LDN 2026 Mental Health

PTSD, Trauma-Stress disorders, Anxiety, Depression, ADHD, OCD, behavioral addictions, weight loss and eating disorders.

Most mental health (MH) patients respond well to a weight-based regimen of multiple LDN doses of 0.06 mg/kg/b/w (mg per kilogram of body weight — typically 3 to 6 mg each dose) administered b.i.d. or t.i.d. While a single dose provides immune system benefits, present-time behavioral benefits and symptom reduction typically require multiple LDN doses during waking hours; this maintains a serum blood presence adequate to support a constant partial antagonism of the opioid system (NTX half-life is 4 hours).

Many MH patients will tolerate starting at a 0.06 mg dose, but it is best to start at half that dose to minimize transient side effects. Once a lower dose is well-tolerated, the dose can be rapidly increased to the target dose. This can take as little as two or three days, though fragile patients may require two months or more to fully adjust. In cases where the patient lacks the awareness to manage multiple doses, the 0.06 mg/kg dose can sometimes be doubled or tripled into a higher single dose to extend LDN's behavioral benefits.
Some patients notice a benefit before reaching the 0.06 mg dose level; others must reach this level before symptoms are reduced.

Exceptionally sensitive patients may find a smaller dose ratio equally effective and tolerate it better. Most cases, and especially complex disorders, will benefit from close monitoring and dose adjustments.

Naltrexone (NTX) alters the stress response, a complex psycho-biological response involving synergistic relationships between endogenous opioids, corticosteroids, endocannabinoids, dopamine, and other systems. When one part is altered, the whole is altered (Valentino, & Van Bockstaele, 2015). The opioid system plays a significant role in protective sympathetic and parasympathetic responses, and in the creation and maintenance of traumatic dissociation, a key factor in many MH disorders, as well as pain syndromes. By antagonizing the opioid system, NTX disrupts pathological dissociation, reduces stress and improves response flexibility (Lanius, R. et al., 2018; Lanius, U. et al., 2014).

NTX appears to disrupt addictions by prioritizing top-down attention to present-time reward over past conditioning (Spencer et al., 2023). This is also a key component of its anti-dissociative effects and why many MH disorders benefit from NTX and LDN treatment (Escamilla et al., 2023). This likely contributes to NTX's ability to positively alter the processing of social and emotional stimuli (Wardle et al., 2016). In contrast to the emotional and cognitive blunting associated with many psychotropic medications, NTX and LDN enhance present-time emotional awareness and mental clarity with improved emotional regulation.

Psychological Trauma: Patients with severe trauma -stress disorders, anxiety disorders, and dissociative disorders (Pape, 2020) — particularly DID, a history of severe early neglect or abuse, or a recent opiate addiction should be closely monitored as they adjust to the medication (see pages 159-160 in "The LDN Book Volume Two"). Repeated psycho-education is often required.

It is common for patients who have phobic responses to experiencing affect (positive as well as negative) to mistake greater body awareness and feeling emotions for a negative side effect due to reduced dissociative buffering. Discomfort typically

diminishes within a few weeks as they come to appreciate their enhanced emotional experience and improved ability to regulate emotions. Intrusive recall of previously dissociated traumatic memories may occur with high doses of NTX, but is relatively rare with LDN. Due to enhanced bioavailability from the addition of LDN, medications that need to be at a specific blood level, such as blood thinners, neuroleptics and antipsychotics, may need to be adjusted to avoid side effects from overmedicating patients.

Depression: Some forms of depression respond adequately to a single LDN dose, but, like anxiety, OCD, eating disorders, and ADHD, depression often benefits from multiple daily doses. A pilot study by Mischoulon and colleagues concluded that LDN (a very low dose of 1 mg, b.i.d.) may have beneficial effects for patients with relapsing major depression as an augmentation for dopamine-enhancing antidepressants (2017).

