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# Disorders of Sexual Impulse Control in Neuropsychiatric Conditions

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**This article reviews hypersexuality in individuals with neuropsychiatric disorders and its psychopharmacologic treatment. A brief review of the neurology, neuroendocrinology, and neuropharmacology of sexual behavior is presented. Literature describing the occurrence and treatment of hypersexuality in individuals with neuropsychiatric disorders is reviewed along with literature which discusses the pharmacologic treatment of individuals with hypersexual disorders in nonneuropsychiatric populations. Finally, a clinical algorhithm for approaching and treating such disorders in a neuropsychiatric population is presented.**


Recently, there has been renewed interest in hypersexuality and in paraphilic and nonparaphilic sexual behaviors.[1-3] In a recent review of the subject Stein et al[2] propose a new category of "hypersexual disorder" which would supplement the current Diagnostic and Statistical Manual, Fourth Edition (DSM-IV) diagnostic entities of paraphilias.[4] They define "hypersexual disorder" as consisting of "recurrent, intense, sexually arousing fantasies, sexual urges, or behaviors that persist over a period of at least 6 months, and do not fall under the definition of paraphilia." As with the paraphilias, these fantasies, urges and behaviors to be diagnosed would have to cause clinically significant distress or impairment in social, occupational, or other important areas of functioning and would not be accounted for by another axis I disorder, such as a manic episode, or be attributable to a direct physiologic effect of a substance or a general medical condition. For cases in which there is an apparent neuropsychiatric or medical condition which causes such hypersexual behavior the suggestion is made that there also be a category of paraphilia or of hypersexual disorder considered to be secondary to a general medical disorder or to substance abuse.[1] Within the current DSM-IV[4] nosology, hypersexual behavior related to a neuropsychiatric condition would fall under the specific paraphilia which the individual might be involved in, or would be considered as a sexual disorder not otherwise specified or as an impulse control disorder not otherwise specified. However, it seems as though the suggestion of Stein et al[1] would be a useful addition to the DSM-IV terminology in identifying and studying these disorders.

This report will briefly present elements of what is known regarding the relevant neuroendocrinology, neuroanatomy, and neuropharmacology of normal sexual functioning and hypersexuality, a review of descriptions of sexual impulse disorders or paraphilias related to neurologic disease or injury with a description of treatment where available, a succinct review of pharmacologic treatments for individuals with hypersexual or paraphilic disorders without apparent additional neuropsychiatric conditions, and suggest an algorithm for the evaluation and treatment of neuropsychiatric patients with such hypersexual or paraphilic disorders.

## Neuroendocrinology, Neuroanatomy, and Neuropharmacology of Sexual Behavior

### *Neuroendocrinology of Sexual Behavior*

Sexual behavior is a highly complex behavior involving the central and peripheral nervous system, as well as the endocrine system; the central nervous system modulates the endocrine system through the hypothalamus and pituitary; and the endocrine system in turn modulates the central nervous system. There is a vast literature exploring the neuroendocrinology of animal models of sexual behavior.[5-7] Generally speaking, the lower phylogenetically an animal is the more its sexual behavior is directly controlled by gonadal hormones; the higher phylogenetically it is the more its sexual behavior is under cortical control. Testosterone is essential for copulatory behavior in male rodents and primates.[5] Sexual behavior in

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the female rodent is completely dependent on the presence of estrogen; in female primates arousal and proceptive behavior are dependent on steroids, but not copulatory behavior.[5] Castration of adult male primates results in a gradual decline in mounting and ejaculation.[5] Reports on the sexual behavior of castrated sex offenders in Germany[8,9] found a marked decrease in sexual functioning and activity in individuals studied over time. In human males, testosterone is metabolized to dihydrotestosterone and this appears to be the most important androgen in determining male sexual behavior.[10] Other evidence suggests that other substances, such as estrogen, prolactin, and endogenous opiate peptides may modulate sexual desire and arousal in men.[11] The role of reproductive hormones in mediating sexual behavior in healthy adult females remains unclear.[12] A recent study[13] showed an increase in arousal in sexually functional women after sublingual testosterone, but the influence of naturally occurring levels of testosterone in women is not clear.

### *Neuroanatomy of Sexual Behavior*

Fig 1 gives an overview of neural structures and endocrine factors which influence sexual function in the human. Sexual functioning involves coordinated activity of the motor, sensory, cortical, limbic, and peripheral nervous system structures as well as endocrinologic factors. Many environmental and other factors also affect sexual functioning, as the figure suggests.

A substantial literature exists which presents information on the neuroanatomy of sexual behavior in other species. In rodents, the medial preoptic area, ventral tegmentum area, nucleus accumbens, olfactory bulb, amygdala, and medial forebrain bundle have been implicated in the control of male sexual behavior[5] and the ventromedical nucleus, midbrain central gray area, preoptic area, and septal area in the control of female sexual behavior.[5] Using lithium to chronically induce limbic seizures in rats Persinger[14] showed persistent hypersexuality. Blumer et al[15] in a review suggest that in virtually all species studied, evidence supports the hypothalamus in the expression of sexual behavior, with implants of estrogen or testosterone or electrical stimulation in the preoptic hypothalamic region eliciting a copulatory response, and with lesions in this region resulting in a decrease or elimination of sexual behavior not restored by exogenous hormone treatment.

