Differential Pharmacological Treatment of Paraphilias and Sex Offenders

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Abstract: *This article gives an overview of current pharmacological treatment of paraphilias and sex offenders focusing on the situation in Germany. Information about selective serotonin reuptake inhibitors (SSRI) is followed by data about established antihormonal substances (cyproterone acetate/CPA, and medroxyprogesterone acetate/MPA), as well as a more detailed account on luteinizing hormone-releasing hormone agonists (LHRH agonists). The results of open, uncontrolled clinical studies with SSRIs (*n = *16) and LHRH agonists (*n = *11) in paraphilic outpatients confirm the positive effects of these substances. A survey about the use of CPA and LHRH agonists in forensic hospitals in Germany shows that half of the patients treated with any kind of (anti-) hormonal agents received an LHRH agonist. The authors present a protocol on side effects, contraindications, and monitoring of CPA and LHRH agonists and develop an algorithm for differential pharmacotherapy of paraphilias.*

Keywords: *pharmacotherapy; paraphilia; sex offender; SSRI; LHRH agonist; CPA*

Over the past decade, the interest in pharmacological treatments of paraphilias and sex offenders has been increasing. There are a number of reasons for this development: (a) the effects of psycho- and sociotherapeutic interventions have been assessed in different meta-analyses (Furby, 1989; Hall, 1995; Hanson & Bussiere, 1998) and are viewed more skeptically than, for example, in the 1970s or 1980s; (b) the short- and long-term sequelae of sexual traumatization have received much attention in the academic as well as in the popular discourse, and more rigorous management of sex offenders has been called for; and (c) new pharmacological agents have been used in the treatment of paraphilias and sex offenders, such as the selective serotonin reuptake inhibitors (SSRIs) and the luteinizing hormone-releasing hormone (LHRH) agonists.

Assessing pharmacological treatment of sex offenders, it should be kept in mind that the terms *sex offender* and *sex offense* are not diagnoses. Therefore, prior to any treatment, a thorough psychiatric, somatic, and criminological diag-

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nostic assessment is mandatory to identify underlying psychiatric and/or somatic disorders as well as other important criminological and prognostic factors. Besides paraphilias (*DSM-IV*), or disorders of sexual preference (*ICD-10*), in sex offenders, underlying psychiatric disorders are often personality disorders—particularly antisocial, narcissistic, borderline, but also schizoid, anxious-avoidant, and other personality disorders (Berger, Berner, Bolterauer, Gutierrez, & Berger, 1999; Kraus, Berner, & Nigbur, 1999; McElroy et al., 1999)—impulse control disorders, and mental retardation (Berner & Karlick-Bolten, 1986; McElroy et al., 1999). There exist often comorbid disorders such as substance disorders, attention deficit hyperactivity disorder (ADHD) (Blocher et al., 2001; Vaih-Koch, Ponseti, & Bonsinki, 2001), affective disorders, organic psychiatric disorders, but also schizophrenia (Smith & Taylor, 1999). However, this distinction between underlying and comorbid disorders in sex offenders is sometimes difficult—theoretically and practically. If a sex offender suffers from one of these psychiatric disorders, he might need adequate pharmacological treatment beside specific psycho- and pharmacotherapy regarding his sexual violence. Comorbid psychiatric disorders should therefore be considered in an algorithm for pharmacological treatment of sex offenders with paraphilias (see Figure 2).

In this article, however, we want to focus on the pharmacotherapy of paraphilias in sex offenders. The optimal pharmacotherapy for paraphilias should (a) reduce selectively the sexual deviant behavior, impulses, and fantasies; (b) support or at least not impair nondeviant sexuality; and (c) not cause other adverse side effects. It is no secret that the development of such a pharmacological agent still appears more like a utopian than a realistic goal for the near future.

