



ADVOCACY

We're in the midst of a major Scientific Revolution regarding our understanding of BEHAVIOR and the IMMUNE System.

This has many ripple effects, including within:

- The Public Health System, and
- The Criminal Justice System

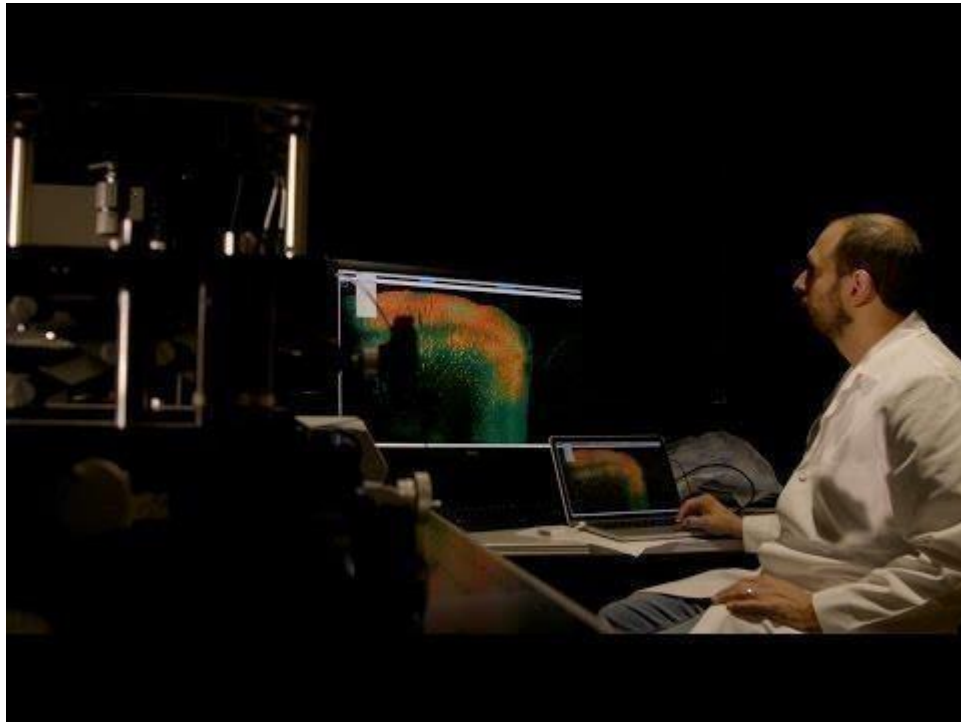
Innate & Adaptive Immunity in:

- Neurodevelopmental Disorders
- Psychiatric Disorders
- Substance Use
- Brain Injury
- Physical Illnesses often with co-morbid Psychiatric Disorders
- Trauma

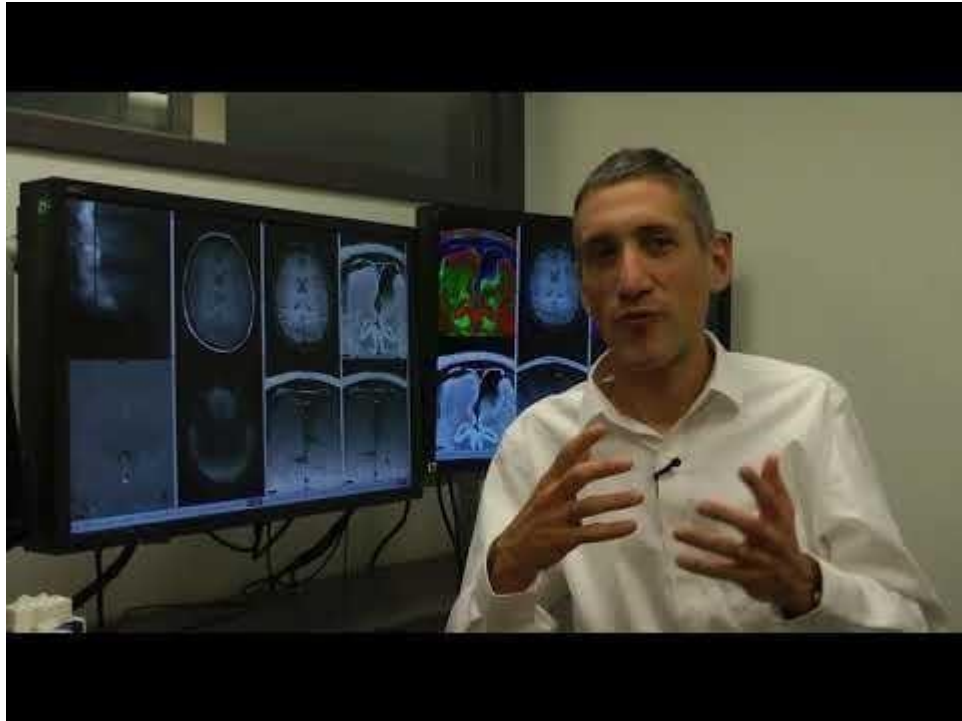
October 2020

Orchid Mental Health Legal Advocacy of Colorado, Inc.

www.orchidadvocacy.org



University of Virginia researchers determine that the immune system affects – and even controls – social behavior (2016)



National Institutes of Health: Scientists Uncover Drain Pipes in Our Brains – a lymphatic system for the brain – the lymph system plays an integral role in the immune functions of the body. (2017) (See also Igdalliance.org)

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EXECUTIVE SUMMARY	
GENERAL CONSIDERATIONS <ul style="list-style-type: none">• Maternal Immune Activation• Cognitive and Social Abilities Rely on Fine-Tuned Equilibrium of Innate & Adaptive Immune Responses• Innate Immune Cells as Regulators of Brain Development & Behavioral Function	

<ul style="list-style-type: none">• Vagus Nerve serves as Modulator of the Brain-Gut Axis in Psychiatric and Inflammatory Disorders.	
ADHD	
Allergies	
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Celiac Disease & Gluten Sensitivities	
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Innate & Adaptive Immunity

in Neuropsychiatric & Developmental Disorders, Substance Use & Brain Injury

General Research Regarding Innate & Adaptive Immune System in Neuropsychiatric Disorders

Maternal Immune Activation

[The fetal origins of mental illness.](#)

Al-Haddad BJS, Oler E, Armistead B, Elsayed NA, Weinberger DR, Bernier R, Burd I, Kapur R, Jacobsson B, Wang C, Mysorekar I, Rajagopal L, Adams Waldorf KM. **Am J Obstet Gynecol.** 2019 Dec;221(6):549-562. doi: 10.1016/j.ajog.2019.06.013. Epub 2019 Jun 15. PMID: 31207234 Review.

In summary, we discuss the current evidence and mechanisms linking infections and inflammation with the increased lifelong risk of neuropsychiatric **disorders** in the child, and how we might improve prenatal care to protect the fetal brain....

[Maternal immune activation in neurodevelopmental disorders.](#)

Solek CM, Farooqi N, Verly M, Lim TK, Ruthazer ES. **Dev Dyn.** 2018

Apr;247(4):588619. doi: 10.1002/dvdy.24612. Epub 2017 Dec 23.PMID: 29226543

Free article.

Review.

Converging lines of evidence from basic science and clinical studies suggest a relationship between maternal immune activation (MIA) and neurodevelopmental disorders such as **autism** spectrum **disorder** (ASD) and schizophrenia. ...

[Reversing behavioural abnormalities in mice exposed to maternal inflammation.](#)

Shin Yim Y, Park A, Berrios J, Lafourcade M, Pascual LM, Soares N, Yeon Kim J, Kim S, Kim H. Waisman A, Littman DR, Wickersham IR, Harnett MT, Huh JR, Choi GB.

Nature. 2017

Sep 28;549(7673):482-487. doi: 10.1038/nature23909. Epub 2017 Sep

13.PMID: 28902835 **Free PMC article.**

Viral infection during pregnancy is correlated with increased frequency of neurodevelopmental **disorders**, and this is studied in mice prenatally subjected to maternal immune activation (MIA). ...

Cognitive and Social Abilities Rely on Fine-Tuned Equilibrium of Innate & Adaptive Immune Responses

Immunoneuropsychiatry - novel perspectives on brain disorders.

Pape K, Tamouza R, Leboyer M, Zipp F. **Nat Rev Neurol.** 2019 Jun;15(6):317-328. doi: 10.1038/s41582-019-0174-4.PMID: 30988501 Review.

Our cognitive and social abilities rely on a highly sensitive and fine-tuned equilibrium of immune responses that involve both **innate** and adaptive **immunity**. ...These discoveries challenge our traditional classification of neurological and **psychiatric** diseases ...

Immunity and mental illness: findings from a Danish population-based immunogenetic study of seven psychiatric and neurodevelopmental disorders.

Nudel R, Benros ME, Krebs MD, Allesøe RL, Lemvig CK, Bybjerg-Grauholm J, Børglum AD, Daly MJ, Nordentoft M, Mors O, Hougaard DM, Mortensen PB, Buil A, Werge T, Rasmussen S, Thompson WK. **Eur J Hum Genet.** 2019 Sep;27(9):1445-1455. doi: 10.1038/s41431-019-0402-9. Epub 2019 Apr 11. PMID: 30976114 **Free PMC article.**

Human leukocyte antigen (HLA) genes encode proteins with important roles in the regulation of the **immune** system. Many studies have also implicated HLA genes in psychiatric and neurodevelopmental disorders. However, these studies usually focus on one **disorder** and/or ...