In primates, the classic studies of Kluver et al[16] implicate the temporal lobes as being important in the control of sexual behavior. In those studies temporal lobectomy resulted in a constellation of symptoms with hypersexuality being prominent. Hypersexuality has been described in Rhesus monkeys and cats after removal of both temporal lobes, the amygdala, and overlying piriform cortex, or after small lesions in the piriform cortex.[15] For humans, Stein et al[1] in their review of the case literature suggest that frontal lesions may be accompanied by disinhibition, with, in particular, impulsive hypersexual responses to external cues; striatal lesions may be related to repetitive triggering of internally generated response patterns; and temporal-limbic lesions may be accompanied by disturbances in sexual appetite and, in particular, a change in the direction of the sexual drive.

Stoleru et al[17] reported on a study involving single photon emission computed tomography in eight healthy right-handed heterosexual men examined during orgasm and reported that cerebral blood flow was decreased during orgasm in all cortical areas except the right prefrontal cortex, where cerebral blood flow increased significantly. A recent positron emission tomography study[18]

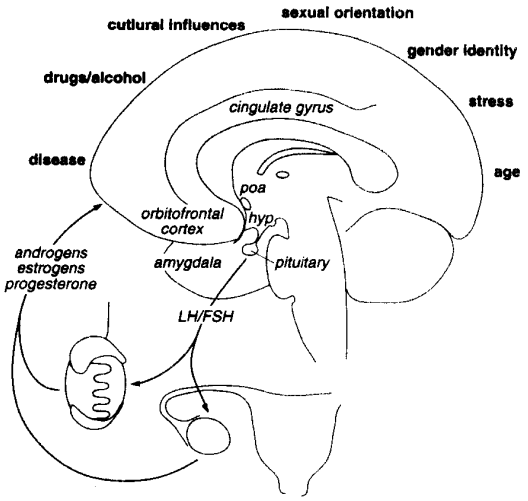


**Figure 1.** Factors which influence human sexuality and neural structures that subserve sexual activity. Abbreviations: LH, luteinizing hormone; FSH, follicle-stimulating hormone; hyp, hypothalamus; poa, preoptic area. (Reprinted with permission from Charney DS, Nestler EJ, Benney BS: Neurobiology of Mental Illness. New York, Oxford University Press, 1999.[79]

of eight male subjects presented with visual sexual stimuli and monitored phalometrically showed a threefold pattern of activation, with bilateral activation of the inferior temporal cortex, a visual association area; the activation of two paralimbic areas, the right insula and right inferior frontal cortex, and activation of the left anterior cingulate cortex, a paralimbic area involved in the control of autonomic and neuroendocrine functions.

### *Neuropharmacology of Sexual Behavior*

The peripheral and autonomic sympathetic and parasympathetic nervous system all innervate the testes, prostrate, seminal vesicles, and vas deferens, as well the uterine and pelvic area and are involved in sexual excitation and orgasm.[35]

Numerous neurotransmitters have been implicated in animal models of sexual behavior including dopamine, noradrenalin, 5-hydroxytryptamine, acetylcholine, gamma-amino-buteric acid, endogenous opioids, prolactin, oxytocin, arg-vasopressin, angiotensin II, gonadotrophin-releasing hormone, substance P, neuropeptide Y, cholecystokinin-8, prostaglandins, corticotrophin-releasing hormone, and corticosterone.[5,20] Many drugs, both medicinal and associated with abuse, have been implicated in the modulation of sexual desire and functioning.[21] Antipsychotic drugs have usually been associated with decreased libido and erectile dysfunction.[12] Amphetamines and L-dopa have been associated with hypersexuality and aggression.[22]

In sum, sexual behavior appears to require adequate amounts of testosterone in the male; the determinates of female sexual behavior are more unclear, with evidence suggesting that testosterone may play a role; the limbic, septal, frontal, and temporal areas are all involved in sexual behavior, which also in higher mammals is under greater cortical control. Many substances have been shown to have some effect on sexual behavior both in animal models or in humans. Many drugs and substances of abuse may have some impact on sexuality, either through a central mechanism of action, or peripherally.

## Neuropsychiatric Syndromes Associated With Hypersexual Behavior or Paraphilias and Their Treatment

### *Dementia*

Dementia of one cause or another has been associated with hypersexual behavior. Cooper[23] reported on four institutionalized male patients with mild to moderate dementia who manifested public masturbation and attempts to molest female patients. He reported that medroxyprogesterone acetate had an excellent effect on reducing deviant behavior and was used without adverse effects. Leo et al[24] reported on the successful use of clomipramine to treat exhibitionism and public masturbation and repetitive sexualized touching of female staff in two elderly men with dementia. Stewart et al[25] reported on the successful use of paroxetine to treat a patient with alcoholic dementia and sexual disinhibiton.