The neurobiological basis of sexuality is highly complex. Many physiological substances produce exciting (stimulating) or inhibiting effects on different sexual processes in the central nervous system, the peripheral nerves, and the primary and secondary genital organs (overview in Meston & Frohlich, 2000). These substances can be divided in hormones on one side (androgens, estrogens, progesterone, prolactin, oxytocin, cortisol, and pheromones) and neurotransmitters and neuropeptides on the other side (nitrous oxide, serotonin, dopamine, adrenaline, nor-adrenaline, opioides, acetylcholine, histamine, gamma-aminobutyric acid). In the treatment of paraphilias and sex offenders, mainly two groups of pharmacological substances have been used: agents influencing the production and effects of androgens (cyproterone acetate/CPA, medroxyprogesterone acetate/MPA, and LHRH agonists, synonymous: gonadotropin-releasing hormone agonists/GnRH agonists) and SSRIs. Focusing on SSRIs and LHRH agonists, for each group of these substances, we present an overview about the pathophysiological basis and mechanism of action, its efficacy in paraphilic patients, adverse effects, monitoring, and dosage followed by results from our department. In the concluding section, we make an attempt to integrate the findings from the literature and our own data into an algorithm for the pharmacological treatment of paraphilias.

SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIs)

Serotonin inhibits sexual arousal and reduces orgasmic and ejaculatory capacity (Meston & Frohlich, 2000). The effects of serotonin vary according to different serotonin receptors (e.g., the activation of 5-HT_{1A} receptors accelerates ejaculation, the activation of 5-HT_{2C} receptors inhibits ejaculation) (Waldinger, Berendsen, Blok, Olivier, & Holstege, 1998). The latter effect has been used in the treatment for premature ejaculation (Mendels, Camera, & Sikes, 1995; Waldinger et al., 1998).

Despite the efficacy of SSRIs in paraphilias, no dysfunction of serotonin metabolism or receptors has yet been established in these patients. However, low CSF levels of 5-HIAA (5-hydroxyindoleacetic acid), a serotonin metabolite, have been found in men with impulsive aggression (Virkkunen, Dejong, Bartko, & Linnoila, 1989; Virkkunen, Rawliongs, et al., 1994, overview in Brown, Botsis, & van Praag, 1994) and in one study on sexual murderer (Lidberg, Tuck, Asberg, Scalia-Tomba, & Bertilsson, 1985). In a small experimental study, Maes et al. (2001) found some evidence for an up-regulation of 5-HT_{2A} and 5-HT_{2C} postsynaptic receptors in pedophiles ($n = 8$).

Possible mechanisms of action of SSRIs in paraphilias are (a) general inhibition of sexual activity; reduction (b) of impulsiveness; (c) of obsessive-compulsive characteristics; (d) of underlying depressive symptoms; and (e) an indirect reduction of testosterone serum levels. Because nefazodone, a serotonin as well as nor-adrenaline reuptake inhibitor, with the fewest side effects on sexual desire and arousal, was effective in reducing sexual obsessions and compulsions (Coleman, Gratzer, Nesvacil, & Raymond, 2000), it is unlikely that this effect is due only to the general inhibitory effect of this drug.

The effectiveness of SSRIs in depressions, anxiety, and obsessive-compulsive disorders has been demonstrated in many controlled, double-blind clinical studies. Nowadays, SSRIs are often used as standard medication for these indications, more so because they have fewer and less severe side effects than the classical tricyclic antidepressants. Since the early 1990s, SSRIs have also been used in the treatment of paraphilias and sexual impulsiveness. That SSRIs reduce sexual fantasies, desire, masturbation, and sexual deviant behavior in patients with various paraphilias has been shown in different clinical trials (Coleman, Cesnik, Moore, & Dwyer, 1992; Kafka, 1994; Kafka & Prentky, 1992; overviews in Bradford, 2000; Bradford & Greenberg, 1996; Gijs & Gooren, 1996; Greenberg & Bradford, 1997; Greenberg, Bradford, Curry, & O'Rourke, 1996). Some of the studies also used penile plethysmography to assess the sexual arousal. In one controlled study, the combination of SSRI with psychotherapy was more effective than psychotherapy alone (Bradford & Greenberg, 1996). Different SSRIs have been used in these studies (fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram) as well as the primarily serotonergic tricyclic antidepressant clomipramine. No dif-