Innate Immune Cells as Regulators of Brain Development & Behavioral Function

Microglia and Beyond: Innate Immune Cells As Regulators of Brain Development and Behavioral Function.

Lenz KM, Nelson LH. **Front Immunol.** 2018 Apr 13;9:698. doi: 10.3389/fimmu.2018.00698. eCollection 2018. PMID: 29706957 **Free PMC article.** Review.

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In contrast, it is only recently becoming clear that **innate** immune cells, primarily brain resident macrophages called microglia, are also key regulators of brain development. ...We also summarize the effects of early life perturbations on microglia function in the developi ...

Vagus Nerve

Vagus Nerve as Modulator of the Brain-Gut Axis in Psychiatric and Inflammatory Disorders.

Breit S, Kupferberg A, Rogler G, Hasler G. **Front Psychiatry.** 2018 Mar 13;9:44. doi: 10.3389/fpsyt.2018.00044. eCollection 2018. PMID: 29593576 **Free PMC article.** Review.

The vagus nerve represents the main component of the parasympathetic nervous system, which oversees a vast array of crucial bodily functions, including control of mood, **immune** response, digestion, and heart rate. ...In this review article, we discuss various functions of t ...

Sterile Inflammation of Brain, due to Activation of Innate Immunity, as a Culprit in Psychiatric Disorders.

Ratajczak MZ, et al. **Front Psychiatry**. 2018. PMID: 29541038 **Free PMC article.**

Review.

Trained innate immunity: a salient factor in the pathogenesis of neuroimmune psychiatric disorders.

Salam AP, et al. **Mol Psychiatry. 2018.** PMID: 29230022 Review.

Genetic Correlations Between Immune-Related Disorders and Psychiatric Disorders

Genetic correlations among psychiatric and immune-related phenotypes based on genome-wide association data.

Tylee DS, Sun J, Hess JL, Tahir MA, Sharma E, Malik R, Worrall BB, Levine AJ, Martinson JJ,

Nejentsev S, Speed D, Fischer A, Mick E, Walker BR, Crawford A, Grant SFA, Polychronakos C, Bradfield JP, Sleiman PMA, Hakonarson H, Ellinghaus E, Elder JT, Tsoi LC, Trembath RC, Barker JN, Franke A, Dehghan A; 23 and Me Research Team; Inflammation

Working Group of the CHARGE Consortium; METASTROKE Consortium of the International Stroke Genetics Consortium; Netherlands Twin Registry; neuroCHARGE

Working Group; Obsessive Compulsive and Tourette Syndrome Working Group of the Psychiatric Genomics Consortium, Faraone SV, Glatt SJ. **Am J Med Genet B**

Neuropsychiatr Genet. 2018 Oct;177(7):641-657. doi: 10.1002/ajmg.b.32652. Epub 2018 Oct 16. PMID: 30325587 **Free PMC article.**

Using LDSC, we observed significant genetic correlations between **immune**-related disorders and several psychiatric disorders, including anorexia nervosa, **attention deficit-hyperactivity disorder**, bipolar **disorder**, major depression, obsessi ...

The role of IL-6 in neurodevelopment after prenatal stress.

Gumusoglu SB, Fine RS, Murray SJ, Bittle JL, Stevens HE. **Brain Behav Immun.** 2017 Oct;65:274-283. doi: 10.1016/j.bbi.2017.05.015. Epub 2017 May 22. PMID: 28546058 **Free PMC article.**

Prenatal stress exposure is associated with adverse psychiatric outcomes, including autism and **ADHD**, as well as locomotor and social inhibition and anxiety-like behaviors in animal offspring. Similarly, maternal **immune** activation also contributes to psychiatric risk ...

The role of the innate immune system in psychiatric disorders.

Jones KA, Thomsen C. **Mol Cell Neurosci.** 2013 Mar;53:52-62. doi: 10.1016/j.mcn.2012.10.002. Epub 2012 Oct 12. PMID: 23064447 Review.

In this review we draw reference to biochemical, cellular and animal disease models, as well as clinical observations to elucidate the role of the **innate** immune system in **psychiatric disorders**. ...Effects of these signaling molecules on neurotransmission, mem

...

ADHD

Maternal serum C-reactive protein (CRP) and offspring attention deficit hyperactivity disorder (ADHD).

Chudal R, Brown AS, Gyllenberg D, Hinkka-Yli-Salomäki S, Sucksdorff M, Surcel HM, Upadhyaya S, Sourander A. **Eur Child Adolesc Psychiatry.** 2020 Feb;29(2):239-247. doi: 10.1007/s00787-019-01372-y. Epub 2019 Jul 16. PMID: 31312974 **Free PMC article.**

The results were similar in both sexes as well as among **ADHD** cases with or without comorbid ASD or conduct **disorder**. In this first study examining CRP, a biomarker for inflammation, during early pregnancy in relation to offspring **ADHD**, we report no significant ...

“In this first study examining CRP, a biomarker for inflammation, during early pregnancy in relation to offspring ADHD, we report no significant associations.

“The lack of any association, when considered with positive findings seen in ASD (Autism Spectrum Disorder) and schizophrenia, and negative findings in bipolar disorder suggests different pathways linking maternal immune activation and development of various neuropsychiatric disorders.”

Oxidative stress and immune aberrancies in attentiondeficit/hyperactivity disorder (ADHD): a casecontrol

comparison.

Verlaet AAJ, Breynaert A, Ceulemans B, De Bruyne T, Franssen E, Pieters L, Savelkoul HFJ, Hermans N. **Eur Child Adolesc Psychiatry**. 2019 May;28(5):719-729. doi:

10.1007/s00787-018-1239-4. Epub 2018 Oct 22. PMID: 30350094

The objective of this study is to compare oxidative stress and **immune** biomarkers between **attention-deficit/hyperactivity disorder (ADHD)** patients and controls without **ADHD**.

...These results point at the potential involvement of sli ...

ADHD pathogenesis in the immune, endocrine and nervous systems of juvenile and maturing SHR and WKY rats.

Kozłowska A, Wojtacha P, Równiak M, Kolenkiewicz M, Huang ACW.

Psychopharmacology (Berl). 2019 Oct;236(10):2937-2958. doi:

10.1007/s002130195180-0. Epub 2019 Feb 8. PMID: 30737597 **Free PMC article**.

RATIONALE: **Attention-deficit/hyperactivity disorder (ADHD)** is one of the most common neurobehavioural disorders with morphological and functional brain abnormalities. However, there is a growing body of evidence that abnormalities in the **immu ...**

Rationale: Attention-deficit/hyperactivity disorder (ADHD) is one of the most common neurobehavioural disorders with morphological and functional brain abnormalities. However, there is a growing body of evidence that abnormalities in the immune and endocrine systems may also account for the ADHD pathogenesis.

Conclusions: Significant elevations of serum and/or tissue contents of cytokines, chemokines and oxidative stress markers as well as volumetric and neurochemical alterations in the mPFC of juvenile SHRs may suggest the cooperation of neurological and immune systems in the ADHD pathogenesis. Elevated levels of steroid hormones in maturing SHRs may be a compensatory effect involved in reducing inflammation and ADHD symptoms.

Alcohol Use Disorder

Neuroimmune signaling in alcohol use disorder.

Erickson EK, Grantham EK, Warden AS, Harris RA. **Pharmacol Biochem Behav.** 2019 Feb;177:34-60. doi: 10.1016/j.pbb.2018.12.007. Epub 2018 Dec 24. PMID: 30590091 **Free PMC article.** Review.

Alcohol modulates **innate** immune signaling in different cell types in the brain by altering gene expression and the molecular pathways that regulate neuroinflammation.

...**Psychiatric disorders** that are comorbid with AUD, such as post-traumatic stress disorder, ...

Innate Immune Signaling and Alcohol Use Disorders.

Coleman LG Jr, Crews FT. **Handb Exp Pharmacol.** 2018;248:369-396. doi: 10.1007/164_2018_92. PMID: 29500721 **Free PMC article.**

Innate immune signaling is an important feature in the pathology of alcohol use **disorders**. Alcohol abuse causes persistent **innate** immune activation in the brain. ...This suggests that **innate** immune activation may play a role both in the development and ...

• Alcohol Use Disorder & Bipolar Disorder

[Bipolar disorder and alcohol use disorder: practical recommendations for treatment, based on a literature review.](#)

Spijker AT, van Zaane J, Koenders MA, Hoekstra R, Kupka RW. *Tijdschr Psychiatr.* **2018**;60(2):87-95.PMID: 29436699 **Free article.** Review. **Dutch.**

A fairly large proportion (25-50%) of patients with **bipolar disorder** (bd) also suffer from comorbid **alcohol use disorder** (aud). ...There is also limited evidence that other effective treatments may include the **use** of integrated psychologi ...

[Add-On Memantine Treatment for Bipolar II Disorder Comorbid with Alcohol Dependence: A 12-Week Follow-Up Study.](#)

Lee SY, Wang TY, Chen SL, Chang YH, Chen PS, Huang SY, Tzeng NS, Wang LJ, Lee IH, Chen KC, Yang YK, Hong JS, Lu RB. *Alcohol Clin Exp Res.* **2018** Jun;42(6):1044-1050. doi: 10.1111/acer.13640. Epub 2018 May 17.PMID: 29656414 **Free PMC article.** Clinical Trial.

