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### Neuroinflammation & Mood Disorders

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# Neuroinflammation & Mood Disorders

Andrea Zanders, BSN, RN

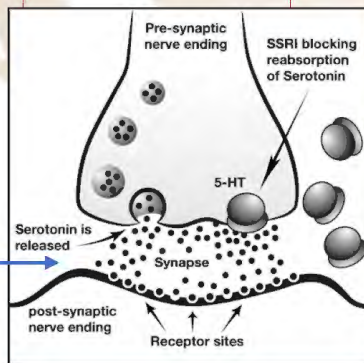
Otterbein University, Westerville, Ohio

## Introduction

This poster aims to discuss the pathophysiology of the two main mood disorders: major depressive disorder and bipolar disorder. The exact etiology of these two disorders remains not fully understood, but it is known that the pathophysiology is complex and multifaceted. This poster discusses theories concerning neuroinflammation and their contribution to the pathophysiology of mood disorders. The role of neuroinflammation in mood disorders is a relatively recent area of research that has shown promising results making it worthy of continued attention. By continuing to progress research in this area new and effective treatment can be developed to help individuals all over the world who do not achieve remission with traditional treatments or who continue to have residual lifelong symptoms even after remission.

## Monoamine hypothesis of depression: the traditional theory of mood disorder pathophysiology which states an imbalance in neurotransmitters is the cause of depression or mania.

- Depression: low concentration of norepinephrine, dopamine, and/or serotonin
- Mania: high concentration of monoamines such as dopamine, norepinephrine, serotonin, and/or gamma-aminobutyrate
- Antidepressant medications balance the levels of these neurotransmitters in the brain by preventing their reuptake and thus increasing the amount available to receptors (Ashok et al., 2017; McCance & Huether, 2019;)



(Cottone, 2020)

## Pathophysiology

### Some recent theories investigate the role of inflammation

Inflammation is an innate protective response in the body that activates when an injury or threat is detected. Cellular signals release chemicals, or cytokines, that work synergistically to eradicate infection and repair tissue (Rainville & Hodes, 2019). Chronic inflammation results when the initial response is ineffective at achieving homeostasis within the body or if the assault to the body is prolonged (Dey & Hankey Giblin, 2018; Rainville & Hodes, 2019). Chronic inflammation leads to pathosis. (Dey & Hankey Giblin, 2018; Rainville & Hodes, 2019)

### Role of inflammation in pathophysiology of mood disorders

Normal brain function relies on low levels of inflammatory cytokines (McCance & Huether, 2019).

Patients with mood disorders have been found to be in a state of chronic pro-inflammatory production causing elevated numbers (Dey & Hankey Giblin, 2018)

Elevated proinflammatory cytokines contribute to:

- Neural atrophy
- Decreased synaptogenesis
- Compromised blood-brain barrier
- Diversion of tryptophan metabolism from serotonin towards excitotoxic chemicals
- Chronic cortisol release and hippocampal damage
- Increase in reactive oxidative species

These elements have all been found to play a role in the development of mood disorders (McCance & Huether, 2019; Offor et al., 2021; Rakofsky & Rapaport, 2018)

Most common proinflammatory cytokines found in patients with mood disorders include IL-1 $\alpha$ , IL-6, tumor necrosis factor (TNF- $\alpha$ ), and C-reactive protein (Dey & Hankey Giblin, 2018; Gourguvelis et al., 2018; McCance & Huether, 2019; Mikkelsen et al., 2017)

High levels of IL-6 are associated with suicidality (Mikkelsen et al., 2017).

Most common anti-inflammatory cytokines found in decreased levels include IL-1 receptor antagonist and IL-10 (Gourguvelis et al., 2018).

**Antidepressants have been found to also work by decreasing the production of pro-inflammatory cytokines and reversing neural atrophy (Dey & Hankey Giblin, 2018; McCance & Huether, 2019; Rakofsky & Rapaport, 2018)**

## Major Mood Disorder Symptomology

### Major depressive disorder

- Loss of interest or pleasure in activities
- Sleep and eating pattern changes
- Irritable or down mood
- Fatigue, difficulty concentrating
- Suicidal ideation

### Bipolar

- Bipolar 1 – Manic episode usually followed by hypomanic or a major depressive episode
  - Bipolar 2 – Major depressive episode for at least two weeks and a hypomanic episode for 4 days
  - Manic episode
    - Elevated or irritable mood
    - Increased energy and decreased need for sleep
    - Pressured speech and racing thoughts
    - Distractibility
    - Excessive risk taking
    - Inflated self-confidence
- (McCance & Huether, 2019)

## Mood disorder treatments addressing the role of inflammation

Poor diet and a sedentary lifestyle have been shown to exacerbate mood disorders and contribute to low-grade chronic inflammation (Gourguvelis et al., 2018 & Offor et al., 2021). Poor diet also effects production and function of neurotransmitters making someone more susceptible to developing a psychiatric condition (Mikkelsen et al., 2017).

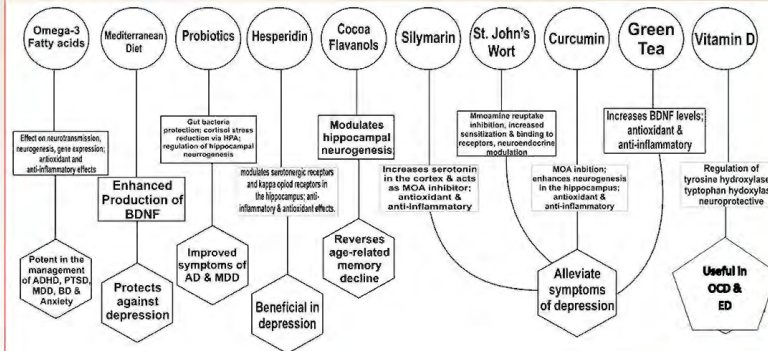
**A healthy diet and regular exercise have been shown to alleviate mood disorder symptoms (Gourguvelis et al., 2018; Mikkelsen et al., 2017; Offor et al., 2021)**

- Several dietary interventions have been shown to decrease systemic inflammation as depicted in the above right illustration (Offor et al., 2021)
- Exercise inhibits pro-inflammatory cytokine release and increases anti-inflammatory cytokines production (Mikkelsen et al., 2017)
- Large adipocytes increase proinflammatory cytokine release. Regular exercise decreases adipose tissue, and therefore reduces systemic inflammation (Mikkelsen et al., 2017)
- The vagus nerve regulates inflammation. Exercise strengthens vagal tone reducing systemic inflammation (Mikkelsen et al., 2017)
- Exercise interventions have been shown to be as effective as pharmacological and cognitive behavioral therapy treatments (Gourguvelis et al., 2018)



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## Effects of dietary interventions on bio-markers of mental conditions



(Offor et al., 2021)

## Conclusion

The benefits of a healthy diet and regular physical activity are more pronounced for individuals with mood disorders (Kruisdijk et al., 2018). With the role that neuroinflammation plays in the pathophysiology of mood disorders, new treatments that reduce proinflammatory cytokines and reverse their negative effects on the brain could be essential to the future of psychiatric treatment. However, neuroinflammation is only one factor in a complex interaction between genetics, anatomy, physiology, and environment that together either protect against or make one at risk for a mood disorder. Research must continue to progress in the investigation of mood disorder pathophysiology in order to develop diversity in treatment options. The possibility of treatment choice will lead to increased remission rates, decreased relapse rates, and individuals with mood disorders who are able to function more independently and successfully within their families, their communities, and society

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