Huntington's disease has been found to be mostly associated with hypoactive sexual disorder, but has also been associated with increased sexual interest and with paraphilias.[26,27] Rich et al[28] described the successful use of leuprolide acetate, a gonadotropin-releasing hormone agonist, to eliminate exhibitionism in one patient with Huntington's disease. Janati[29] reported on the occurrence of the Kluver-Bucy syndrome in a patient with Huntington's Chorea with hypersexual behavior with successful treatment with high dose, but not low dose, haloperidol.

### *Kluver-Bucy Syndrome*

Friedman et al[30] reported on the development of sexually flavored conversation in a 50-year-old man with an acute nectrotizing encephalitis which involved the limbic system. Terzian et al[31] reported on the development of hypersexuality and Kluver-Bucy syndrome in a 19-year-old man with bilateral removal of the temporal lobes and epilepsy. Stewart,[32] reviewing such case reports of Kluver-Bucy in humans, decided to use carbamazepine to treat inappropriate sexual verbalizations and rage attacks in a 20-year-old man who had sustained frontal and temporal encephalomalacia as the result of a head injury; this was successful in treating both. Lilly et al[33] reported on 12 patients with Kluver-Bucy syndrome which followed head trauma, Alzheimer's disease, Pick's disease, and herpes encephalitis. This syndrome was noted to be transient after head trauma, but persistent in postencephalitc syndromes; aphasia, amnesia or dementia were associated findings. Treatment was not discussed.

### *Brain Injury*

Sexual dysfunction is a common sequalae of traumatic brain injury.[19] Sabhesan et al[34] reported on the development of sexual dysfunction in 34 brain-injured patients, finding mostly decreased,

but some increased interest in sex, with the use of lewd language, frotteurism, exhibitionism, sadism, and rape being sequalae. Given the vulnerability of subfrontal and temporal cortex to traumatic injury[35] one might expect a relatively high incidence of Kluver-Bucy syndrome in this population. Gerstenbrand et al[36] reported on 40 patients with severe brain injury, 30 of whom developed a complete or partial Kluver-Bucy syndrome, which included hypersexuality, during recovery. At 1 year of follow-up no persisting "complete" Kluver-Bucy syndromes were observed. Stein et al[1] described the case of a 24-year-old man who developed symptoms of hypersexuality related to head trauma, with aggressive outbursts, inappropriate sexual remarks, and, on, many occasions, attempts to kiss, touch or hug staff members. A behavioral modification program and valproate had only minimal effect.

### *Patients Receiving L-Dopa Treatment for Parkinsonism*

Bowers et al[37] reported on 19 patients who were receiving L-dopa for Parkinson's Disease; seven reported increased sexual behavior at some time in their therapy; three patterns that emerged included increased sexuality as a part of general overall improvement in functioning, a specific increase in sexual drive, and an apparent disinhibition of sexual impulses. Brown et al[38] studied seven men with Parkinson's disease treated with L-dopa and found approximately one-half reported increased sexual interest not related to an increase in locomotion. Uitti et al[39] reported on 13 Parkinsonian patients, 11 men and 2 women, selected from a large clinical population at two parkinsonism clinics. Two patients developed hypersexuality after bilateral thalamotomy; all developed increased sexuality while on drug treatment. A reduction in dosage of L-dopa described in some of these cases resulted in an improvement of the hypersexuality.

### *Epilepsy*

Blumer et al[40] reported that of 11 patients with temporal lobe epilepsy who were hyposexual and were treated with unilateral temporal lobectomy a transient or permanent postoperative increase of sexual responsiveness occurred in seven of these; this improvement was related to the improvement of seizures. Shukla et al[41] reported on 70 cases of temporal lobe epilepsy and grand mal epilepsy who were studied for their sexual functioning, and found only one case of hypersexuality in this group. Demerdash et al[42] examined a sample of 700 female epileptic outpatients and found an incidence of 18% of psychosexual disorders and of 5% of paraphilias. Exhibitionism was said to be the most common paraphilia; this was further characterized as taking the form of disrobement or exposure of the breast or genitalia in the immediate postictal period. Saunders et al[43] reported on 100 noninstitutionalized male epileptics, 33 of whom had temporal lobe epilepsy; one of these had evidence of sexual deviation or hypersexuality. Epstein et al[44] reported on five cases of fetishism and transvestitism related to temporal lobe dysfunction. Erickson[45] reported on a case of nymphomania in a woman coincident with a neoplasm around the topical projection of the genital structures of the right paracentral lobule. Operative removal of the neoplasm resulted in a cessation of hypersexual behavior. Goldberg et al[46] reported on the case of a 34-year-old man with complex partial seizures and several paraphilias (pedophilia, voyeurism, scatologia, and hypersexuality) all of which responded to treatment with carbamazepine, after unsuccessful trials of dilantin and phenobarbital. Hunter et al[47] reported on the occurrence of temporal lobe epilepsy supervening on longstanding transvestism and fetishism which, after failing to respond to medication, responded to a temporal lobectomy with resolution of the seizure disorder and of the paraphilias. Remillard et al[48] reported on 12 women with temporal lobe epilepsy who reported sexual arousal or orgasm as part of their epileptic seizures and reviewed the literature on 11 similar women. Hypersexual behavior was a feature in some of these; three responded to surgical treatment.