BACKGROUND: **Bipolar disorder** (BD), especially BD-II, is frequently comorbid with **alcohol** dependence. Because BD-II and **alcohol** dependence are neurodegenerative disorders, agents with anti-inflammatory and neurotrophic effects might provide effective th ...

Pharmacological Treatment of Bipolar Disorder with Comorbid Alcohol Use Disorder.

Naglich A, Adinoff B, Brown ES. **CNS Drugs.** 2017 Aug;31(8):665-674. doi: 10.1007/s40263-017-0449-5.PMID: 28669022

Bipolar disorder (BD) spectrum and **alcohol use** disorders (AUDs) commonly occur together. Comorbidity between the two conditions predisposes patients to elevated risks of adverse outcomes, including hospitalization and suicide, compared with either cond ...

• **Alcohol Use Disorder & Depression**

Alcohol Use Disorder and Depressive Disorders.

McHugh RK, Weiss RD. **Alcohol Res.** 2019 Jan 1;40(1):arcr.v40.1.01. doi: 10.35946/arcr.v40.1.01. eCollection 2019 Oct 21.PMID: 31649834 **Free PMC article.** Review.

Alcohol use disorder (AUD) and **depressive** disorders are among the most prevalent psychiatric disorders and co-occur more often than expected by chance. The aim of this review is to characterize the prevalence, course, and treatment of co-occurring AUD ...

Double screening for dual disorder, alcoholism and depression.

Pavkovic B, Zaric M, Markovic M, Klacar M, Huljic A, Caricic A. **Psychiatry Res.** 2018 Dec;270:483-489. doi: 10.1016/j.psychres.2018.10.013. Epub 2018 Oct 9. PMID: 30326431

Comorbidity of **alcohol use disorder** and major **depressive disorder** has been reported in samples. The aim of this study was to examine the relationship between **alcoholism** and **depression** in undiagnosed patients by simultaneously apply ...

Co-occurring depression and alcohol misuse is under-identified in general practice: A cross-sectional study.

Hobden B, Bryant J, Sanson-Fisher R, Oldmeadow C, Carey M. **J Health Psychol.** 2018 Jul;23(8):1085-1095. doi: 10.1177/1359105316643855. Epub 2016 Apr 25. PMID: 27114213

Depression and **alcohol** misuse are common co-occurring conditions. This study aimed to determine the accuracy of general practitioner identification of **depression** and **alcohol** misuse. ...Those with severe **alcohol** misuse, no chronic diseases and lo ...

An Online Intervention for Co-Occurring Depression and Problematic Alcohol Use in Young People: Primary Outcomes From a Randomized Controlled Trial.

Deady M, Mills KL, Teesson M, Kay-Lambkin F. **J Med Internet Res.** 2016 Mar 23;18(3):e71. doi: 10.2196/jmir.5178. PMID: 27009465 **Free PMC article.** Clinical Trial.

BACKGROUND: **Depression** and problematic **alcohol use** represent two of the major causes of disease burden in young adults. These conditions frequently co-occur and this is associated with increased harm and poorer outcomes than either **disorder** in isolation ...

• Alcohol Use Disorder and PTSD

Effects of oxytocin on stress reactivity and craving in veterans with co-occurring PTSD and alcohol use disorder.

Flanagan JC, Allan NP, Calhoun CD, Badour CL, Moran-Santa Maria M, Brady KT, Back SE. **Exp Clin Psychopharmacol.** 2019 Feb;27(1):45-54. doi: 10.1037/pha0000232. Epub 2018 Nov 1. PMID: 30382728 **Free PMC article.** Clinical Trial.

Posttraumatic **stress disorder (PTSD)** and **alcohol use disorder (AUD)** are highly prevalent and commonly co-occur. The dual diagnosis of **PTSD/AUD** is associated with serious negative sequelae, and there are currently no effective pharm ...

The Epidemiology of Post-Traumatic Stress Disorder and Alcohol Use Disorder.

Smith ND, Cottler LB. **Alcohol Res.** 2018;39(2):113-120.PMID: 31198651 **Free PMC article.** Review.

For more than 40 years, research has shown that individuals with **post-traumatic stress disorder (PTSD)** use alcohol and experience **alcohol use disorder (AUD)** to a greater degree than those with no **PTSD**. . . .

Doxazosin for the treatment of co-occurring PTSD and alcohol use disorder: Design and methodology of a randomized controlled trial in military veterans.

Back SE, Flanagan JC, Jones JL, Augur I, Peterson AL, Young-McCaughan S, Shirley DW, Henschel A, Joseph JE, Litz BT, Hancock AK, Roache JD, Mintz J, Wachen JS, Keane TM, Brady KT; Consortium to Alleviate PTSD. **Contemp Clin Trials.** 2018 Oct;73:8-15. doi: 10.1016/j.cct.2018.08.009. Epub 2018 Aug 24.PMID: 30145268 **Free PMC article.** Clinical Trial.

Posttraumatic **stress disorder (PTSD)** and **alcohol use disorders (AUD)** are two of the most common mental health **disorders** affecting civilians as well as military populations. ...In addition, functional magnetic resonance imaging (fMR ...

Treatment of alcohol use disorder and co-occurring PTSD.

Taylor M, Petrakis I, Ralevski E. **Am J Drug Alcohol Abuse.** 2017 Jul;43(4):391-401. doi: 10.1080/00952990.2016.1263641. Epub 2016 Dec 23. PMID: 28010130 Review.

BACKGROUND: **Alcohol use disorder** (AUD) is a serious psychiatric **disorder** with medical, psychiatric, and social consequences. In individuals with comorbid **post-traumatic stress disorder (PTSD)**, treatment outcomes are n ...

• Alcohol Use Disorder & Traumatic Brain Injury

Does pediatric traumatic brain injury cause adult alcohol misuse: Combining preclinical and epidemiological approaches.

Weil ZM, Karelina K, Corrigan JD. **Exp Neurol.** 2019 Jul;317:284-290. doi: 10.1016/j.expneurol.2019.03.012. Epub 2019 Mar 22. PMID: 30910407 Review.

Traumatic **brain injury** (TBI) is closely interrelated with **alcohol** use disorders. This is mediated, in part, by the large number of individuals who are intoxicated at the time of their **injuries**. ...However, for a number of reasons including potential co ...

Alcohol Use Disorder and Traumatic Brain Injury.

Weil ZM, Corrigan JD, Karelina K. **Alcohol Res.** 2018;39(2):171-180. PMID: 31198656 **Free PMC article.** Review.

Alcohol use and traumatic **brain injury** (TBI) are inextricably and bidirectionally linked. **Alcohol** intoxication is one of the strongest predictors of TBI, and a substantial proportion of TBIs occur in intoxicated individuals. ...Critically, **alcohol** ...

An Examination of Behavioral and Neuronal Effects of Comorbid Traumatic Brain Injury and Alcohol Use.

Mayer AR, Hanlon FM, Claus ED, Dodd AB, Miller B, Mickey J, Quinn DK, Hagerty SL, Seaman B, Hutchison KE. **Biol Psychiatry Cogn Neurosci Neuroimaging.** 2018 Mar;3(3):294-302. doi: 10.1016/j.bpsc.2017.09.012. Epub 2017 Oct 10. PMID: 29486871 **Free PMC article.**

BACKGROUND: Chronic **alcohol** use disorders (AUDs) and traumatic **brain injury** (TBI) are highly comorbid and share commonly affected neuronal substrates (i.e., prefrontal cortex, limbic system, and cerebellum). ...Future studies should examine the potential long ...

Minocycline blocks traumatic brain injury-induced alcohol consumption and nucleus accumbens inflammation in adolescent male mice.

Karelina K, Nicholson S, Weil ZM. **Brain Behav Immun.** 2018 Mar;69:532-539. doi: 10.1016/j.bbi.2018.01.012. Epub 2018 Feb 1. PMID: 29395778 **Free PMC article.**

Alcohol use is a well characterized risk factor for traumatic **brain injury** (TBI); however, emerging clinical and experimental research suggests that TBI may also be an independent risk factor for the development of **alcohol** use disorders. ...Moreover, a ...

Acute Alcohol Exposure and Risk of Mortality of Patients with Traumatic Brain Injury: A Systematic Review and Meta-Analysis.

Ding Q, Wang Z, Shen M, Su Z, Shen L. **Alcohol Clin Exp Res.** 2017 Sep;41(9):1532-1540. doi: 10.1111/acer.13436. Epub 2017 Jul 18.PMID: 28654159 Review.

After traumatic **brain injury** (TBI), patients usually live with significant disability and socioeconomic burdens. Acute exposure to **alcohol** is considered a major risk factor for TBI. ...Further studies assessing the effect of **alcohol** between the BAC-pos ...

Alcohol abuse after traumatic brain injury: Experimental and clinical evidence.

Weil ZM, Corrigan JD, Karelina K. **Neurosci Biobehav Rev.** 2016 Mar;62:89-99. doi: 10.1016/j.neubiorev.2016.01.005. Epub 2016 Jan 24.PMID: 26814960 Review.

Brain injury survivors, particularly those injured early in life are very likely to abuse drugs and **alcohol** later in life. **Alcohol** abuse following traumatic **brain injury** (TBI) is associated with poorer rehabilitation outcomes and a greatl ...