BPD/Self-injury: NTX appears to be more effective than other medications for borderline personality disorder (Timäus et al., 2021), and it has been identified as a treatment for non-suicidal self-injury patients (Zeng et al., 2025).

Eating disorders: Eating disorders such as bulimia often require high doses of NTX (Roudbaraki et al., 2025); in some cases, the multiple dosing of LDN may be helpful. NTX is a primary component of the FDA-approved weight loss medication Contrave.

ADHD: Some ADHD patients benefit from LDN alone; others will need additional stimulant medication. Patients already taking stimulant medication may benefit by adding LDN, especially when anxiety or a trauma history is a contributing factor.

Autism Spectrum: Subgroups on the autism spectrum have the potential to benefit from NTX/LDN treatment, and LDN is being studied as a potential supplemental therapy for children with autism spectrum disorder (ASD), with a focus on inflammation and behavioral symptoms (Roy et al., 2015).

Traumatic Brain Injury & Post-traumatic Seizures

Recent acute traumatic brain injuries (TBI) will likely require aggressive treatment with high doses of NTX, 50-125 mg BID. The dose can be increased until alterations to consciousness, such as brain fog, are maximally diminished. Consider neuropsychological testing such as the Trail Making Test (TMT) or the MOCA to track improvements. After cognitive benefits plateau, maintain the high dose for one month or as long as is required for symptom management, then reduce to LDN. In some cases, a transdermal application of LDN to the carotid artery - with the patient lying down - can be utilized to increase the concentration of naltrexone delivered to the brain.

Similar to MH disorders, starting with half the 0.06/mg/kg/b/w dose and quickly titrating up to a well-tolerated higher dose works well; periodically monitor compliance and dose effectiveness. Similar to LDN dosing, some patients will benefit from multiple high NTX doses.

In the case of concurrent orthopedic injuries that require opioid pain control, use N-Acetyl Cysteine (NAC) initially (see Hoffer et al., 2013). Both NTX (e.g., Greeneltc et al., 2004) and NAC (e.g., Sakai et al., 2023) share anti-TNF-alpha effects that are likely beneficial in limiting inflammatory effects. Titrate down from opiates as soon as possible and use alternative pain control; then slowly titrate in NTX.

Early on, NTX should be used in high doses, 50-125 mg b.i.d. Increase the dose until brain fog, feeling like in a dream, and other consciousness alterations are maximally diminished.

Ideally, NTX treatment for TBI is initiated no later than one week after injury, though good lasting effects have been observed when initiating four weeks later by using NAC in the interim. Use simple neuropsychological testing (Trailmaking Test, MOCA) to track when functional improvement plateaus. Maintain full dose 1 month after plateau and then go to LDN.
Research on opioid antagonists for treating TBI has been neglected in the West. Nevertheless, extensive Chinese research shows that every domain impacted by severe TBI benefits from treatment with the opioid antagonist naloxone (Zhang et al., 2014).

Following hospitalization, NTX and LDN treatment have the potential to enhance gains in the recovery phase of treatment. Anecdotal reports show that injuries in an advanced stage of recovery or mild concussions may be treated with the standard LDN MH protocol once patients no longer report benefits from higher doses. Stroke patients may also benefit from this TBI protocol (see Peyravian, 2019).

For a review of the literature on opioid antagonist treatment for concussion and TBI, see the 2017 presentation by the authors (…Link: https://ldnresearchtrust.org/ulrich-lanius-and-galyn-forster%E2%80%99s-presentation-opioid-antagonists-ldn-2017-conference …). Access their PowerPoint at https://ldnresearchtrust.org/opioid-antagonists-traumatic-brain-injury-0

LDN may also benefit the treatment of seizure disorders: In a case study of 5 children with intractable epilepsy, Abokrysha and colleagues report, "…adding LDN (1-5 mg) to the treatment of intractable epileptic patients was noticed to show marked improvement even in symptomatic epilepsy." Improvements were clinically observable and evident in follow-up electroencephalograms (EEG) (2021). The 2024 study, *Neuroprotective effects of naltrexone in a mouse model of post-traumatic seizures* (PTS), demonstrated that, "naltrexone reduced the severity of many of the sequelae of TBI," NTX treatment ameliorated neuroinflammation, neurodegeneration, reduced interictal events and prevented seizures in all TBI mice, showing NTX to be a promising candidate against PTS, TBI-associated neuroinflammation and epileptogenesis .71% of untreated mice developed PTS.

