THE TURKISH JOURNAL ON ADDICTIONS
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INVITED REVIEW

A Narrative Review on Bio-Physiology of Naltrexone Treatment in Pornography Addiction

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Main Points

- Problematic pornography is a debatable entity with challenges in formulating management plans as there exists no proven pharmacotherapy.
- Naltrexone has been considered a pan-addiction treatment proving effective for substance as well as behavioural addictions.
- Our literature review identified 8 case reports and open-label studies exploring the role of naltrexone in sexual addiction.
- The case reports identified successful use of naltrexone in specific cases of problematic pornography use. However, rigorous randomized controlled studies are needed to fully establish the role of Naltrexone in Management of PPU.

Abstract

Problematic pornography use remains a debatable entity, with features overlapping behavioral addictions and impulse control disorders. The controversial nosological status also provides challenges in formulating management plans as there exists no proven pharmacotherapy. We reviewed the bio-physiological basis and available evidence for naltrexone for the management of pornography addiction. Evidence supporting naltrexone as a standalone or adjunctive treatment in pornography addiction is limited. The case report suggesting positive outcomes represents a heterogeneous clinical entity and thus cannot be generalized. More rigorous clinical trials are needed to establish naltrexone's efficacy in the management of problematic pornography use.

Keywords: Hypersexual disorder, naltrexone, pornography, problematic sexual behaviors

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Received: May 22, 2023
Revision Requested: August 27, 2023
Last Revision Recieved: October 24, 2023
Accepted: December 3, 2023
Publication Date: March 21, 2024

Introduction

Hypersexual disorder/sexual addiction is an umbrella construct encompassing a number of problematic sexual behaviors (cybersex, problematic pornography use (PPU), excessive masturbation, telephone sex, etc.) (Karila et al., 2014). Pornography use is one of such problematic conditions and is defined as "a stigmatized behaviour, in which one or more people intentionally expose themselves to representations of nudity, which may or may not include depictions of sexual behaviour, or who seek out, create, modify, exchange, or store such materials, evoking immediate sexual and affective responses "(Kohut et al., 2020). Despite five decades of research, the prevalence of pornography in the general population remains debatable, with literature suggesting higher rates of PPU in sexual minorities than heterosexual individuals and men reporting more PPU than women (Borgogna et al., 2022). As there is no consensus among professionals over the nosological status of pornography addiction, hypotheses swing from obsessive-compulsive spectrum to impulse control to behavioral addiction. This confusion also leads to challenges in the management of such conditions (de Alarcón et al., 2019; Grubbs et al., 2020).

Cite this article as: Ravish, H., Arya, S., & Sharma, M. K. (2024). A narrative review on bio-physiology of naltrexone treatment in pornography addiction. *Addicta: The Turkish Journal on Addictions*, 11(1), 112-116.

DOI: 10.5152/ADDICTA.2024.23049

Naltrexone has been studied and is commonly used as an anti-craving agent for alcohol and opioid use disorders. Naltrexone acts by blocking mu-opioid receptor opioid receptors on γ-aminobutyric acid interneurons in the ventral tegmental area (VTA) as well as modifying the hypothalamic-pituitary-adrenal axis. This eventually inhibits dopaminergic neurons in VTA, a region underlying the reinforcing properties of addictive and compulsive behaviors (Aboujaoude & Salame, 2016). Since opioid receptors indirectly regulate dopamine release in the mesolimbic pathway as well as modulate impulsivity, drugs acting on these receptors may prove effective for all addictions, including pornography (Aboujaoude & Salame, 2016; Piquet-Pessôa & Fontenelle, 2016). While naltrexone's effectiveness at reducing sexual urges to masturbate to pornography remains largely unexplored, its feasibility and tolerability have been recently documented (Savard et al., 2020).

Since there are no well-defined treatment protocols for the management of pornography, we therefore synthesized current evidence on the frequently used pharmacology approach for such conditions and discussed naltrexone's role in the management of PPU.