### *Tourette's Syndrome*

Eldridge et al[49] reported that out of a sample of 15 patients with Tourette's, three had a history of sexual exposure and five had a history of touching or having the urge to touch their own or other's genitals. Nee et al[50] described 50 patients with Tourette's syndrome and characterized 16 as having engaged in inappropriate sexual activity. Comings[51] summarized his study of individuals with Tourette's syndrome and noted that sexual touching was one symptom and suggested that this was one aspect of limbic system disinhibition in this disorder. Comings et al[52] reported on a case of familial exhibitionism in this disorder which was suc-

cessfully treated with haloperidol. McDougle et al[53] also used haloperidol to successfully treat both the characteristic tics of Tourette's disorder and multiple associated sexual paraphilias; all of these behaviors returned when the haloperidol was discontinued. Kerbeshian et al[54] were able to use fluoxetine to treat a young man with Tourette's and compulsive masturbation involving fantasies of homosexual behavior associated with guilt.

### *Other Entities Associated With Hypersexuality*

A variety of other neurologic disorders can be associated with hypersexuality. Langworthy et al[55] in an early series reported that overt sexual activity in cases of "disseminated sclerosis" (presumably multiple sclerosis) was problematic; no treatment was discussed. Huws et al[56] described progressive hypersexuality and a foot fetish in a 26-year-old man with multiple sclerosis which relentlessly progressed despite counseling, behavioral therapy, cyproterone acetate, neuroleptics, and carbamazepine and resulted in the patient's containment in a maximum security hospital.

Gorman et al[57] presented two cases of markedly increased sexual behavior related to septal damage sustained in the course of placement of ventriculoperitoneal shunts, suggesting that the brain circuit involving septal nuclei has a role in the sexual behavior. Heath[58] reported on in-depth electroencephalograms during orgasms in two patients which showed activity in the septal region.

Miller et al[59] described the occurrence of disinhibition of sexual activity and hypersexuality in four cases of individuals with medial basal-frontal or diencephalic injury and four cases of patients with altered sexual preference with patients whose injuries involved limbic system structures.

Akil et al[60] reported on sexual preoccupation and reduced sexual inhibitions in six patients with Wilson's disease and summarized findings of others. Anticopper therapy was associated with improvement. Monga et al[61] reported on hypersexuality in three stroke patients, with involvement of the temporal lobe being a common factor in all three cases.

Freeman[62] in an early narrative report of his experience involving some 3,400 patients indicated that frontal lobotomy was followed at least temporarily by an increase in libido and an increased rate of illegitimate pregnancy in women.

Boast et al[63] reported on a case of homosexual erotomania in a patient with AIDS-related complex (ARC) which remitted when his ARC progressed to frank AIDS.

Myers[64] reviewed the literature on the treatment of sexual offenses in individuals with developmental disabilities and discussed a case history of a young man who was successfully treated with medroxyprogesterone acetate.

Kafka et al[65] in a study of 60 men with paraphilias and nonparaphilic sexual impulsivity found that 71% had a mood disorder, 45% had a substance abuse disorder and 40% had a history of childhood attention deficit hyperactivity disorder (ADHD). Kafka[66] reported on his use of psychostimulants or buproprion in 30 patients with paraphilias and paraphila-related disorders if they failed to respond to serotonin-reuptake inhibitors (SRIs) or if they continued with symptoms of depression or ADHD despite treatment with an SRI.

Finally, hypersexual behavior and poor judgment are one of the commonly recognized features of mania.

## Psychopharmacologic Treatment of Paraphilias and Paraphilia-Related Disorders

There are relatively few systematic treatment studies of sexual disorders in individuals with neurologic disease. Thus, we must draw on what is known about treatment in other populations.