Allergies [a mixed bag]

Allergies, asthma, and psychopathology in a nationally representative US sample.

Kelly K, Ratliff S, Mezuk B .**J Affect Disord.** 2019 May 15;251:130-135. doi: 10.1016/j.jad.2019.03.026. Epub 2019 Mar 6.PMID: 30921596

The objective of this study was to use a large, population-based sample to examine the association between several common **psychiatric** conditions and two atopic **disorders: seasonal allergies** and asthma. This study also examined whether comorbidity betwe ...

"Approximately 36.6% had a history of allergies and 11.5% a history of asthma. **Seasonal allergies were positively associated with odds of MDD [Major Depressive Disorder]**(Odds ratio (OR): 1.24, 95% Confidence Interval (CI): 1.06-1.46), GAD (OR: 1.54 (1.28-1.84)), PD (OR: 1.54 (1.24-1.91)), and PTSD (OR: 1.32 (1.09-1.59)).

Asthma was not significantly associated with any psychiatric disorder. All significant associations persisted after adjustment for psychiatric comorbidities. [But see contrarian studies in our section on Asthma. Those studies are from China, Iran, the US and involving the US military]

Allergies, asthma, and psychopathology in a nationally representative US sample.]

Kelly K, Ratliff S, Mezuk B .**J Affect Disord.** 2019 May 15;251:130-135. doi: 10.1016/j.jad.2019.03.026. Epub 2019 Mar 6.PMID: 30921596

The objective of this study was to use a large, population-based sample to examine the association between several common **psychiatric** conditions and two atopic **disorders: seasonal allergies** and asthma. This study also examined whether comorbidity betwe ...

“A history of seasonal allergies was associated with greater odds of mood disorders, anxiety disorders, and eating disorders, but not alcohol or substance use disorders, after adjusting for socio-demographic characteristics and tobacco use.

“The associations between seasonal allergies and mood disorders, substance use disorders, and alcohol use disorders were particularly strong for Latino Americans.

“The association between seasonal allergies and eating disorders was stronger for men than women. Seasonal allergies are a risk factor for psychiatric disorders. Individuals complaining of seasonal allergies should be screened for early signs of mental health problems and referred to specialized services accordingly.”

Seasonal allergies and suicidality: results from the National Comorbidity Survey Replication.

Messias E, Clarke DE, Goodwin RD. **Acta Psychiatr Scand.** 2010 Aug;122(2):139-42. doi: 10.1111/j.1600-0447.2009.01518.x. Epub 2009 Dec 11. PMID: 20003091

RESULTS: After weighting and adjustment, a positive and statistically significant association was found between history of **seasonal allergies** and history of suicidal ideation [adjusted OR = 1.27 (1.01-1.58)]. We found no association between history of **seasonal** ...

“After weighting and adjustment, a positive and statistically significant association was found between history of seasonal allergies and history of suicidal ideation [adjusted OR = 1.27 (1.01-1.58)].

“We found no association between history of seasonal allergies and history of suicide attempts [adjusted OR = 1.17 (0.89-1.52)].”

Altitude

(see also Hypoxia and Sleep Apnea)

Living High and Feeling Low: Altitude, Suicide, and Depression.

Kious BM, Kondo DG, Renshaw PF. **Harv Rev Psychiatry.** 2018 Mar/Apr;26(2):43-56. doi: 10.1097/HRP.000000000000158.PMID: 29517615 Review.

After participating in this activity, learners should be better able to:• Assess epidemiologic evidence that increased **altitude** of residence is linked to increased risk of **depression** and suicide• Evaluate strategies to address hypoxia related **depression** and s ...

Altitude and risk of depression and anxiety: findings from the intern health study.

Kious BM, Bakian A, Zhao J, Mickey B, Guille C, Renshaw P, Sen S. *Int Rev Psychiatry*.

2019 Nov-Dec;31(7-8):637-645. doi: 10.1080/09540261.2019.1586324. Epub 2019 May 14. PMID: 31084447

Multiple studies suggest that the risks of **depression** and suicide increase with increasing **altitude** of residence, but no studies have assessed whether changing **altitude** changes these risks. ...The data suggest that moving from low to high **altitude** is a ...

Association between altitude, prescription opioid misuse, and fatal overdoses.

Ombach HJ, Scholl LS, Bakian AV, Renshaw KT, Sung YH, Renshaw PF, Kanekar S. *Addict Behav Rep*. 2019 Feb 18;9:100167. doi: 10.1016/j.abrep.2019.100167. eCollection 2019 Jun. PMID: 31193784 **Free PMC article.**

Living at **altitude** has been linked to greater reward benefits of other drugs of abuse, and living at **altitude** may also exacerbate the respiratory **depression** linked to opioid use. ...This increased misuse of both stimulants and opioids may increase likelihood ...

Exaggerated systemic oxidative-inflammatory-nitrosative stress in chronic mountain sickness is associated with cognitive decline and depression.

Bailey DM, Brugniaux JV, Filipponi T, Marley CJ, Stacey B, Soria R, Rimoldi SF, Cerny D, Rexhaj E, Pratali L, Salmòn CS, Murillo Jáuregui C, Villena M, Smirl JD, Ogoh S, Pietri S, Scherrer U, Sartori C. **J Physiol.** 2019 Jan;597(2):611-629. doi: 10.1113/JP276898. Epub 2018 Nov 24. PMID: 30397919 **Free PMC article.** Clinical Trial.

KEY POINTS: Chronic mountain sickness (CMS) is a maladaptation syndrome encountered at high **altitude** (HA) characterised by severe hypoxaemia that carries a higher risk of stroke and migraine and is associated with increased morbidity and mortality. ...Systemic OXINOS was m ...

Suicide and High Altitude: An Integrative Review.

Reno E, Brown TL, Betz ME, Allen MH, Hoffecker L, Reitingger J, Roach R, Honigman B. *High Alt Med Biol.* 2018 Jun;19(2):99-108. doi: 10.1089/ham.2016.0131. Epub 2017 Nov 21. PMID: 29161114 Review.

All the studies found that high **altitude** was independently associated with suicide. One study found that many individual characteristics of those who committed suicide were different at high **altitudes** than low **altitude**, including a lack of access or barriers ...

Asthma

Shared genetics of asthma and mental health disorders: a large-scale genome-wide cross-trait analysis.

Zhu Z, Zhu X, Liu CL, Shi H, Shen S, Yang Y, Hasegawa K, Camargo CA Jr, Liang L. **Eur Respir J.** 2019 Dec 19;54(6):1901507. doi: 10.1183/13993003.01507-2019. Print 2019 Dec.PMID: 31619474

Thus, we aimed to investigate shared genetics and the causal link between asthma and mental health disorders. We conducted a large-scale genome-wide cross-trait association study to investigate genetic overlap between asthma from the UK Biobank and eight mental health disorders fr ...

“We identified that ADHD, ANX (Anxiety Disorder) and MDD (Major Depressive Disorder) have a strong genetic correlation with asthma at the genome-wide level.”

Associations of Behavioral Disorders with Asthma in Iranian Children.

Tajdini M, Effatpanah M, Zaki-Dizaji M, Movahedi M, Parvaneh N, Shariat M, Gharagozlou M. **Iran J Allergy Asthma Immunol.** 2019 Jun 8;18(3):340-345. doi: 10.18502/ijaai.v18i3.1127.PMID: 31522441 **Free article.**

This case-control study was performed in a pediatric referral health care center(Children's Medical CenterinTehran University of Medical Sciences) in 2017.With random selection, the 80 children with **asthma** and 92 controls with age range of 5 to 11 years were enrolle

...

Asthma, allergy, and psychiatric disease.

Bellanti JA, Setticone RA. **Allergy Asthma Proc.** 2015 Nov-Dec;36(6):415-7. doi: 10.2500/aap.2015.36.3919.PMID: 26534746 **Free PMC article.** No abstract available.

Asthma and psychiatric disorders in male army recruits and soldiers.

Lev-Tzion R, Friedman T, Shochat T, Gazala E, Wohl Y. **Isr Med Assoc J.** 2007 May;9(5):361-4.PMID: 17591373 **Free article.**

BACKGROUND: Numerous studies have shown an association between **asthma** and **mental disorders**. While elevated rates of **asthma** have been noted among **psychiatric** patients with anxiety **disorders** and post-traumatic stress disorder, several studi ...

Psychiatric disorders and asthma outcomes among high-risk inner-city patients.

Feldman JM, Siddique MI, Morales E, Kaminski B, Lu SE, Lehrer PM. **Psychosom Med.** 2005 Nov-Dec;67(6):989-96. doi: 10.1097/01.psy.0000188556.97979.13.PMID: 16314605
OBJECTIVE: The purpose of this study was to examine the rate of **psychiatric disorders** among patients attending an ethnically diverse, innercity **asthma** clinic for an initial visit and assess the association between **psychiatric disorders** and a ...

Atopic Dermatitis

Association Between Atopic Dermatitis and Suicidality: A Systematic Review and Meta-analysis.