Citations: PTSD, Trauma-Stress disorders, Anxiety, Depression, OCD:

Escamilla, I., Juan, N., Peñalva, C., Sánchez-Llorens, M., Renau, J., Benito, A., & Haro, G. (2023). "Treatment of dissociative symptoms with opioid antagonists: a systematic review," *European journal of psychotraumatology*, *14*(2), 2265184. https://doi.org/10.1080/20008066.2023.2265184

Forster, G., "Introduction to LDN as an Adjunctive to Psychotherapy," in The LDN Book 4, ed. Linda Elsegood (LDN Research Trust, 2025), ISBN 9781739107062.

Lanius, R. A., Boyd, J. E., McKinnon, M. C., Nicholson, A. A., Frewen, P., Vermetten, E., Jetly, R., & Spiegel, D. (2018). "A Review of the Neurobiological Basis of Trauma-Related Dissociation and its Relation to Cannabinoid- and Opioid-Mediated Stress Response: a Transdiagnostic, Translational Approach," *Current Psychiatry Reports*, *20*(12), 118. https://doi.org/10.1007/s11920-018-0983-y

Lanius, U. and Forster, G., "Chapter 10: Post Traumatic Stress Disorder," in The LDN Book, Volume Two, ed. Linda Elsegood (White River Junction, VT: Chelsey Green Publishing, 2020). ISBN-13: 978-1603589901

Lanius, U F, Corrigan, F M (2014). "Opioid antagonists and Dissociation: adjunctive pharmacological interventions," in UF Lanius, S Paulsen and FM Corrigan (Eds.): Neurobiology and treatment Lanius U., Paulsen S., & Corrigan F., "Neurobiology and Treatment of Traumatic Dissociation: Towards an Embodied Self," (New York: Springer Publishing Company, 2014).

Mischoulon, D., Hylek, L., Yeung, A. S., Clain, A. J., Baer, L., Cusin, C., Ionescu, D. F., Alpert, J. E., Soskin, D. P., & Fava, M. (2017). "Randomized, proof-of-concept trial of low dose naltrexone for patients with breakthrough symptoms of major depressive disorder on antidepressants," *Journal of affective disorders*, *208*, 6–14.

Pape, W. (2020). "Dissociative Disorders," in L. Elsegood (ed.) The LDN Book, Volume Two: The latest research on how Low Dose Naltrexone could revolutionize treatment for PTSD, Pain, IBD, Lyme Disease.

Roy, A., Roy, M., Deb, S., Unwin, G., & Roy, A. (2015). "Are opioid antagonists effective in attenuating the core symptoms of autism spectrum conditions in children: a systematic review," *Journal of intellectual disability research : JIDR*, *59*(4), 293–306. https://doi.org/10.1111/jir.12122

Roudbaraki, S. N., Salimi, M., Esmailpour, S., & Mohammadi, F. (2025). "Efficacy of naltrexone and bupropion combination in patients with binge eating disorder: a systematic review and meta-analysis," *Eating and weight disorders : EWD*, *30*(1), 75. https://doi.org/10.1007/s40519-025-01786-5

Spencer C., Elton A., Dove S., Faulkner M., Robinson D., and Boettiger C., "Naltrexone Engages a Brain Reward Network in the Presence of Reward-Predictive Distractor Stimuli in Males," *Addiction Neuroscience* 7 (2023): 100085, https://doi.org/10.1016/j.addicn.2023.100085