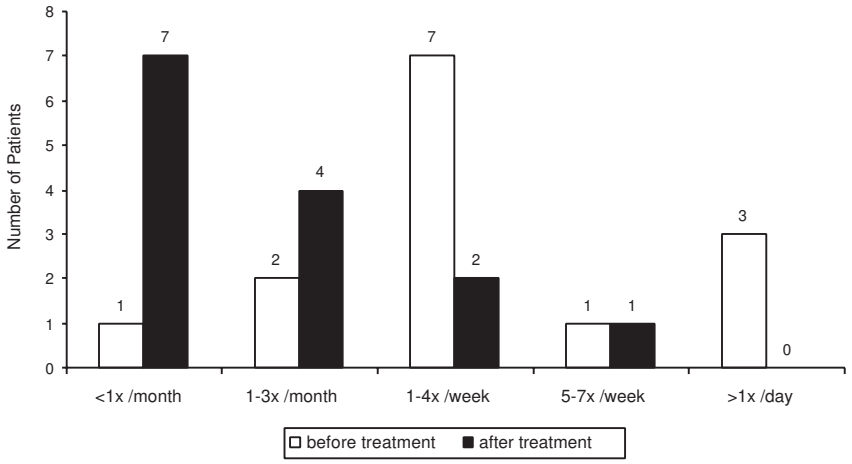

Figure 1 **Masturbation With Paraphilic Fantasies Before and After Selective Serotonin Reuptake Inhibitors Treatment (n = 16)**

ferences in treatment outcome were found for different SSRIs (Greenberg et al., 1996 compared fluoxetine, fluvoxamine and sertraline). According to Stein et al. (1992), SSRIs are helpful only in patients with sexual compulsive symptoms; according to Kafka and Prentky (1992), patients with comorbid affective symptoms experienced greater benefit. However, it should be stressed that these studies often relied on rather small samples, short follow-up periods (generally 12 weeks), and they were not placebo-controlled or double-blind. Rösler and Witztum (2000) warn about overestimating the effect of SSRIs in paraphilic patients and sex offenders and recommend more randomized studies.

In an open, uncontrolled, retrospective study at our department (preliminary data, Strohm & Berner, 2001), 16 male outpatients (mean age 49 years, range 30 years to 70 years) were treated for different paraphilias (8 pedophilia, 4 sadomasochism, 3 exhibitionism, 2 fetishism, and 1 paraphilia-related disorder). These patients suffered from high rates of comorbid psychiatric disorders (8 substance abuse or dependency, 8 personality disorders, 5 depression, 2 psychosis, 2 mental retardation, 1 obsessive-compulsive disorder). Mean treatment duration was 23 months (range 2 to 78). Besides the SSRIs (9 patients with fluoxetine, 4 citalopram, 2 sertraline, 1 paroxetine), all patients received—supportive or more intensive—psychotherapy. There was a marked reduction in paraphilic fantasies and masturbation (see Figure 1).

Despite high rates of sexual dysfunctions as side effects (11 patients with reduced desire, 6 erectile dysfunction, 6 retarded ejaculation or orgasm), most patients reported high overall treatment satisfaction (7 patients very high, 4 high, 3 moderate).

Under SSRIs, first improvements of paraphilic symptoms are generally seen after 2 to 4 weeks (maximum after 2 or 3 months). The dosages are the same as for depressive disorders; only in some patients it is necessary to increase the dosage to those used in obsessive-compulsive disorders. If retardation of ejaculation or orgasm leads to increased recruitment of paraphilic fantasies to reach orgasm, the dosage should be individually titrated, smaller doses are often sufficient to reduce paraphilic symptoms. The side effects of SSRIs in paraphilic patients are the same as in other indications (restlessness, anxiety, decreased sleep, drowsiness, nausea, decreased appetite, hepatocellular damage, very rarely hyponatremia with the syndrome of inappropriate secretion of antidiuretic hormone/SIADH) and are often only transient. Monitoring includes blood tests for liver and renal function, electrolytes, blood cell count, as well as blood pressure and a pretreatment electrocardiography (ECG).

