

PARAPHILIAS

# Treatment of Paraphilic Disorders in Sexual Offenders or Men With a Risk of Sexual Offending With Luteinizing Hormone-Releasing Hormone Agonists: An Updated Systematic Review



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## ABSTRACT

**Background:** Different pharmacologic agents are used in the treatment of paraphilic disorders in sexual offenders or men with a risk of sexual offending, with luteinizing hormone-releasing hormone (LHRH) agonists being the agents introduced more recently to treatment regimens.

**Aim:** To summarize the relevant literature concerning LHRH agonist treatment of paraphilic disorders in sexual offenders and update the previously published systematic review by Briken et al (J Clin Psychiatry 2003;64:890–897).

**Methods:** The PubMed and Google Scholar databases were searched for literature published from January 2003 through October 2017 using the following key words: *LHRH agonists, GnRH agonists, antiandrogens AND paraphilia, pedophilia, sex offenders.*

**Outcomes:** Evaluation of the effectiveness and side effects of LHRH agonist treatment of paraphilic disorders in sexual offenders.

**Results:** After screening for duplicates and applying specific selection criteria, the search yielded 24 eligible studies reporting on a sample of 256 patients. There is increasing evidence that LHRH agonists are more effective than steroidal antiandrogens in lowering paraphilic sexual thoughts and behaviors. Current research also is based on methods that might be less susceptible to faking (eg, eye-tracking, brain imaging, and viewing-time measures). Side effects occurring most frequently are fatigue, hot flashes, depressive mood, weight gain, high blood pressure, diabetes, gynecomastia, loss of erectile function, and loss of bone mineral density.

**Clinical Implications:** Although LHRH agonists seem to be the most effective drugs in the treatment of paraphilic fantasies and behaviors, they should be reserved for patients with a paraphilic disorder and the highest risk of sexual offending because of their extensive side effects.

**Strengths and Limitations:** This systematic review considers all types of research on LHRH agonist treatment in patients with paraphilic disorders, thereby providing a complete overview of the current state of research. However, most studies are case reports or observational studies and randomized controlled clinical trials have not been conducted or published.

**Conclusions:** LHRH agonists are a useful treatment when combined with psychotherapy in patients with a paraphilic disorder and the highest risk of sexual offending. However, throughout treatment, close monitoring of side effects is needed and ethical concerns must always be kept in mind. **Turner D, Briken P. Treatment of Paraphilic Disorders in Sexual Offenders or Men With a Risk of Sexual Offending With Luteinizing Hormone-Releasing Hormone Agonists: An Updated Systematic Review. J Sex Med 2018;15:77–93.**

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**Key Words:** Gonadotropin-Releasing Hormone Agonists; Luteinizing Hormone-Releasing Hormone Agonists; Sexual Offender; Treatment; Antiandrogens; Paraphilia; Pedophilia; Paraphilic Disorder; Pedophilic Disorder

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## INTRODUCTION

In the *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition*, paraphilic interests are defined as “any intense and persistent sexual interest other than sexual interest in genital stimulation or preparatory fondling with phenotypically normal,

physiologically mature, consenting human partners.”<sup>1</sup> To be differentiated from paraphilic interests, paraphilic disorders also must cause distress or impairments in normal daily functioning to the patient or harm to others.<sup>1</sup> Although discussed controversially, the distinction between paraphilic interests and disorders could lead to a de-stigmatization and de-pathologization of non-normative sexual interests.<sup>2</sup> Prevalence rates of a paraphilic disorder of approximately 50% have been found in sexual offenders, with pedophilic disorder (40%–47%) and sexual sadism disorder (6%–13%) being among the diagnoses found most frequently.<sup>3–5</sup> A deviant sexual preference is one of the strongest predictors for sexual recidivism in adult and adolescent sexual offenders.<sup>6</sup>