There have been several reviews of antiandrogen therapy in the treatment of paraphilias[67,68] and of more comprehensive pharmacologic treatments of the paraphilias.[66,69,70] Medroxyprogesterone acetate and cyproterone acetate (the latter not being available in the United States) have been studied in double-blind fashion and generally have tended to show good effect, although most studies have involved small numbers.[69] Aside from a study by Kruesi et al[71] there have been no organized double-blind studies of anti-depressant agents. In that study Kruesi et al[71] described a double-blind crossover comparison of clomipramine versus desipramine; of 15 subjects enrolled in the protocol only eight completed it and it was concluded that these antidepressants had efficacy compared with placebo. Other studies of antidepressant agents[72-74] have been open clinical trials involving the successful use of sertraline or fluoxetine in individuals with paraphilas or paraphilia-related disorders. One might expect that the selective SRI agents might have

particular efficacy in treating hypersexual behavior for several reasons. First, they are effective for the treatment of obsessive-compulsive disorder, and many of the paraphilias, particularly high-frequency ones such as exhibitionism or frotteurism, have obsessive and compulsive aspects. Second, the well-known side effects of decreased libido and impairment in ejaculation could actually be treatment effects for this population. Finally, depression is a common comorbid condition in individuals with paraphilias. Alleviation of depressive symptoms could conceivably help them to have better control over their sexual impulses. Other studies and case reports have presented information on fluoxetine, clomipramine, fluvoxamine, buspirone, lithium carbonate, and imipramine with efficacy reported for individuals with paraphilias.[69] However, they are all uncontrolled single case reports or small series.

The most recent study to date involving antiandrogens[75] was an uncontrolled observational study which reported on the use of triptorelin (an analogue of gonadotropin-releasing hormone which inhibits pituitary-gonadal functioning and suppresses testosterone) and supportive psychotherapy in 30 men with long-standing paraphilias. This study found a reduction in deviant sexual fantasies and desires from a mean of 48 ± 10 per week before therapy to zero during therapy and a decrease in the number of incidents of abnormal sexual behavior from 5 ± 2 per month to zero while receiving triptorelin. The main side effects were erectile failure, hot flashes, and a decrease in bone mineral density in some men. This study relied on patient's self-report and did not include objective physiologic assessment of sexual interest patterns.

The reasons for the lack of systematic study of pharmacologic agents in this population are numerous. Patient compliance is one factor. Baine et al[76] reported on a sample of 100 men accused of sexual assault of a child who they tried to enroll on a randomized, double-blind trial involving medroxyprogesterone acetate (MPA). A total of 48 men completed the assessment; 18 agreed to participate in a drug trial, but only 11 completed a 3-month course of MPA or placebo therapy. Ethical problems exist in establishing a study where one of the outcome measures could be victimization of a child or another individual. Finally, paraphilic and hypersexual behavior is often egosyntonic and individuals are reluctant to be treated for it unless legal circumstances or other consequences result in motivation for treatment.

## Suggested Algorithm for the Treatment of Disorders of Sexual Impulse Control in Neuropsychiatric Conditions

### *Clinical Assessment*

It is apparent from the above review that disorders of sexual impulse control are common sequalae of many neuropsychiatric conditions. As always, it is important to clearly identify the problematic behaviors. Oftentimes, patients themselves are poor self-observers and reporters and the observations of staff or of family members or significant others must be relied on. An assessment of urgency and dangerousness must be performed to establish adequate protection for the patient as well as the staff or public. One-to-one observation, hospitalization, or removal of an individual from a family where children or others might be possible victims should be considered.

A thorough clinical assessment of the behavior should be initiated. The underlying diagnoses should be confirmed, and any factors which could be causing an exacerbation of hypersexual behavior should be considered. These would involve a consideration of medications that a patient may be receiving, the possibility of substance use or abuse, or the progression of the underlying neurologic condition such as an extension of a brain tumor or the development of elevated intracranial pressure. Appropriate corrective measures should be taken.

### *Treatment*

In some situations, such as with recent brain injury, it may be appropriate to observe and wait, as evidence suggests that hypersexual behavior occurring in this condition may be transient. Patients with epilepsy and associated hypersexual behavior should be treated for their seizure disorder vigorously. Hypersexual behavior in several of the cases of temporal lobe epilepsy noted above responded to anticonvulsant treatment. Some of the newer anticonvulsants may offer better opportunities to treat such disorders. Surgery to correct underlying neurologic problems, such as the removal of a tumor or seizure focus, has been reported to have beneficial effects on the hypersexual behavior, but should be used only as a last resort.

In cases of Tourette's syndrome, haloperidol has proven effective for treating hypersexual or paraphilic behaviors. For such behaviors in patients with dementia paroxetine, clomipramine, medroxyprogesterone acetate and depot-leuprolide have proven effective. In patients with developmental disabilities refractory to behavior therapy, MPA has been found to be useful, although in our experience depot-leuprolide acetate could be considered instead because of its favorable side-effect profile compared with MPA.

Patients receiving L-dopa for Parkinson's disease who become hypersexual should have their medication regimen reviewed with a consideration of a reduction of L-dopa; possibly treatment with an agent more specifically targeting sexual behavior could be effective in lowering hypersexuality.

Copper-lowering treatment has helped treat hypersexual behavior in Wilson's disease.

Reports of current treatment of the paraphilias and/or paraphilia-related disorders would suggest that SRIs or adrenergic antidepressants may be useful, although these have not been directly compared and current studies consist of mostly series of individuals who have been given open treatment. The caveat that individuals with neurologic conditions, like the elderly, can be exquisitely sensitive to the effects and side effects of medication should be observed and appropriate caution exercised.