Sandhu JK, Wu KK, Bui TL, Armstrong AW. **JAMA Dermatol.** 2019 Feb 1;155(2):178-187. doi: 10.1001/jamadermatol.2018.4566.PMID: 30540348 **Free PMC article.**

The search criteria for PubMed were as follows: (dermatitis, atopic [MeSH] OR eczema [MeSH]) AND (**suicidal** ideation [MeSH] OR **suicide**, attempted [MeSH] OR **suicide** [MeSH]

OR **suicidality** OR **suicidal** behavior). The search criteria for Embase, Psycl ...

“In the meta-analyses, patients with AD [Atopic Dermatitis] were 44% more likely to exhibit suicidal ideation (pooled odds ratio, 1.44; 95% CI, 1.25-1.65) and 36% more likely to attempt suicide (pooled odds ratio, 1.36; 95% CI, 1.09-1.70) compared with patients without AD.

“Studies investigating completed suicides in patients with AD had inconsistent results.”

Major Comorbidities of Atopic Dermatitis: Beyond Allergic Disorders.

Paller A, Jaworski JC, Simpson EL, Boguniewicz M, Russell JJ, Block JK, Tofte S, Dunn JD, Feldman SR, Clark AR, Schwartz G, Eichenfield LF. **Am J Clin Dermatol.** 2018 Dec;19(6):821-838. doi: 10.1007/s40257-018-0383-4.PMID: 30168085 Review.

Atopic dermatitis is also associated with several mental health comorbidities particularly **attention-deficit hyperactivity disorder, anxiety, and depression.**

...Atopic dermatitis may also be associated with obesity, cardiovascular disease, and autoimmu ...

Autism

Associations between Monocyte and T Cell Cytokine Profiles in Autism Spectrum Disorders: Effects of Dysregulated Innate Immune Responses on Adaptive Responses to Recall Antigens in a Subset of ASD Children.

Jyonouchi H, Geng L. **Int J Mol Sci.** 2019 Sep 24;20(19):4731. doi: 10.3390/ijms20194731.PMID: 31554204 **Free PMC article.**

Altered **innate** immune responses in a subset of ASD children are not restricted to TLR pathways and correlated with changes in T cell cytokine production. Altered trained **immunity** may play a role in the above described changes....

The Role of the Immune System in Autism Spectrum Disorder.

Meltzer A, Van de Water **J.Neuropsychopharmacology.** 2017 Jan;42(1):284-298. doi: 10.1038/npp.2016.158. Epub 2016 Aug 18.PMID: 27534269 **Free PMC article.** Review.

While much effort has focused on the identification of genes associated with autism, research emerging within the past two decades suggests that **immune** dysfunction is a viable risk factor contributing to the neurodevelopmental deficits observed in autism spectrum **disord** ...

Bipolar Disorder

The Neuropeptide CGRP Induces Bipolar Syndrome in Group 2 Innate Lymphoid Cells.

Motomura Y, Kobayashi T, Moro K. **Immunity**. 2019 Oct 15;51(4):598-600. doi: 10.1016/j.immuni.2019.09.015.PMID: 31618650

In this issue of **Immunity**, Nagashima et al., Wallrapp et al., and Xu et al. demonstrate that the neuropeptide calcitonin gene-related peptide (CGRP) fine tunes type

2 **innate** immune response via suppressing group 2 **innate** lymphoid cells (ILC2s)...

Targeting the immune system in the treatment of bipolar disorder.

Rosenblat JD. **Psychopharmacology (Berl)**. 2019 Oct;236(10):2909-2921. doi: 10.1007/s00213-019-5175-x. Epub 2019 Feb 13.PMID: 30756134 Review.

RATIONALE: **Immune** dysfunction has been strongly implicated in the pathophysiology of **bipolar** disorder (BD). As such, numerous clinical trials have investigated the effects of anti-inflammatory agents in the treatment of BD. ...Future larger studies, using stratified

...

The Relationship Between Neuroimmunity and Bipolar Disorder: Mechanism and Translational Application.

Niu Z, Yang L, Wu X, Zhu Y, Chen J, Fang Y. **Neurosci Bull**. 2019 Aug;35(4):595-607. doi:

10.1007/s12264-019-00403-7. Epub 2019 Jun 18. PMID: 31214924 **Free PMC article.**
Review.

Neuroimmune **system** may be involved in the pathological process of **bipolar** disorder (BD), but the essential association is not fully understood. Accumulating evidence has shown that BD involves the activation of **immune** cells and the release of inflammatory sub ...

Dysregulation of the gut-brain axis in schizophrenia and bipolar disorder: probiotic supplementation as a supportive treatment in psychiatric disorders.

Genedi M, Janmaat IE, Haarman BBCM, Sommer IEC. **Curr Opin Psychiatry.** 2019 May;32(3):185-195. doi: 10.1097/YCO.000000000000499. PMID: 30920970 Review.

PURPOSE OF REVIEW: Schizophrenia (SCZ) and **bipolar** disorder are severe mental disorders, both placing a significant burden on individuals' wellbeing and global health generally. ...Increased activation of components of the **immune system** may be involved, inclu ...

Natural killer cells protect white matter integrity in bipolar disorder.

Furlan R, Melloni E, Finardi A, Vai B, Di Toro S, Aggio V, Battistini L, Borsellino G, Manfredi E, Falini A, Colombo C, Poletti S, Benedetti F. **Brain Behav Immun.** 2019 Oct;81:410-421. doi: 10.1016/j.bbi.2019.06.037. Epub 2019 Jun 26. PMID: 31254622

BACKGROUND: **Bipolar** Disorder (BD) associates with disrupted white matter (WM) microstructure and functional connectivity, and with a perturbation of the **immune system**. ...A core component of the innate **immune system**, natural killer (NK) cells we ...

Revisiting inflammation in bipolar disorder.

Fries GR, Walss-Bass C, Bauer ME, Teixeira AL. **Pharmacol Biochem Behav.** 2019 Feb;177:12-19. doi: 10.1016/j.pbb.2018.12.006. Epub 2018 Dec 24. PMID: 30586559 Review.

Bipolar disorder (BD) has been associated with **immune** changes, and yet their underlying mechanisms are still not fully understood. ...BD immunology is an evolving field and current studies indicate this disease is more than a brain disorder, and it can be conceptual ...

Clinically relevant and simple immune system measure is related to symptom burden in bipolar disorder.

Köhler-Forsberg O, Sylvia L, Deckersbach T, Ostacher MJ, McInnis M, Iosifescu D, Bowden C, McElroy S, Calabrese J, Thase M, Shelton RC, Tohen M, Kocsis J, Friedman E, Ketter T, Nierenberg AA. **Acta Neuropsychiatr.** 2018 Oct;30(5):297-305. doi: 10.1017/neu.2017.34. Epub 2017 Dec 7. PMID: 29212563

CONCLUSION: **Immune system** alterations were associated with increased severity of specific mood symptoms, particularly among men. Our results support the sickness syndrome theory, but furthermore emphasise the relevance to study **immune** suppression in **bipola** ...

The microbiome, immunity, and schizophrenia and bipolar disorder.

Dickerson F, Severance E, Yolken R. **Brain Behav Immun.** 2017 May;62:46-52. doi: 10.1016/j.bbi.2016.12.010. Epub 2016 Dec 18. PMID: 28003152 **Free PMC article.** Review.

Schizophrenia and **bipolar** disorder are serious neuropsychiatric disorders of uncertain etiology. Recent studies indicate that **immune** activation may contribute to the etiopathogenesis of these disorders. Numerous studies in animal models indicate that the mucosal mic ...

Bipolar Disorder and Inflammation.

Rosenblat JD, McIntyre RS. **Psychiatr Clin North Am.** 2016 Mar;39(1):125-37. doi: 10.1016/j.psc.2015.09.006. Epub 2015 Dec 10. PMID: 26876323 Review.

The pathophysiology of **bipolar** disorder (BD) remains poorly understood. Current psychopharmacologic treatments are often poorly tolerated and carry high rates of treatment resistance. Mounting evidence has suggested that innate **immune system** dysfunction may p ...

Bipolar and panic disorders may be associated with hereditary defects in the innate immune system.

Foldager L, Köhler O, Steffensen R, Thiel S, Kristensen AS, Jensenius JC, Mors O. **J Affect Disord.** 2014 Aug;164:148-54. doi: 10.1016/j.jad.2014.04.017. Epub 2014 Apr 19. PMID: 24856568

BACKGROUND: Mannan-binding lectin (MBL) and mannan-binding lectin-associated serine protease-2 (MASP-2) represent important arms of the innate **immune system**, and different deficiencies may result in infections or autoimmune diseases. Both **bipolar** and panic di ...

Immune dysregulation and autoimmunity in bipolar disorder:

Synthesis of the evidence and its clinical application.

Rege S, Hodgkinson SJ. *Aust N Z J Psychiatry*. 2013 Dec;47(12):1136-51. doi: 10.1177/0004867413499077. Epub 2013 Aug 1. PMID: 23908311 Review.

METHOD: This article reviews the literature on peripheral and central **immune** dysregulation and autoimmunity in **bipolar** disorder. ...RESULTS: Neuroinflammation and peripheral **immune** dysregulation may play a role in the pathophysiology of **bipolar** disorder ...

Brain Injury

Targeting innate immunity for neurodegenerative disorders of the central nervous system.