ANTIHORMONAL SUBSTANCES (CPA, MPA, AND LHRH- OR GnRH AGONISTS)

Androgens (testosterone and dihydrotestosterone) play a crucial role in the hormonal regulation of male sexuality (for an overview, see Rubinow & Schmidt, 1996). The behavioral effects of testosterone and dihydrotestosterone are mediated through androgen receptors, which are widely but selectively distributed throughout the brain (i.e., in the septal region, the pituitary, and the hypothalamus) (Bradford, 2001; Rubinow & Schmidt, 1996). Testosterone also influences erection and ejaculation (Bradford, 2001), and, vice versa, sexual activity seems to increase testosterone levels (Jannini et al., 1999). Androgens appear to regulate the action of a wide range of neurotransmitters. Testosterone enhances the sensitivity of dopaminergic receptors, and (in animal studies) modulates 5-HT_{1A} and 5-HT_{1B} receptor effects on impulsive aggression (Simon, Cologer-Clifford, Lu, McKenna, & Hu, 1998).

The role of testosterone in human aggression is less clear (overview in Volavka, 1995). Male prisoners with a history of violent crime during adolescence (Kreuz & Rose, 1972) or chronic violent behavior (Ehrenkranz, Bliss, & Sheard, 1974) had higher testosterone levels than prisoners convicted for nonviolent crimes. High free testosterone levels in the cerebrospinal fluid (CSF) discriminated violent from nonviolent alcoholic offenders (Virkkunen, Rawlings, et al., 1994). Research on aggression in rhesus monkeys has distinguished the following two types of offensive aggression: impulsive aggression, resulting from loss of impulse control and associated with low CSF 5-HIAA (5-hydroxyindoleacetic acid) concentrations, and assertive, competitive (and less violent) aggression, associated with high levels of CSF free testosterone (Higley et al., 1996). However, most correlative studies of androgens and aggression are characterized by their inconsistency and wide variations in subject characteristics, sample size, hormonal measures (e.g., total vs. free levels, plasma vs. CSF), and aggression

measures used (Archer, 1991; Rubinow & Schmidt, 1996). In paraphilic patients and sex offenders, testosterone levels are generally within the normal range for adults (Rösler & Witztum, 1998, 2000; Seim & Dwyer, 1988).

Surgical castration has been shown to substantially reduce recidivism rates of sex offenders (Hansen, 1991; Langelüddeke, 1963; Stürup, 1972, Wille, & Beier, 1989). Because surgical castration is irreversible and poses many ethical problems, it has been restricted to severe, treatment-resistant single cases, after the introduction of pharmacological antihormonal treatment with CPA and MPA in the 1970s. First positive outcomes under CPA were reported by Laschet and Laschet (1971). Since then, a number of studies on the use of CPA or MPA have been published (overview in Gijs & Gooren, 1996). In controlled, double-blind studies, a reduction of sexual desire, arousability, and behavior in paraphilic patients and sex offenders has been demonstrated (Bradford & Pawlak, 1993). CPA (which is not officially approved in the United States) antagonizes the biological effects of testosterone mainly through a competitive inhibition at androgen receptors. A number of side effects such as gynaecomastia, weakness, weight gain, thromboembolism, depression, and hepatocellular damage limit its use (Gijs & Gooren, 1996). MPA is a potent progestational agent with a dose-dependent inhibition of gonadotropin secretion reducing testosterone production in the testes. However, in Germany, MPA is not used in paraphilias. Dosages for CPA range from 50 to 200 mg/d p.o. or 300 to 600 mg i.m. every 10 to 14 days. Possible side effects include weight gain, malaise, nightmares, headaches, muscular cramps, dyspepsia, gallstones, and diabetes mellitus (Gijs & Gooren, 1996). In Table 1, the side effects, contraindications, and monitoring of CPA treatment are listed and compared to those of LHRH agonists.