Finally, antiandrogens could be considered. The severe progestational side effects of MPA which include thromboembolic problems[77] can be avoided by the use of LHRH agonists. If LHRH agonists are used, or, indeed, if any of the medications discussed earlier are used, patients should be informed that such treatment involves an off-label indication for such medicaton. Depot leuprolide acetate and the other LHRH agonists cause a brief flare in levels of testosterone which can be counteracted by the administration of a testosterone antagonist such as flutamide. The process of desensitization of GnRH receptors in the anterior pituitary cells which eventually results in the lowering of lutenizing hormone and follicle-stimulating hormone, and thus testosterone, takes from 1 to 4 weeks, during which time testosterone and dihydrotestosterone are well above normal levels,[78] and we have arbitrarily administered flutamide for 30 days coincident with the initiation of leuprolide acetate to prevent any hypersexuality related to a testosterone flare. A thorough medical evaluation including a baseline assessment for bone density should be performed before the initiation of such therapy, and we have suggested annual bone-density evaluations to monitor for the development of osteoporosis. Leuprolide acetate is available in 1-month and 3-month sustained-release depot forms. The main effects are reduction in serum testosterone, sexual fantasy and behavior; the main side-effects include hot flashes, decreased growth of facial and body hair, gynecomastia, asthenia, and a decrease in bone mineral density. Most of the effects and side effects of the GnRH agaonists are reversible with cessation of the medication; testosterone and sexual functioning were reported to return to normal within 2 months after cessation of GnRH agonists used to treat individuals with paraphilias.[75] However, side effects such as demineralization, osteoporosis, and gynecomastia may be more enduring or permanent. Further study of these agents in this population is clearly warranted.

There are few systematic studies which address the treatment of sexual disorders in individuals with neurologic diseases. The case report and case series literature suggests that it is reasonable to approach these problems using interventions developed for those without brain disorders, although more cautious dosing strategies are warranted.

## References

1. Stein DJ, Hugo F, Oosthuizen P, et al: Neuropsychiatry of hypersexuality. CNS Spectrums 5:36-46, 2000
2. Stein DJ, Black DW, Pienaar W: Sexual disorders not otherwise specified: Compulsive, addictive, or impulsive? CNS Spectrums 5:60-64, 2000
3. Black DW: The epidemiology and phenomenology of compulsive sexual behavior. CNS Spectrums 5:26-72, 2000
4. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders (ed 4). American Psychiatric Association, Washington, DC, 1994
5. Wilson CA: Pharmacological targets for the control of male and female sexual behavior, in Riley AJ, Peet M, and Wilson C (eds): Sexual Pharmacology. Oxford, United Kingdom, Oxford University Press, 1993
6. Ahlenius S: The effect of dopaminergic and serotonergic agents on the lordosis response in female rats, in Riley AJ, Peet M, and Wilson C (eds): Sexual Pharmacology. Oxford, United Kingdom, Oxford University Press, 1993
7. Barfield RJ: Animal models of human sexual behaviour, in Riley AJ, Peet M, and Wilson C (eds): Sexual Pharmacology. Oxford, United Kingdom, Oxford University Press, 1993