Andreasson KI, Bachstetter AD, Colonna M, Ginhoux F, Holmes C, Lamb B, Landreth G, Lee DC, Low D, Lynch MA, Monson A, O'Banion MK, Pekny M, Puschmann T, Russek-Blum N, Sandusky LA, Selenica ML, Takata K, Teeling J, Town T, Van Eldik LJ. *J Neurochem*. 2016 Sep;138(5):653-93. doi: 10.1111/jnc.13667. PMID: 27248001 **Free PMC article**. Review.

This mini review series originated from the 4th Venusberg Meeting on Neuroinflammation held in Bonn, Germany, 7-9th May 2015, **presenting updates on innate immunity in acute brain injury and chronic neurodegenerative disorders, such as traumatic brain injury a ...**

Celiac Disease & Non-Celiac Gluten Sensitivities

A Comprehensive Review of Celiac Disease/Gluten-Sensitive Enteropathies.

McAllister BP, Williams E, Clarke K. **Clin Rev Allergy Immunol.** 2019 Oct;57(2):226-243. doi: 10.1007/s12016-018-8691-2.PMID: 29858750 Review.

More recently, several entities including gluten intolerance, non-**celiac** gluten sensitivity, and seronegative **celiac disease** have been described. ...Finally, the association of other **disease** states including **psychiatric** illness, infertility, lym ...

Psychiatric Comorbidity in Children and Adults with GlutenRelated Disorders: A Narrative Review.

Slim M, Rico-Villademoros F, Calandre EP. **Nutrients.** 2018 Jul 6;10(7):875. doi: 10.3390/nu10070875.PMID: 29986423 **Free PMC article.** Review.

A systematic literature search using MEDLINE, Embase and PsycINFO from inception to 2018 using terms of '**celiac disease**’ or '‘gluten-sensitivityrelated **disorders**’ combined with terms of '‘**mental disor** ...

Celiac Disease Is Associated with Childhood Psychiatric Disorders: A Population-Based Study.

Butwicka A, Lichtenstein P, Frisén L, Almqvist C, Larsson H, Ludvigsson JF. **J Pediatr.** 2017 May;184:87-93.e1. doi: 10.1016/j.jpeds.2017.01.043. Epub 2017 Mar 7. PMID: 28283256

OBJECTIVES: To determine the risk of future childhood **psychiatric disorders** in **celiac disease**, assess the association between previous **psychiatric disorders** and **celiac disease** in children, and investigate the risk of childho ...

Neurological disorders and celiac disease.

Casella G, Bordo BM, Schalling R, Villanacci V, Salemme M, Di Bella C, Baldini V, Bassotti G. *Minerva Gastroenterol Dietol.* 2016 Jun;62(2):197-206. Epub 2015 Nov 30. PMID: 26619901 Review.

Celiac disease (CD) determines neurologic manifestations in 10% of all CD patients. We describe the most common clinical manifestations as cerebellar ataxia, gluten encephalopathy, multiple sclerosis, peripheral neuropathies, sensorineural hearing loss, epilepsy, he ...

Cocaine Use

A potential role for the gut microbiome in substance use disorders.

Meckel KR, Kiraly DD. **Psychopharmacology (Berl).** 2019 May;236(5):1513-1530. doi:

10.1007/s00213-019-05232-0. Epub 2019 Apr 14.PMID: 30982128 **Free PMC article.** Review.

In recent years, there has been a growing interest to explore interactions between the peripheral **immune system**, the gut microbiome, and the CNS. ...

Activation of the Immune System During a Developmental Window May Provide a Link Between Early Life Stress and Future Susceptibility to Cocaine Abuse.

Brown KT, Bachtell RK. **Biol Psychiatry.** 2018 Dec 15;84(12):865-866. doi: 10.1016/j.biopsych.2018.10.002.PMID: 30466507 No abstract available.

From Traumatic Childhood to Cocaine Abuse: The Critical Function of the Immune System.

Lo Iacono L, Catale C, Martini A, Valzania A, Viscomi MT, Chiurchiù V, Guatteo E, Bussone S, Perrone F, Di Sabato P, Aricò E, D'Argenio A, Troisi A, Mercuri NB, Maccarrone M, PuglisiAllegra S, Casella P, Carola V.**Biol Psychiatry.** 2018 Dec 15;84(12):905-916. doi: 10.1016/j.biopsych.2018.05.022. Epub 2018 Jun 11.PMID: 30029767

Adverse childhood experiences affect the **immune system**, and the **immune system** mediates the effects of psychostimulants. However, whether this **system** is involved in the etiology of substance use disorder in individuals who have experienced early ...

Systems-level view of cocaine addiction: the interconnection of the immune and nervous systems.

Marasco CC, Goodwin CR, Winder DG, Schramm-Sapyta NL, McLean JA, Wikswow JP. **Exp Biol Med (Maywood).** 2014 Nov;239(11):1433-42. doi: 10.1177/1535370214537747. Epub 2014 Jun 5.PMID: 24903164 **Free PMC article.** Review.

In this paper, we probe the current research regarding **cocaine** and the **immune system**, and map a systems-level view to outline a broader perspective of the biological response to **cocaine**. ...The focus of this review is on the connection between the nerv ...

Cognitive Deficits/ Executive Functioning

Associations between maternal cytokine levels during gestation and measures of child cognitive abilities and executive functioning.

Dozmorov MG, Bilbo SD, Kollins SH, Zucker N, Do EK, Schechter JC, Zhang JJ, Murphy SK, Hoyo C, Fuemmeler BF. **Brain Behav Immun.** 2018 May;70:390-397. doi: 10.1016/j.bbi.2018.03.029. Epub 2018 Mar 26. PMID: 29588230 **Free PMC article.**

Yet, the relationship between **maternal** cytokines during gestation and later cognitive ability and **executive function** remains understudied. ...Results suggest that dysregulation in gestational **immune activity** are associated with child cognitive a ...

Immune activation in lactating dams alters sucklings' brain cytokines and produces non-overlapping behavioral deficits in adult female and male offspring: A novel neurodevelopmental model of sex-specific psychopathology.

Arad M, Piontkewitz Y, Albelda N, Shaashua L, Weiner I. **Brain Behav Immun.** 2017 Jul;63:35-49. doi: 10.1016/j.bbi.2017.01.015. Epub 2017 Feb 9. PMID: 28189716

Early **immune activation** (IA) in rodents, prenatal through the mother or early postnatal directly to the neonate, is widely used to produce behavioral endophenotypes relevant to schizophrenia and depression. Given that **maternal immune** response plays a c ...

Evidence that aetiological risk factors for psychiatric disorders cause distinct patterns of cognitive deficits.

Wallace J, Marston HM, McQuade R, Gartside SE. *Eur Neuropsychopharmacol.* 2014 Jun;24(6):879-89. doi: 10.1016/j.euroneuro.2013.12.005. Epub 2013 Dec 14. PMID: 24377755

Here we used **maternal immune activation** (MIA) as a rat model of **maternal** infection, and sub-chronic low dose corticosterone treatment as a rat model of flattened glucocorticoid rhythm. ...The effects of these three treatments on neurocognition were exp ...

Depression

An immune gate of depression - Early neuroimmune development in the formation of the underlying depressive disorder.

Kowalczyk M, Szemraj J, Bliźniewska K, Maes M, Berk M, Su KP, Gałecki P. **Pharmacol Rep.** 2019 Dec;71(6):1299-1307. doi: 10.1016/j.pharep.2019.05.022. Epub 2019 May 28. PMID: 31706254 Review.

The **immune system** plays a coordinating role in mediating inflammatory process. Beginning from foetal life, dendritic cells have the ability to react to bacterial and viral antigens, stimulating T lymphocytes in a similar way to adult cells. ...As a

□
result, Th lympho ...

Inflammation and depression: a causal or coincidental link to the pathophysiology?

Leonard BE. *Acta Neuropsychiatr.* 2018 Feb;30(1):1-16. doi: 10.1017/neu.2016.69. Epub 2017 Jan 23. PMID: 28112061 Review.

This review summarises the evidence that chronic low grade inflammation triggers changes that contribute to the mental and physical ill health of patients with major **depression**. Inflammation, and the activation of the hypothalamic pituitary axis by stress, are normal compo ...

Depression and postoperative complications: an overview.

Ghoneim MM, O'Hara MW. **BMC Surg.** 2016 Feb 2;16:5. doi: 10.1186/s12893-016-0120y.PMID: 26830195 **Free PMC article.** Review.

Major **depressive disorder** is a frequent complication of surgery, which may lead to further morbidity and mortality. LITERATURE SEARCH: Several electronic data bases, including PubMed, were searched pairing "**depression**" with surgery, postoperative complication ...

Inflammation-Associated Co-morbidity Between Depression and Cardiovascular Disease.

Halaris A. **Curr Top Behav Neurosci.** 2017;31:45-70. doi: 10.1007/7854_2016_28.PMID: 27830572 Review.

Specific pathophysiologic factors across these systems include homeostatic imbalance between the sympathetic and the parasympathetic systems with loss of heart rate variability (HRV) in **depression**, sympathoadrenal activation, hypothalamicpituitaryadrenal (HPA) axis activ ...

Probiotics for the treatment of depressive symptoms: An antiinflammatory mechanism?

Park C, Brietzke E, Rosenblat JD, Musial N, Zuckerman H, Raguett RM, Pan Z, Rong C, Fus D, McIntyre RS. **Brain Behav Immun.** 2018 Oct;73:115-124. doi: 10.1016/j.bbi.2018.07.006. Epub 2018 Jul 18.PMID: 30009996 Review.