Material and Methods

We conducted the literature review using Arksey and O'Malley's methodological framework. Studies were identified through a comprehensive search in PubMed, PsycINFO, ScienceDirect, and Google Scholar using keywords "Naltrexone or Opioid receptor antagonist, Pornography, and Addiction," with no country or study design restrictions. Peer-reviewed studies (original articles, narratives, systematic reviews, pre-prints, and case reports) were included. We excluded studies primarily focusing on social perspective (psychological or social aspects of pornography) and paraphilic sexual behavior as well as reviews on the topic. All databases were searched for English-language articles from January 2000 to December 2021. Two authors independently screened the article titles and abstracts initially; for those whose relevance could not be determined by title and abstract, the full text was read for further inclusion. The reference list of primary retrieved articles was also examined to locate any missing relevant articles in the database search. Using a customized data collection form, information was collected on domains like study type, participant characteristics, intervention, and outcomes and documented in the relevant fields from the selected studies. Since the aim of our narrative review was to focus on naltrexone's role in the management of PPU, we focused on the underlying neural and chemical deficits and the hypothetical role of opioid antagonists in addressing those. Therefore, data were extracted in broad categories of 1. physiological, 2. biochemical, 3. naltrexone as a treatment modality.

Physiological Changes in Problematic Pornography Use

Evidence suggests that both substance and behavioral addictions may be associated with similar neural deficits related to error processing and inhibitory control, with the dorsal anterior cingulate cortex being the core area for these underlying deficits (Luijten et al., 2014). Substance and behavioral addiction are associated with the dysregulation of endogenous opioids while the former is also related to baseline higher mu-opioid receptor availability (Mick et al, 2016). Problematic pornography use is associated with increased neural activity in the mesolimbic pathway of the ventral striatum (Balodis & Potenza, 2015; Klucken et al., 2016), similar to activation observed in financial rewards (Koob, 2013). In both pornography and addiction, decreased connectivity of the prefrontal cortex exists with the ventral striatum and amygdala (Kelly et al, 2008; Love et al., 2015). In addition to defects in these connections, hypersexual subjects show gray matter deficits and reduced functional connectivity between the temporal cortex and caudate region (Seok & Sohn, 2018). Data from functional MRI and PET (Positron Emission Tomography) studies have found dopamine dysfunction in the mesocorti-colimbic region, suggesting an imbalance between hyperactive subcortical reward systems and hypoactive prefrontal control mechanisms (Limbrick-Oldfield, van Holst & Clark, 2013).

Biochemical Changes in Problematic Pornography Use

Individuals with PPU typically show a dysfunctional response to stress in the hypothalamus-pituitary-adrenal axis, with alterations observed in individuals with substance addiction (Koob, 2013; Chatzittofis et al., 2016). These responses may be explained as a result of epigenetic changes in classic inflammatory markers involved in the pathophysiology of addictions (Jokinen et al., 2017). Additionally, studies have shown that individuals with hypersexual disorders have high levels of tumor necrosis factor (TNF) and a strong correlation between higher hypersexuality rating scale scores and TNF (Jokinen et al., 2016). A study has found that higher sexuality leads to increased expression of Delta-FosB in the nucleus accumbens of the ventral striatum, as well as overexpression of Delta-FosB-induced a hypersexual syndrome (Hilton & Watts, 2011). Delta-FosB thus has the potential to serve as a biomarker for the reward circuitry activation as well as the severity of addiction (Pitchers et al., 2010).

Naltrexone as a Treatment Option in Problematic Pornography Use

Ryback (2004), in an open-label study, provided the earliest evidence for the role of naltrexone in reducing problematic sexual behaviors among "sexual offenders." Based on our literature search, we retrieved seven case reports suggesting some role of naltrexone in different compulsive sexual behaviors (Table 1). Among these, only four explicitly focused on pornography addiction.

Bostwick & Bucchi (2008), published a case report of a young male with a 10-year history of porn addiction and major depression who improved on 150 mg of naltrexone after unsuccessful treatment attempts with sertraline, individual therapy, group therapy, sex anonymous, and pastoral counseling. Capurso (2017), reported that 50 mg of naltrexone led to a significant improvement in time spent on pornography as well as nicotine use within two months of initiation. Further, a few case reports provide evidence that naltrexone can be a useful adjunct to Cognitive Behavior Therapy(CBT) for pornography addiction (Kraus et al, 2015; Sharma et al, 2022).