Because of the crucial role testosterone plays in male sexuality, it could be a significant factor contributing to the etiology of paraphilic urges and behaviors.<sup>7</sup> Physiologically, testosterone is produced in the Leydig cells of the testes and to a lesser extent in the adrenal cortex and brain.<sup>8</sup> Testosterone production in the brain is *de novo* from cholesterol or through transformation of classic steroids such as progesterone that enter the nervous system through the blood stream.<sup>9</sup> Its production and secretion are controlled by the hypothalamic-pituitary-gonadal axis and follow a negative feedback mechanism. Testosterone receptors have been found in different brain areas of humans and animals, such as the mammillary body, hippocampus, amygdala, orbitofrontal cortex, inferior temporal cortex, and hypothalamus. According to the 4-component model of sexual arousal proposed by Stoleru et al,<sup>10</sup> these brain structures are involved in cognitive (eg, orbitofrontal cortex), emotional (eg, amygdala), and motivational (eg, hypothalamus) processes that take place during sexual arousal and overt sexual behaviors.<sup>7,10–17</sup> Alterations in these brain areas could lead to changes in sexual arousal patterns, including sexual arousal to non-normative objects or sexual practices. Underscoring this suggestion, imaging studies have found structural and functional alterations in most of these brain areas in sexual offenders with a pedophilic disorder.<sup>18–20</sup> Structural imaging studies have found decreased gray matter volumes in the orbitofrontal and dorsolateral prefrontal cortex, insula, ventral striatum, cingulate gyrus, parahippocampal gyrus, and right amygdala in pedophilic sexual offenders compared with healthy controls.<sup>18,19</sup> Furthermore, using functional magnetic resonance imaging (fMRI), decreased activity in the left dorsolateral prefrontal cortex, right occipital and right parietal cortex, hypothalamus, and insula has been reported in pedophilic sexual offenders during the presentation of sexual stimuli.<sup>20</sup>

However, it is not clear how changes in testosterone concentrations are associated with these changes in brain activation patterns and, hence, with paraphilic behaviors or sexual offending. Giotakos et al<sup>21</sup> found higher plasma testosterone levels in a sample of sexual offenders against adults but not in sexual offenders against children (not necessarily with a paraphilic disorder) compared with healthy controls. However, in all 3 groups,

the plasma testosterone level was still within the normal range. Studer et al<sup>22</sup> reported a positive association between higher serum testosterone levels and sexual recidivism in a sample of 501 sexual offenders (also not necessarily with a paraphilic disorder). In their study, 14.5% of sexual offenders had testosterone concentrations above the normal range, although the investigators estimated that a rate of 2.5% would be expected for the general population.<sup>22</sup> In contrast, other studies did not find an association between serum testosterone concentrations and sexual recidivism and some found even significantly higher serum testosterone levels in healthy controls compared with child sexual abusers.<sup>23,24</sup> A recent meta-analysis concluded that serum testosterone concentrations are not altered in sexual offenders, but that sexual offenders against adults could have higher serum testosterone concentrations than child sexual abusers; however, these are usually within the normal range.<sup>25</sup> Furthermore, many studies did not distinguish between sexual offenders with a paraphilic disorder and those without a paraphilic disorder. The investigators suggested that increased testosterone concentrations could lead to more violent and antisocial, rather than more paraphilic, behaviors and that increased antisocial behaviors in turn could facilitate committing sexual offenses in certain individuals.<sup>21,25,26</sup> Nonetheless, previous research has suggested that suppressed serum testosterone concentrations might cause not only decreased sexual functioning but also decreased frequency of paraphilic fantasies and behaviors.<sup>27,28</sup>

In addition to testosterone, dopamine and serotonin play an important role in male sexuality. While dopamine is mainly involved in processes of sexual excitation, serotonin is associated with sexual inhibition processes.<sup>29</sup> Dopamine receptors relevant for sexual functioning can be found in mesolimbic, nigrostriatal, and hypothalamic brain structures.<sup>29</sup> Some case studies found an association between the onset of paraphilic fantasies and behaviors and treatment with dopamine-enhancing drugs in patients with Parkinson disease.<sup>30</sup> However, no differences in genetic polymorphisms in dopamine receptor or dopamine transporter genes were found between sexual offenders with a paraphilic disorder and healthy controls.<sup>31</sup>

After an extensive review of the literature published until 2009, the current guidelines of the World Federation of Societies of Biological Psychiatry (WFSBP) advocated for the use of selective serotonin reuptake inhibitors (SSRIs), steroidal anti-androgens (cyproterone acetate [CPA] and medroxyprogesterone acetate [MPA]), and luteinizing hormone-releasing hormone (LHRH) agonists in the treatment of paraphilic disorders.<sup>32</sup> Although antipsychotics lead to alterations in dopamine metabolism and some small studies have shown that antipsychotics can lead to a decrease of paraphilic fantasies and behaviors, they should be applied only if comorbid diagnoses justify their use.<sup>32</sup> Furthermore, in patients with a comorbid depressive or obsessive-compulsive disorder, SSRIs should be preferred over other agents.<sup>32–37</sup> In antisocial individuals, a recent Cochrane

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