LHRH is a decapeptid that is synthesized by a loose network of cells in the basal forebrain (within the hypothalamus) and is secreted directly into the hypophysioportal circulation. The secretion is pulsatile and stimulates the release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the pituitary, which drives the production of testosterone in the testes (Conn & Crowley, 1991). LHRH neurons project also to extra-pituitary sites, such as the olfactory bulb and amygdala, where the hormone may act as a neuromodulator (Rösler & Witztum, 2000). The continuous (in contrast to the physiologically pulsatile) application of long-acting LHRH agonists suppresses reversibly the pituitary-gonadal axis by a down regulation of the gonadotrophic cells. Secretion of LH and FSH is inhibited, testosterone and dihydrotestosterone drop to castration levels. Synthetic LHRH agonists (leuprolide, nafarelin, goserilin and triptorelin) have an enhanced potency relative to the native LHRH (Rösler & Witztum, 2000).

After the injection of short-acting LHRH, pedophilic patients show a greater increase in LH but not in FSH (Bain et al., 1988; Gaffney & Berlin, 1984). These findings support the hypothesis of disorders in hormone regulation in pedophilia, such as endocrine changes in pre- or neonatal life imprinted into the hypothala-

TABLE 1
TREATMENT PROTOCOL FOR
CYPROTERONE ACETAT UND LHRH AGONISTS

Item	*Cyproterone Acetate*	*LHRH Agonists*
Side effects	Changes in blood pressure, ischaemia, deterioration of cardiac diseases	
	Thromboembolism	
	Osteoporosis (possibly increased risk under LHRH agonists)	
	Hypogonadism	
	Gynaecomastia (possibly increased risk under CPA)	
	Hot flashes, cold sweats	
	Weight gain	
	Changes in blood glucose levels	
	Anaemia	
	Dry skin, hair loss	
	Depressive moods	
	Fatigue, headaches, sleep disturbances	
	Nausea, vomiting, constipation	
	Hepatocellular damage (↑ liver-enzymes)	Temporary renal dysfunction Pituitary failure
Contraindications	Allergy against the drugs	
	Active pituitary pathology	
	History of thromboembolism	
	Severe liver dysfunction, liver tumors	Osteoporosis
Pretreatment assessment	FSH, LH, testosterone, prolactin	
	Serum calcium, phosphate	
	Blood glucose, liver-enzymes (AST, ALT, GGT)	
	Urea nitrogen and blood creatinine	
	Blood cell count	
	Body weight, blood pressure, ECG	
	Bone density scan	
Monitoring during treatment	Testosterone, liver-enzymes (CPA), urea nitrogen and blood creatinine (LHRH agonists), and blood cell count monthly for the first 4 months, then every 6 months	
	LH, FSH, blood glucose, calcium, phosphate, body weight, and blood pressure every 6 months	
	(If suspected osteoporosis: bone density scan)	Bone-density scan every year

NOTE: LHRH = luteinizing hormone-releasing hormone agonists. CPA = cyproterone acetate. AST = aspartate amino-transferate. ALT = alanine amino-transferate . GGT = gamma-glutamyl transferate. ECG = electrocardiography. LH = luteinizing hormone. FSH = follicle-stimulating hormone.

mus or other hormone sensitive areas, decreased hormone catabolism, or increased end-organ sensitivity (Bain et al., 1988).