Among the remaining three case reports, the focus was on sexual compulsions rather than pornography addiction (Grant & Kim, 2001; Raymond et al, 2002; Camacho, Moura & Oliveira-Maia, 2018). These reports suggest that naltrexone can lead

Table 1.
Description of Case Reports Highlighting the Role of Naltrexone in the Management of Problematic Pornography

Author & Year	Sociodemographic	Duration of Illness	Symptoms	Comorbidity	Naltrexone Dose	Improvement	Other Comments	Other Failed Therapies
[28]Grant & Kim, 2001	58 years/ male	8 years	Sexual compulsion	Kleptomania	SD- 25 mg FD- 150 mg	Almost complete resolution of symptoms at 150 mg	Maintained well for 20 weeks while on medications	fluoxetine, behavioral therapy, and psychotherapy
[29]Raymond 2002a Raymond 2002b	42/ female 62/ male	6 years 20 years	Compulsive sexual behavior Compulsive sexual behavior	Major depression cocaine use disorder	SD - 50 mg FD - 100 mg SD - 50 mg FD - 100 mg	Partial improvement at 50 mg. Significant improvement (75%) within 2 weeks of 100 mg. Significant improvement at 50 mg after 4 weeks, complete resolution at 100 mg	Maintained well for 1 year 8 months. Maintained well for 8 months	Fluoxetine individual and group therapy. Fluoxetine Bupropion Buspirone Citalopram
[24]Bostwick & Bucchi 2008	30/male	10 years	Porn addiction	Major depression	SD - 50 mg FD - 150 mg	Noticeable improvement in the first week, with almost complete improvement at 150 mg	Maintained well for a period of 3 years on medication	sertraline, individual therapy, group therapy, sex anonymous, and pastoral counseling
[25]Capruso, 2017	69/female	ND	Pornography	Nicotine dependence	SD - 50 mg FD - 25 mg	>50% improvement in 2 weeks	Patient reported naltrexone-induced anhedonia, and as a result, the dose was reduced to 25 mg, which led to partial resurfacing of symptoms	Imipramine 200 mg
[30]Camacho, 2018	27/male	ND	Sexual compulsion	Depression anxiety	SD - 50 mg FD - 100 mg	Significant improvement at 50 mg after 8 weeks of treatment, sustained improvement at 100 mg	m. well for 10 months	Fluoxetine supportive therapy
[26]Kraus, 2018	Early 30's/male	10 years	Internet pornography addiction		50 mg	50 mg naltrexone as an adjunct to CBT led to significant improvement in the urges within two weeks of initiation	CBT led to 70% improvement and adding naltrexone as an adjunct led to further improvement	
[27]Sharma et al., 2021	26/male	9 years	Internet pornography addiction		25 mg	25 mg naltrexone after 10-week CBT. Introduction of naltrexone led to a significant decrease in craving	CBT led to 50% improvement in his symptoms	

Note: FD = full dose; SD = starting dose.

to improvements in sexual compulsions, even in cases where Selective Serotonin Reuptake Inhibitors (SSRIs) and psychotherapy failed to show any response.

Conclusion

Our review suggests that there are limited studies exploring the role of altrexone alone or in combination for problematic porno graphy.pornography use The case reports we identified do suggest that naltrexone can be a useful option for problematic pornography use. Further, in patients who respond to naltrexone treatment, the response may be positive and with rapid onset during the first 6 – 8 weeks. Despite these reports, the findings need to be taken with caution. It is very likely that these cases are heterogeneous and represent different disorders, with no specific agreed diagnosis and unstructured outcomes. Our review highlights that there is a paucity of research on the pharmacological management of pornography addiction, with no controlled trials. Many of these challenges are due to the uncertain status of this entity and the lack of well-defined diagnostic criteria. However, since naltrexone has been considered a pan-addiction treatment, promising findings from case reports justify further research into the efficacy and tolerability of naltrexone for the management of pornography addiction.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – M.S., H.R., S.A.; Design – M.S., H.R., S.A.; Supervision – M.S.; Resources – M.S., H.R., S.A.; Materials – M.S., H.R., S.A.; Data Collection and/or Processing – M.S., H.R., S.A.; Analysis and/or Interpretation – M.S., H.R., S.A.; Literature Search – H.R., S.A.; Writing Manuscript – H.R., S.A.; Critical Review – M.S.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

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