Emerging evidence suggests that modifying the composition of the gut microbiota via probiotic supplementation may be a viable adjuvant treatment option for individuals with major **depressive disorder** (MDD). ...The objectives of this review are to (1) evaluate the evi ...

Depression and sterile inflammation: Essential role of danger associated molecular patterns.

Franklin TC, Xu C, Duman RS. **Brain Behav Immun.** 2018 Aug;72:2-13. doi: 10.1016/j.bbi.2017.10.025. Epub 2017 Nov 2. PMID: 29102801 Review.

Stress is a major risk factor for psychiatric **disorder** including major **depressive disorder** (MDD) and can induce **inflammation**, which is known to be dysregulated in **depression**. ..Conversely, administration of anti-inflammatory agents has been sho ...

Inflammation and depression: a causal or coincidental link to the pathophysiology?

Leonard BE. **Acta Neuropsychiatr.** 2018 Feb;30(1):1-16. doi: 10.1017/neu.2016.69. Epub 2017 Jan 23. PMID: 28112061 Review.

This review summarises the evidence that chronic low grade **inflammation** triggers changes that contribute to the mental and physical ill health of patients with major **depression**. ...This results in the synthesis of the neurotoxic N-methyl-d-aspartate (NMDA) glutamate ...

Evidence for Inflammation-Associated Depression.

Liu CS, Adibfar A, Herrmann N, Gallagher D, Lanctôt KL. *Curr Top Behav Neurosci.* **2017**;31:3-30. doi: 10.1007/7854_2016_2.PMID: 27221622 Review.

This chapter explores the evidence supporting **inflammation**-associated **depression**. Data to date suggest a bidirectional relationship between **inflammation** and **depression** wherein one process can drive the other. ...Taken together, the reviewed preclinical ...

Inflammation in Depression and the Potential for Antiinflammatory Treatment.

Kohler O, Krogh J, Mors O, Benros ME. *Curr Neuropharmacol.* **2016**;14(7):732-42. doi: 10.2174/1570159x14666151208113700.PMID: 27640518 **Free PMC article.** Review.

Accumulating evidence supports an association between **depression** and inflammatory processes, a connection that seems to be bidirectional. ...Within this paper, we review the association between **inflammation** and **depression** together with the current evidence on ...

Innate and adaptive immunity in the development of depression: An update on current knowledge and technological advances.

Haapakoski R, Ebmeier KP, Alenius H, Kivimäki M. *Prog Neuropsychopharmacol Biol Psychiatry.* **2016** Apr 3;66:63-72. doi: 10.1016/j.pnpbp.2015.11.012. Epub 2015 Nov 26.PMID: 26631274 **Free PMC article.** Review.

Observational studies have shown that indicators of **immunity**, especially C reactive protein and proinflammatory cytokines, such as interleukin 6, are associated with an increased risk of depressive **disorders**, although the evidence from randomized trials remains limi ...

Inflammation: depression fans the flames and feasts on the heat.

Kiecolt-Glaser JK, Derry HM, Fagundes CP. **Am J Psychiatry.** 2015 Nov 1;172(11):107591. doi: 10.1176/appi.ajp.2015.15020152. Epub 2015 Sep 11. PMID: 26357876 **Free PMC article.** Review.

Depression and **inflammation** fuel one another. **Inflammation** plays a key role in **depression's** pathogenesis for a subset of **depressed** individuals; **depression** also primes larger cytokine responses to stressors and pathogens that do not ...

Hypoxia

(not getting enough oxygen to tissues)

Perinatal hypoxia as a risk factor for psychopathology later in life: the role of dopamine and neurotrophins.

Giannopoulou I, Pagida MA, Briana DD, Panayotacopoulou MT. **Hormones (Athens).** 2018 Mar;17(1):25-32. doi: 10.1007/s42000-018-0007-7. Epub 2018 Apr 16. PMID: 29858855 Review.

Fetal **hypoxia** (intrapartum oxygen deprivation), **hypoxia**-related obstetric complications, and **hypoxia** during the early neonatal period are major environmental risk factors shown to be associated with an increased risk for later psychopathology. ...The aim of t ...

Pathological Impacts of Chronic Hypoxia on Alzheimer's Disease.

Zhang F, Niu L, Li S, Le W. *ACS Chem Neurosci.* **2019** Feb 20;10(2):902-909. doi: 10.1021/acschemneuro.8b00442. Epub 2018 Nov 26. PMID: 30412668 Review.

Chronic **hypoxia** is considered as one of the important environmental factors contributing to the pathogenesis of Alzheimer's disease (AD). ...Since chronic **hypoxia** is common in the elderly and may contribute to the pathogenesis of AD, prospective prevention an ...

Regulation of immunity and inflammation by hypoxia in immunological niches.

Taylor CT, Colgan SP. *Nat Rev Immunol.* **2017** Dec;17(12):774-785. doi: 10.1038/nri.2017.103. Epub 2017 Oct 3. PMID: 28972206 **Free PMC article.** Review.

The impact of **hypoxia** on immunity and inflammation can vary depending on the microenvironment and **immune** processes occurring in a given niche. ...Furthermore, we discuss the possibility of targeting **hypoxia**-sensitive pathways in **immune** cells for the tr ...

Migraine and psychiatric disorders co-morbidity explained by sinus hypoxic nitric oxide theory - a new hypothesis on the Sino rhinogenic theory.

Rathnasiri Bandara SM. *Med Hypotheses.* 2014 Mar;82(3):257-65. doi: 10.1016/j.mehy.2013.11.045. Epub 2013 Dec 12. PMID: 24411127

This article explains a new pathophysiological initiation between central effects of sinorhinogenic nitric oxide phenomena and **psychiatric disorders**. It also provides an

etiologically important neuro vascular impulse generating pathway to cause or aggravate
psych ...

[Study of hypoxia-induced immune injury and its intervention measure].

Tian YM, Nie HJ, Liu JY, Zan JP, Zhang YK, Zhang DX, Wang H. Zhongguo Ying Yong Sheng Li Xue Za Zhi. **2010 Nov**;26(4):404-10. PMID: 21328972 Chinese.

OBJECTIVE: To explore the characteristic of **hypoxia**-induced **immune** injury, its mechanisms and the intervention measure. METHODS: The change of **immune** organ index, T lymphocyte subsets of peripheral blood and **immune** organ in mice during **hypoxia** w ...

Marijuana

Methamphetamine

Attention-Deficit Hyperactivity Disorder in Adults Using Methamphetamine: Does It Affect Comorbidity, Quality of Life, and Global Functioning?

Mihan R, Shahrivar Z, Mahmoudi-Gharaei J, Shakiba A, Hosseini M. *Iran J Psychiatry*. 2018 Apr;13(2):111-118.PMID: 29997656 **Free PMC article.**

Objective: **Attention-deficit hyperactivity disorder (ADHD)** is common in adulthood, and it is associated with different high- risk behaviors, particularly substance use. Evidence suggests a high prevalence of **ADHD** in adults who take **met** ...

Managing attention deficit hyperactivity disorder in adults using illicit psychostimulants: A systematic review.

Cook J, Lloyd-Jones M, Arunogiri S, Ogden E, Bonomo Y. *Aust N Z J Psychiatry*. 2017 Sep;51(9):876-885. doi: 10.1177/0004867417714878. Epub 2017 Jun 22.PMID: 28639480 Review.

CONTEXT: **Attention deficit hyperactivity disorder** and stimulant use **disorder** commonly co-exist, and appropriate treatments have not been well established. OBJECTIVE: To provide guidance for treatment of co-existing **attention deficit** ...

Attention-deficit/hyperactivity disorder among chronic methamphetamine users: frequency, persistence, and adverse effects on everyday functioning.

Obermeit LC, Cattie JE, Bolden KA, Marquine MJ, Morgan EE, Franklin DR Jr, Atkinson JH, Grant I, Woods SP; Translational Methamphetamine AIDS Research Center (TMARC) Group. **Addict Behav.** 2013 Dec;38(12):2874-8. doi: 10.1016/j.addbeh.2013.08.010. Epub 2013 Aug 19. PMID: 24018233 **Free PMC article.**

AIMS: **Attention-Deficit/Hyperactivity Disorder (ADHD)** is widely regarded as a common comorbidity of **methamphetamine (MA)** dependence, but the frequency, persistence, and real-world impact of **ADHD** among MA users are not known. ...CON ...

“Findings indicate that ADHD is prevalent among chronic MA [methamphetamine] users, who are at increased risk for persistence of childhood diagnoses of ADHD into their adult years.

“ADHD also appears to play an important role in MA [methamphetamine]-associated disability, indicating that targeted ADHD screening and treatment may help to improve realworld outcomes for individuals with MA use disorders.”

Predictors of methamphetamine psychosis: history of ADHDrelevant childhood behaviors and drug exposure.

Salo R, Fassbender C, Iosif AM, Ursu S, Leamon MH, Carter C. **Psychiatry Res.** 2013 Dec 15;210(2):529-35. doi: 10.1016/j.psychres.2013.06.030. Epub 2013 Jul 26. PMID: 23896355 **Free PMC article.**

The goal of this study was to extend our previous research that reported a significant association between **Attention Deficit Hyperactivity Disorder (ADHD)**-relevant childhood behaviors and the frequency of **methamphetamine (MA)**-induced psyc ...