Long-acting LHRH agonists are widely used in the treatment of prostate cancer (Conn & Crowley, 1991). As treatment for paraphilic patients and sex offenders, LHRH agonists received much attention after the publication of Rösler and Witztum in the *New England Journal of Medicine* (1998; for further clinical studies, see Krueger & Kaplan, 2001; Thibaut, Cordier, & Kuhn, 1993; for a systematic review, see Briken, Hill, & Berner, 2003). They treated 30 "treatment-resistant" paraphilic outpatients in an uncontrolled, observational study with monthly intramuscular injections of 3.75 mg of triptorelin and supportive psychotherapy for 8 to 42 months. Of these, 16 had previously been convicted for sex crimes; and 22 persons had other psychiatric disorders (i.e., 9 personality disorder, 5 schizophrenia in remission) and were receiving other psychotropic medications if necessary. Nine men had previously been treated with CPA without sufficient effect (CPA treatment was stopped 12 months before triptorelin administration). Seven patients had also received SSRIs (serotonergic drug treatment was stopped 2 months before triptorelin administration). No sexual offences were committed during triptorelin therapy. The severity of the paraphilia measured by self-reports and testosterone levels decreased significantly. Six men stopped treatment after 8 to 10 months. Two of these stopped treatment because of side effects and thereafter received CPA (200 mg per day). Both were subsequently prosecuted for sexual offences and sentenced to prison. In 11 of 18 men, the bone mineral density decreased significantly, most men had transient pain at the sites of injection. Other side effects were hypogonadism, hot flashes, decreased growth of facial and body hair, asthenia, and muscle tenderness. In addition, 21 men reported erectile failure. This was proportional to age and found in all men older than 35 years. In a recent article, Rösler and Witztum (2000) reported about the concomitant administration of small doses of testosterone (25 to 50 mg testosterone enanthate per month) to prevent bone mineral loss and to ameliorate the erectile dysfunction, whereas paraphilic fantasies should remain suppressed.

In a less known article, Hansen and Lykke-Olesen (1997) reported about their work in a closed institution for offenders in need of psychiatric treatment. Since 1989, they treated recidivistic dangerous sex offenders with a combination of triptorelin and CPA (both administered by depot; doses were not reported). They used the combination with CPA to block the androgen receptors, thus ensuring against illegal procurement of anabolic steroids. Of the 30 men who started treatment, 7 gave up (1 death due to coronary occlusion, but no relation to medication was found; 2 men had hepatitis C; 4 men did not accept hormonal treatment as a longtime perspective). The other 23 persons were treated with pharmacotherapy and psychotherapy: 5 were still in prison, but with freedom-related privileges; 12 had been released on probation but were still undergoing treatment; and 5 were released on probation with a limited period of supervision and stopped treatment thereafter. Of these 5, 1 relapsed 9 months later. Among the offenders under

triptorelin plus CPA, there had been no relapse. All patients showed dissocial personality structures, and a number of them reported sadistic sexual fantasies. When the latter disappeared in the course of treatment, the patients were able to talk about the fantasies. The majority stated that the effects were positive and they felt more relaxed. Side effects were increased weight and perspiration, individual cases of gynaecomastia, and a single case of temporary urine incontinence.

In our research group (Briken, 2002; Briken, Nika, & Berner, 2001), we treated 11 patients with long-lasting deviant sexual behavior (pedophilia, sadism, sexual impulsiveness) that already had caused legal consequences. The most common comorbid diagnoses were personality disorders and mental retardation. Of these, 6 patients had already received CPA without sufficient improvement on deviant fantasies or suffering from intolerable side effects. All subjects received a 3-month subcutaneous depot of 11.25 mg leuprolide. For the first 2 weeks, we additionally administered CPA (300 mg) to reduce the so-called flare up effect (a transient increase of testosterone at the beginning of treatment with LHRH agonists). Length of follow-up was 1 year. All patients reported a reduction in paraphilic activities, and no sexual offences were committed during therapy. Side effects were depression, weight gain, and pain at the site of the injection. There was also a reduced frequency of erection, ejaculation, and masturbation.

LHRH agonists are not officially approved for the treatment of paraphilic patients in Germany. However, in a survey of German forensic hospitals, we found that 12% of the sex offenders (47% for child abuse, 31% for rape, 7% for homicide and attempted homicide) received either CPA (n = 29) or LHRH agonists (n = 29) (Czerny, Briken, & Berner, 2002). Their diagnoses included pedophilia, sadomasochism, exhibitionism, fetishism, and voyeurism. Mean duration of treatment with CPA was 22.6 months and with LHRH agonists, 10.3 months. In only 19 of 29 patients treated with LHRH agonists was information about treatment response available. According to the psychiatrists' judgment, there were only small differences between CPA (more reduction of sexual activity) and LHRH (more reduction of fantasies) in efficacy. No effect was reported in 3 cases of each group (CPA: 10%; LHRH: 17%). An increase of sexual fantasies was reported in 1 case on CPA. Two patients had previously been treated with CPA without success. After switching to the LHRH agonists, the intensity of sexual desire and symptoms was noticeably reduced. Probably the most severe side effect under CPA was a case of thromboembolism. Allergic reactions, osteoporosis, cardiovascular side effects, or hepatocellular damages were not reported.