8. Heim N: Sexual behavior of castrated sex offenders. Arch Sex Behav 10:11-19, 1981
9. Wille R, Beier KM: Castration in Germany. Ann Sex Res 2:103-133, 1989
10. Mantzoros CS, Georgiadis EI, Trichopoulos D: Contribution of dihydrotestosterone to male sexual behaviour. BMJ 310:1289-1291, 1995
11. Segraves RT: Drugs and desire, in Leiblum SR, Rosen RC (eds): Sexual Desire Disorders. New York, NY, The Guilford Press, 1988
12. Schiavi RC, Segraves RT: The biology of sexual function, in Levine SB (ed): Clinical Sexuality. Philadelphia, PA, W.B. Saunders Company, 1995
13. Tuiten A, Van Honk J, Koppeschaar H, et al: Time course of effects of testosterone administration on sexual arousal in women. Arch Gen Psychiatry 57:149-153, 2000
14. Persinger MA: Maintained hypersexuality between male rats following chronically induced limbic seizures: Implications for bisexuality in complex partial epileptic seizures. Psychol Rep 74:647-652, 1994
15. Blumer D, Walker AE: The neural basis of sexual behavior, in Benson F, Blumer D (eds): Psychiatric Aspects of Neurologic Disease. New York, NY, Grune & Stratton, 1975
16. Kluver H, Bucy PC: Preliminary analysis of functions of the temporal lobes in monkeys. Arch Neurol Psych 42:979-1000, 1939
17. Tiihonen J, Kuikka J, Kupila J, et al: Increase in cerebral blood flow of right prefrontal cortex in man during orgasm. Neurosci Lett 170:241-243, 1994
18. Stoléru S, Grégoire M-C, Gérard D, et al: Neuroanatomical correlates of visually evoked sexual arousal in human males. Arch Sex Behav 28:1-21, 1999
19. Zasler ND: Sexual dysfunction, in Silver JM, Yudofsky SC, Hales RE (eds): Neuropsychiatry of Traumatic Brain Injury. Washington, DC, American Psychiatric Press, 1994
20. Pfaus JG, Everitt BJ: The psychopharmacology of sexual behavior, in Bloom FE, Kupfer DJ (eds): Psychopharmacology: The Fourth Generation of Progress. New York, NY, Raven, 1995
21. Crenshaw TL, Goldberg JP: Sexual pharmacology. Drugs that affect sexual function. New York, NY, W.W. Norton & Company, 1996
22. Angrist B, Gershon S: Clinical effects of amphetamine and L-DOPA on sexuality and aggression. Compr Psych 17:715-722, 1976
23. Cooper AJ: Medroxyprogesterone acetate (MPA) treatment of sexual acting out in men suffering from dementia. J Clin Psychiatry 48:368-370, 1987
24. Leo RJ, Kim KY: Clomipramine treatment of paraphilias in elderly demented patients. J Geriatr Psychiatry Neurol 8:123-124, 1995
25. Stewart JT, Shin KJ: Paroxetine treatment of sexual disinhibition in dementia. Am J Psychiatry 154:1474, 1997
26. Fedoroff JP, Peyser C, Franz ML, et al: Sexual disorders in Huntington's disease. J Neuropsych 6:147-153, 1994
27. Dewhurst K, Oliver JE, McKnight AL: Socio-psychiatric consequences of Huntington's disease. Br J Psychiatry 116:255-258, 1970
28. Rich SS, Ovesiew F: Leuprolide acetate for exhibitionism in Huntington's disease. Mov Disord 9:353-357, 1994
29. Janati A: Kluver-Bucy syndrome in Huntington's chorea. J Nerv Ment Dis 173:632-635, 1985
30. Friedman HM and Allen N: Chronic effects of complete limbic lobe destruction in man. Neurology 19:679-690, 1989
31. Terzian H, Ore GD: Syndrome of Klüver and Bucy. Reproducted in man by bilateral removal of the temporal lobes. Neurology 5:373-380, 1955
32. Stewart JT: Carbamazepine treatment of a patient with Klüver-Bucy syndrome. J Clin Psychiatry 46:496-497, 1985
33. Lilly R, Cummings JL, Benson F, et al: The human Klüver-Bucy syndrome. Neurology 33:1141-1145, 1983
34. Sabhesan S, Natarajan M: Sexual behavior after head injury in Indian men and women. Arch Sex Behav 18:349-356, 1989
35. Adams RD, Victor M, Ropper AH: Principles of Neurology. New York, NY, McGraw-Hill, 1997
36. Gerstenbrand F, Poewe W, Aichner F, et al: Klüver-Bucy syndrome in man: Experiences with posttraumatic cases. Neurosci Biobehav Rev 7:413-417, 1983
37. Bowers MB, Van Woert M, Davis L: Sexual behavior during L-dopa treatment for Parkinsonism. Am J Psychiatry 127:127-129, 1971
38. Brown E, Brown GM, Kofman O, et al: Sexual function and affect in Parkinsonian men treated with L-dopa. Am J Psychiatry 135:1552-1555, 1978
39. Uitti RJ, Rajput AH, Goetz CG, et al: Hypersexuality with antiparkinsonian therapy. Clin Neuropharmacol 12:375-383, 1989
40. Blumer D, Walker AE: Sexual behavior in temporal lobe epilepsy. Arch Neurol 16:37-43, 1967
41. Shukla GD, Srivastava ON, Katiyar BC: Sexual disturbances in temporal lobe epilepsy: A controlled study. Br J Psychiatry 134:288-292, 1979
42. Demerdash A, Shaalan M, Midani A, et al: Sexual behavior of a sample of females with epilepsy. Epilepsia 32:82-85, 1991
43. Saunders M, Rawson M: Sexuality in male epileptics. J Neurolog Sci 10:577-583, 1970
44. Epstein AW: Relationship of fetishism and transvestism to brain and particularly to temporal lobe dysfunction. J Nerv Ment Dis 133:247-253, 1961
45. Erickson TC: Erotomania (nymphomania) as an expression of cortical epileptiform discharge. Arch Neurol Psych 53:226-231, 1945
46. Goldberg RL, Buongiorno PA: The use of carbamazepine for the treatment of paraphilias in a brain damaged patient. Int J Psychiatry Med 12:275-279, 1982-1983
47. Hunter R, Logue V, McMenemy WH: Temporal lobe epilepsy supervening on longstanding transvestism and fetishism. Epilepsia 4:60-65, 1963
48. Rémillard GM, Andermann F, Testa GF, et al: Sexual ictal manifestations predominate in women with temporal lobe epilepsy: A finding suggesting sexual dimorphism in the human brain. Neurology 33:323-330, 1983
49. Eldridge R, Sweet R, Lake CR, et al: Gilles de la Tourette's syndrome: Clinical, genetic, psychologic, and biochemical aspects in 21 selected families. Neurology 27:115-124, 1977

