-, stress- and pain-related disorders. The limited availability of information on the mechanisms, pathways and cause-and-effect relationships hinders us from translating and implementing the knowledge from the bench to the clinic.

Implications: Further understanding of this intricate field might potentially shed light on novel preventive and therapeutic strategies to combat these disorders. Nutritional approaches, microbiome manipulations, enteric and brain barrier reinforcement and sensing and trafficking modulation might improve physical and mental health outcomes.

Harnessing the power of microbiome assessment tools as part of neuroprotective nutrition and lifestyle medicine interventions.
Toribio-Mateas M.
Full text available free at Pub Med:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6027349/

Abstract
An extensive body of evidence documents the importance of the gut microbiome both in health and in a variety of human diseases. Cell and animal studies describing this relationship abound, whilst clinical studies exploring the associations between changes in gut microbiota and the corresponding metabolites with neurodegeneration in the

human brain have only begun to emerge more recently. Further, the findings of such studies are often difficult to translate into simple clinical applications that result in measurable health outcomes. The purpose of this paper is to appraise the literature on a select set of biomarkers from a clinician's perspective. This practical review aims to examine key physiological processes that influence both gastrointestinal, as well as brain health, and to discuss how tools such as the characterization of commensal bacteria, the identification of potential opportunistic, pathogenic and parasitic organisms and the quantification of gut microbiome biomarkers and metabolites can help inform clinical decisions of nutrition and lifestyle medicine practitioners.