Comparisons of leuprolide acetate with medroxyprogesterone acetate or cyproterone acetate suggest that there may be fewer side effects, including less risk of hepatitis, thromboembolism, and gynaecomastia (Grasswick & Bradford, 2002). In general, LHRH agonists as well as CPA (and MPA) result in a marked reduction of overall sexuality (desire, erection, ejaculation, and orgasm), however in CPA and MPA, these sexual dysfunctions may be dose related. Reilly, Delva, and Hudson (2000) proposed protocols for the use of LHRH agonists in the treatment of paraphilias to avoid serious side effects before they have an affect on

patients' health. Integrating Reilly's recommendations and results from the literature, we compared the side effects, contraindications, and necessary monitoring of CPA and LHRH agonists (see Table 1). Administration must always include informed consent. Because osteoporosis is a long-term risk, especially in LHRH agonists, a baseline bone-density scan should be performed prior to treatment and every year thereafter. Osteoporosis may possibly be prevented by administration of calcium and vitamin D or biphosphonates. As noted above, Rösler and Witztum (2000) prescribed small doses of testosterone (25 to 50 mg testosterone enanthate per month) to prevent bone mineral loss and to ameliorate the erectile dysfunction under LHRH agonists.

ALGORITHM FOR PHARMACOTHERAPY OF PARAPHILIAS

How can these different and partially preliminary findings be integrated into practical guidelines for psychopharmacological treatment of paraphilias? Although the scientific database is still insufficient, attempts have been made to formulate a therapeutic algorithm for these disorders. Bradford (2000, 2001) proposed a scheme with six levels according to the severity and criminological risk factors of paraphilias: starting with exclusive psychotherapy or relapse prevention programs, followed by SSRI alone, or in combination with low doses of CPA, then progressing to strong reduction of testosterone levels by oral or intramuscular (if unreliable compliance) application of CPA, and eventually to a complete reduction of testosterone to castration levels by parenteral CPA or LHRH agonists.

Incorporating this stepwise scheme, we have formulated a more flexible algorithm considering comorbid symptoms (see Figure 2).

A treatment program should start with supportive or intensive (cognitive behavioral or psychodynamic) psychotherapy and pharmacological (as well as psychotherapeutic) treatment of comorbid disorders if needed (e.g., neuroleptic treatment in schizophrenic patients, carbamazepine for borderline personality disorders, and so forth).

In mild cases with strong deviant fantasies or impulses and any risk for sexual offences, psychotherapy in combination with SSRI treatment should be considered, especially if the paraphilia is less severe (no hands-on offences, fetishism, exhibitionism), and if the paraphilic patient shows additional symptoms such as anxiety, social phobia, depression, severe feelings of guilt, obsessions, and compulsions because these belong to the well-established target symptoms for SSRI treatment. Using SSRIs as a first step in pharmacological treatment for these patients is justifiable because these substances have been proved effective in some of these patients but carry much less severe side effects and do not reduce overall sexuality as much as antihormonal medications. Therefore, SSRIs are generally well tolerated by the patients even on a long-term basis. SSRI treatment should be attempted with at least one, but usually two different agents (Kafka, 2000). The