Timäus, C., Meiser, M., Wiltfang, J., Bandelow, B., & Wedekind, D. (2021). "Efficacy of naltrexone in borderline personality disorder, a retrospective analysis in inpatients," *Human psychopharmacology*, *36*(6), e2800. https://doi.org/10.1002/hup.2800

Valentino R. and Van Bockstaele E., "Endogenous Opioids: The Downside of Opposing Stress," *Neurobiology of Stress* 1 (2015): 23–32, https://doi.org/10.1016/j.ynstr.2014.09.006

Wardle M., Bershad A., & de Wit H. (2016). "Naltrexone Alters the Processing of Social and Emotional Stimuli in Healthy Adults," *Social Neuroscience*, *11*(6), 579–591. https://doi.org/10.1080/17470919.2015.1136355

Zeng YY, Saeed S, Hu SH. "Non-Suicidal Self-Injury: Pain Addiction Mechanisms, Neurophysiological Signatures, and Therapeutic Advances," *J Clin Med Res.* 2025 Oct 29;17(10):537-549. https://doi.org/10.14740/jocmr6332 PMID: 41209581; PMCID: PMC12591249.

Citations: Traumatic Brain Injury:

Abokrysha NT, Kishk NA, Nawito AM, Mounir N. "Effect of Low-Dose Naltrexone on Egyptian Children with Intractable Epilepsy: A Case Series Study," *Neurol India* 2021;69:1781-4.

Greeneltch, K. M., Haudenschild, C. C., Keegan, A. D., & Shi, Y. (2004). "The opioid antagonist naltrexone blocks acute endotoxic shock by inhibiting tumor necrosis factor-alpha production," *Brain, behavior, and immunity*, *18*(5), 476–484. https://doi.org/10.1016/j.bbi.2003.12.001

Hoffer, M. E., Balaban, C., Slade, M. D., Tsao, J. W., & Hoffer, B. (2013). "Amelioration of acute sequelae of blast induced mild traumatic brain injury by N-acetyl cysteine: a double-blind, placebo controlled study," *PloS one*, *8*(1), e54163. https://doi.org/10.1371/journal.pone.0054163

Peyravian N., Dikici E., Deo S., Toborek M. & Daunert S., "Opioid Antagonists as Potential Therapeutics for Ischemic Stroke," *Progress in Neurobiology* 182 (2019): 101679, https://doi.org/10.1016/j.pneurobio.2019.101679

Rodriguez, S., Sharma, S., Tiarks, G., Peterson, Z., Jackson, K., Thedens, D., Wong, A., Keffala-Gerhard, D., Mahajan, V. B., Ferguson, P. J., Newell, E. A., Glykys, J., Nickl-Jockschat, T., & Bassuk, A. G. (2024). "Neuroprotective effects of naltrexone in a mouse model of post-traumatic seizures," *Scientific reports*, *14*(1), 13507. https://doi.org/10.1038/s41598-024-63942-8

Sakai, M., Yu, Z., Taniguchi, M., Picotin, R., Oyama, N., Stellwagen, D., Ono, C., Kikuchi, Y., Matsui, K., Nakanishi, M., Yoshii, H., Furuyashiki, T., Abe, T., & Tomita, H. (2023). "N-Acetylcysteine Suppresses Microglial Inflammation and Induces Mortality Dose-Dependently via Tumor Necrosis Factor-α Signaling," *International journal of molecular sciences*, *24*(4), 3798. https://doi.org/10.3390/ijms24043798

Zhang, H., Wang, X., Li, Y., Du, R., Xu, E., Dong, L., Wang, X., Yan, Z., Pang, L., Wei, M., & She, L. (2014). "Naloxone for Severe Traumatic Brain Injury: A Meta-Analysis," *PloS one*, *9*(12), e113093. https://doi.org/10.1371/journal.pone.0113093

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