Opioids

PTSD

Gene expression differences in PTSD are uniquely related to the intrusion symptom cluster: A transcriptome-wide analysis in military service members.

Rusch HL, Robinson J, Yun S, Osier ND, Martin C, Brewin CR, Gill JM. **Brain Behav Immun.** 2019 Aug;80:904-908. doi: 10.1016/j.bbi.2019.04.039. Epub 2019 Apr 27. PMID: 31039430 **Free PMC article.**

Posttraumatic **stress** disorder (**PTSD**) is associated with widespread **immune** dysregulation; however, little is known about the gene expression differences attributed to each **PTSD** symptom cluster. ...Pathway analysis identified upregulated **immune** r ...

Inflammation and post-traumatic stress disorder.

Hori H, Kim Y. **Psychiatry Clin Neurosci.** 2019 Apr;73(4):143-153. doi: 10.1111/pcn.12820. Epub 2019 Feb 21. PMID: 30653780 **Free article.** Review.

While **post-traumatic stress** disorder (**PTSD**) is currently diagnosed based solely on classic psychological and behavioral symptoms, a growing body of evidence has

highlighted a link between this disorder and alterations in the **immune** and inflammat ...

Metabolism, Metabolomics, and Inflammation in Posttraumatic Stress Disorder.

Mellon SH, Gautam A, Hammamieh R, Jett M, Wolkowitz OM. **Biol Psychiatry.** 2018 May 15;83(10):866-875. doi: 10.1016/j.biopsych.2018.02.007. Epub 2018 Feb 22. PMID: 29628193 Review.

Posttraumatic **stress** disorder (**PTSD**) is defined by classic psychological manifestations, although among the characteristics are significantly increased rates of serious somatic comorbidities, such as cardiovascular disease, **immune** dysfunction, and metabolic s ...

Posttraumatic stress disorder (PTSD) and the dermatology patient.

Gupta MA, Jarosz P, Gupta AK. **Clin Dermatol.** 2017 May-Jun;35(3):260-266. doi: 10.1016/j.clindermatol.2017.01.005. Epub 2017 Jan 22. PMID: 28511822

Some **PTSD** patients show hypothalamic-pituitary-adrenal axis hyporesponsiveness and higher circulating T lymphocytes, which can exacerbate **immune**-mediated dermatologic **disorders**. **PTSD** should be considered an underlying factor in the chronic, recurrent, ...

PTSD, a Disorder with an Immunological Component.

Wang Z, Young MR. **Front Immunol.** 2016 Jun 6;7:219. doi: 10.3389/fimmu.2016.00219. eCollection 2016.PMID: 27375619 **Free PMC article.** Review.

Post-traumatic stress disorder (**PTSD**) has been associated with an inflammatory state. However, few studies have addressed the mechanisms underlying this **immune** imbalance that favors inflammation or how this imbalance contributes to **PTSD**. ...

Schizophrenia

Gut microbiome and adaptive immunity in schizophrenia.

Agorastos A, Bozikas VP. *Psychiatriki.* 2019 Jul-Sep;30(3):189-192. doi: 10.22365/jpsych.2019.303.189.PMID: 31685450 **Free article.** English, Greek, Modern.

Over the past few years, immunopathogenesis has emerged as one of the most compelling aetiopathological models of **schizophrenia** (SCZ), suggesting a chronic, **immune**-based, low-grade inflammatory background of this devastating disorder.^{1,2}

Mounting evidence points tow ...

Autoimmune phenotypes in schizophrenia reveal novel treatment targets.

Severance EG, Dickerson FB, Yolken RH. **Pharmacol Ther.** 2018 Sep;189:184-198. doi: 10.1016/j.pharmthera.2018.05.005. Epub 2018 May 6. PMID: 29742478 **Free PMC article.** Review.

At the forefront of this investigative effort is the **immune** system and its many components, pathways and phenotypes, which are now known to actively engage the brain. Studies in **schizophrenia** reveal an intricate association of environmentally driven **immune** ac ...

Inflammation in Schizophrenia: Pathogenetic Aspects and Therapeutic Considerations.

Müller N. *Schizophr Bull.* 2018 Aug 20;44(5):973-982. doi: 10.1093/schbul/sby024. PMID: 29648618 **Free PMC article.** Review.

In animal models, pre- or perinatal elicitation of the **immune** response may increase **immune** reactivity throughout life, and similar findings have been described in humans. ...**Schizophrenia** is characterized by risk genes that promote inflammation and by environ ...

The microbiome, immunity, and schizophrenia and bipolar disorder.

Dickerson F, Severance E, Yolken R. **Brain Behav Immun.** 2017 May;62:46-52. doi: 10.1016/j.bbi.2016.12.010. Epub 2016 Dec 18. PMID: 28003152 **Free PMC article.** Review.

Schizophrenia and bipolar disorder are serious neuropsychiatric disorders of uncertain etiology. Recent studies indicate that **immune** activation may contribute to the etiopathogenesis of these disorders. ...The study of **immune** alterations and the microbiome in ...

Neuroimmune biomarkers in schizophrenia.

Tomasik J, Rahmoune H, Guest PC, Bahn S. **Schizophr Res.** 2016 Sep;176(1):3-13. doi: 10.1016/j.schres.2014.07.025. Epub 2014 Aug 12. PMID: 25124519 Review.

Numerous technologies have been employed in search of **schizophrenia** biomarkers. These studies have suggested that neuroinflammatory processes may play a role in **schizophrenia** pathogenesis, at least in a subgroup of patients. ...In line with these findings, certain i ...

Inflammation and immunity in schizophrenia: implications for pathophysiology and treatment.

Khandaker GM, Cousins L, Deakin J, Lennox BR, Yolken R, Jones PB. **Lancet Psychiatry.** **2015** Mar;2(3):258-270. doi: 10.1016/S2215-0366(14)00122-9. Epub 2015 Feb age 54 of 58

25.PMID: 26359903 **Free PMC article.** Review.

A possible association between **schizophrenia** and the **immune** system was postulated over a century ago, and is supported by epidemiological and genetic studies pointing to links with infection and inflammation. ...In this Review, we describe some of the important area ...

Smoking

Trauma/Adversity

Childhood Adversity and Current Stress are related to Pro- and Anti-inflammatory Cytokines in Major Depression.

Müller N, Krause D, Barth R, Myint AM, Weidinger E, Stettinger W, Zill P, Drexhage H, Schwarz MJ. **J Affect Disord.** 2019 Jun 15;253:270-276. doi: 10.1016/j.jad.2019.04.088. Epub 2019 Apr 22.PMID: 31063941

We used Cohen's Perceived Stress Scale (PSS), the list of life-threatening experiences questionnaire (LTE-Q) and the childhood **trauma** questionnaire (CTQ) to assess the level of stress and analyzed IL-6 and IL-10 cytokines in venous blood plasma. ...This study highli ...

Traumagenics: At the intersect of childhood trauma, immunity and psychosis.

Chase KA, Melbourne JK, Rosen C, McCarthy-Jones S, Jones N, Feiner BM, Sharma RP. **Psychiatry Res.** 2019 Mar;273:369-377. doi: 10.1016/j.psychres.2018.12.097. Epub 2018 Dec 19.PMID: 30682559

Early childhood **trauma**, including physical, sexual or **emotional** abuse, neglect, harm or threat of harm, is associated with adulthood dysregulation of the **immune** system. ...Most importantly, persons with schizophrenia and a history of childhood **trauma** d ...

Developmental Trajectories of Early Life Stress and Trauma: A d Stress System Dysregulation.

Agorastos A, Pervanidou P, Chrousos GP, Baker DG. **Front Psychiatry. 2019** Mar 11;10:118. doi: 10.3389/fpsy.2019.00118. eCollection 2019.PMID: 30914979 **Free PMC article.**

Review.

In addition, alterations in **emotional** and autonomic reactivity, circadian rhythm disruption, functional and structural changes in the brain, as well as **immune** and metabolic dysregulation have been lately identified as important risk factors for a chronically impaired ...

Childhood trauma in mood disorders: Neurobiological mechanisms and implications for treatment.

Jaworska-Andryszewska P, Rybakowski JK. **Pharmacol Rep. 2019** Feb;71(1):112-120. doi: 10.1016/j.pharep.2018.10.004. Epub 2018 Oct 11.PMID: 30544098 Review.

Among multiple environmental factors, the experience of childhood **trauma** can be connected with the pathogenesis, course and the treatment of mood disorders. ...Somatic effects of childhood **trauma** include disturbances of stress axis and **immune** inflammatory mechanisms ...

Childhood trauma and adulthood inflammation: a metaanalysis of peripheral C-reactive protein, interleukin-6 and tumour necrosis factor- α .

Baumeister D, Akhtar R, Ciufolini S, Pariante CM, Mondelli V. **Mol Psychiatry. 2016** May;21(5):642-9. doi: 10.1038/mp.2015.67. Epub 2015 Jun 2. PMID: 26033244 **Free PMC article.**

Random-effects meta-analysis showed that individuals exposed to childhood **trauma** had significantly elevated baseline peripheral levels of CRP (Fisher's $z=0.10$, 95% confidence interval (CI)=0.05-0.14), IL-6 ($z=0.08$, 95% CI=0.03-0.14) and TNF- α ($z=0.23$, 95% CI=0.14-0. ...