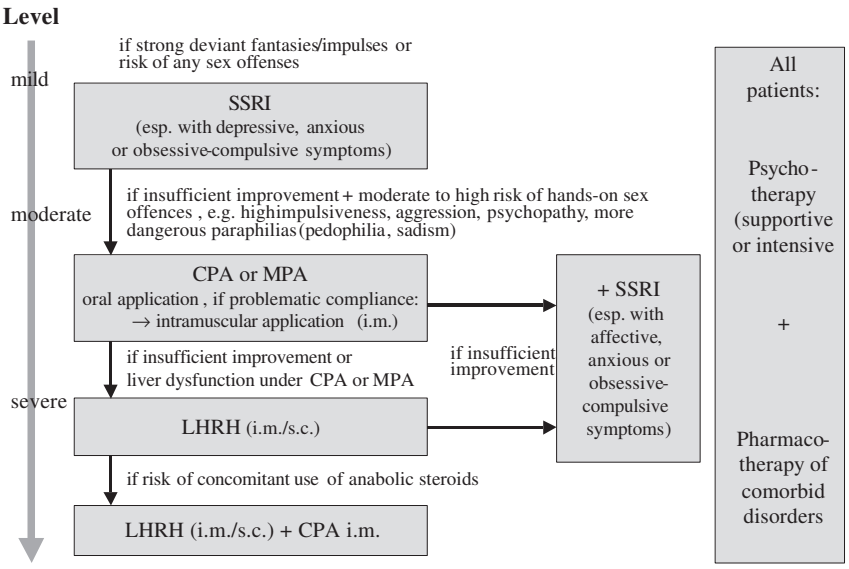

Figure 2 Algorithm for the Pharmacological Treatment of Paraphilias
NOTE: LHRH = luteinizing hormone-releasing hormone agonists. CPA = cyproterone acetate. SSRI = selective serotonin reuptake inhibitors. MPA = medroxyprogesterone acetate.

dosage might be reduced, if delayed orgasm and ejaculation results in an increased use of paraphilic fantasies.

If there is an insufficient improvement and a moderate to high risk for hands-on offenses, especially in more impulsive, aggressive, and psychopathic patients or more dangerous paraphilias such as pedophila and sadism, CPA or MPA should be given. For risk assessment, established instruments should be used (e.g., the Psychopathy Checklist-Revised [Hare, 1991], the SVR-20 [Boer, Hart, Kropp, & Webster, 1997], or the Static-99 [Hanson & Thornton, 2000]). Side effects are dose related so that a careful titration could minimize them and may allow patients to maintain appropriate sexual behavior while eliminating deviant behavior. Taking into account the yet relatively small database and short clinical experience with LHRH agonists in paraphilic patients, as well as the lack of an official approval for these indications by the health authorities, CPA treatment (or MPA in the United States) should still be considered the first line of antihormonal medication. Intramuscular application of CPA should be used especially in cases with unreliable compliance in medication.

Although the number of studies is still small, LHRH agonists seem to be effective in some cases in which CPA and SSRIs failed and can offer an alternative for patients with liver dysfunctions under CPA or for whom preexistent hepatocellular damage is seen as contraindication for CPA treatment. The combination of an antihormonal agent with an SSRI should be considered in patients

with insufficient improvement under CPA, MPA, or a LHRH agonist alone, especially in patients with depressive, anxiety, obsessive-compulsive symptoms.

A caveat must be expressed for cases with severe psychopathy and antisocial personality disorders with unreliable treatment compliance. In such cases, counteracting against the antihormonal treatment may result in secret self-application of testosterone to neutralize the effect of the medication. Even if controlled by regular blood tests, this form of noncompliance may still remain an important contraindication for antihormonal treatment. A combination of LHRH agonists and CPA could be a possible option for these patients (Hansen & Lykke-Olesen, 1997). To prevent or manage osteoporosis under LHRH agonists, the application of calcium and vitamin D or biphosphonates has been recommended as well as concomitant small doses of testosterone, the latter might also prevent or ameliorate erectile dysfunction.

Of course, these preliminary recommendations have to be modified according to further clinical experience and scientific progress. There is an urgent need for further research with prospective, controlled studies using large sample sizes and better methods (especially penile plethysmography) to investigate the use of SSRIs, CPA, MPA, and LHRH agonists. For practical and ethical reasons, such more rigorous and sophisticated study designs, however, are often difficult to realize in populations with forensically relevant disorders.

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