50. Nee LE, Caine ED, Polinsky RJ, et al: Gilles de la Tourette syndrome: Clinial and family study of 50 cases. Ann Neurol 7:41-49, 1980
51. Comings DE: A controlled study of Tourette syndrome. VII. Summary: A common genetic disorder causing disinhibition of the limbic system. Am J Hum Genet 41:839-866, 1987
52. Comings DE, Comings BG: A case of familial exhibitionism in Tourette's syndrome successfully treated with haloperidol. Am J Psychiatry 139:913-915, 1982
53. McDougle CJ, Southwick SM, Rohrbaugh RM: Tourette's disorder and associated complex behaviors: A case report. Yale J Biol Med 63:209-214, 1990
54. Kerbeshian J, Burd L: Tourette's syndrome and recurrent paraphilic masturbatory fantasy. Can J Psych 36:155-157, 1991
55. Langworthy OR, Kolb LC, Androp S: Disturbances of behavior in patients with disseminated sclerosis. Am J Psychiatry 98:243-249, 1941
56. Huws R, Shubsachs APW, Taylor PJ: Hypersexuality, fetishism and multiple sclerosis. Br J Psychiatry 158:280-281, 1991
57. Gorman DG, Cummings JL: Hypersexuality following septal injury. Arch Neurol 49:308-310, 1992
58. Heath RG: Pleasure and brain activity in man. J Nerv Ment Dis 154:3-18, 1972
59. Miller BJ, Cummings JL, McIntyre H, et al: Hypersexuality or altered sexual preference following brain injury. J Neurol Neurosurg Psychiatry 49:867-873, 1986
60. Akil M, Brewer GJ: Psychiatric and behavioral abnormalities in Wilson's disease. Behav Neurol Move Dis 65:171-178, 1995
61. Monga TN, Monga M, Raina MS, et al: Hypersexuality in stroke. Arch Phys Med Rehabil 67:415-417, 1986
62. Freeman W: Sexual behavior and fertility after frontal lobotomy. Biol Psychiatry 6:97-104, 1973
63. Boast N, Coid J: Homosexual erotomania and HIV infection. Br J Psychiatry 164:842-846, 1994
64. Myers BA: Treatment of sexual offenses by persons with development disabilities. Am J Mental Retard 95:563-569, 1991
65. Kafka MP, Prentky RA: Attention-deficit/hyperactivity disorder in males with paraphilias and paraphilia-related disorders: A comorbidity study. J Clin Psychiatry 59:388-396, 1998
66. Kafka M: Psychopharmacologic treatments for nonparaphilic compulsive sexual behaviors. CNS Spectrums 5:49-59, 2000
67. Berlin FS, Meinecke CF: Treatment of sex offenders with antiandrogenic medication: Conceptualization, review of treatment modalities, and preliminary findings. Am J Psychiatry 138:601-607, 1981
68. Bradford JM: The antiandrogen and hormonal treatment of sex offenders, in Marshall W, Laws D, Barbaree H (eds): Handbook of Sexual Assault. Issues Theories and Treatment of the Offender. New York, NY, Plenum Press, 1990
69. Gijs L, Gooren L: Hormonal and psychopharmacological interventions in the treatment of Paraphilias: An update. J Sex Res 33:273-290, 1996
70. Richer M, Crismon ML: Pharmacotherapy of sexual offenders. Ann Pharmacother 27:316-320, 1993
71. Kruesi MJP, Fine S, Valladares L, et al: Paraphilias: A double-blind crossover comparison of clomipramine versus desipramine. Arch Sex Behav 21:587-593, 1992
72. Kafka MP: Sertraline pharmacotherapy for paraphilias and paraphilia-related disorders: An open trial. Ann Clin Psychiatry 6:189-195, 1994
73. Kafka MP: Successful antidepressant treatment of nonparaphilic sexual addictions and paraphilias in men. J Clin Psychiatry 52:60-65, 1991
74. Kafka MP, Prentky R: Fluoxetine treatment of nonparaphilic sexual addictions and paraphilias in men. J Clin Psychiatry 53:351-358, 1992
75. Rosler A, Witztum E: Treatment of men with paraphilia with a long-acting analogue of gonadotropin-releasing hormone. N Engl J Med 338:416-422, 1998
76. Bain J, Langevin R, Dickey R, et al: Hormones in sexually aggressive men. Ann Sex Res 1:63-78, 1988
77. Smith JA, Glode LM, Max DT, et al: Clinical effects of gonadotrophin-releasing hormone analogue in metastatic carcinoma of prostate. Urology 25:106-114, 1985
78. Scaletscky R, Smith JA: Disease flare with gonadotrophin-releasing hormone (GnRH) analogues. How serious is it? Drug Saf 8:265-270, 1993
79. Charney DS, Nestler EJ, Benney BS: Neurobiology of Mental Illness. New York, Oxford University Press, 1999