

## The Role of Testosterone in Sexuality and Paraphilia— A Neurobiological Approach. Part II: Testosterone and Paraphilia

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[Correction added after online publication 28-Jul-2011: Dr. Stolpmann's name has been corrected.]

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### ABSTRACT

**Introduction.** Antiandrogen therapy has been used for 30 years to treat paraphilic patients and sexual offenders. Yet the therapeutic success of antiandrogens is uncertain. Furthermore, there is still a lack of comprehensive knowledge about the effects of androgen-lowering therapy in paraphilic patients.

**Aim.** We discuss endocrinological, neurobiological, and therapeutic aspects of paraphilia with the aim of integrating these on the basis of the current neurobiological and clinical knowledge on testosterone that was set out in Part I of this review.

**Methods.** Our review of the human literature comprises the current knowledge about the neurobiology of paraphilia and the known endocrinological, pathophysiological, and genetic aspects of this disorder. The role of testosterone is discussed. A survey of antiandrogen therapy and its outcome in paraphilic patients and sex offenders is provided.

**Results.** Although not all data are consistent, current imaging research suggests that structural and functional changes in pedophilia appear for the most part in brain regions also involved in sexual functions. Not exclusively testosterone but also some other endocrinological and neurochemical parameters could be disturbed in pedophilic patients and child molesters; these include changes in hypothalamic–pituitary function, prolactin levels, and dopaminergic or serotonergic functions. There appears to be a sex-steroid-related genetic influence on antisocial traits, externalizing behavior, and sexual behavior. Most of the studies in which antiandrogen therapy in paraphilic patients and sex offenders have been examined were case reports, or observational or open-label studies, and many did not include adequate control groups. Only a few placebo-controlled double-blind studies have been published with inconsistent results concerning treatment effects. Outcome measures differ between the studies and do not seem ideally suited to their purpose.

**Conclusions.** On the basis of the current knowledge about testosterone and its effects on brain and behavior as described in Part I, and of available results on the relationship between testosterone and paraphilia as well as antiandrogen therapy, we present from a neurobiological perspective an extended scientific proposal for design features to investigate the effects of antiandrogen treatment in large clinical trials. **Jordan K, Fromberger P, Stolpmann G, and Müller JL. The role of testosterone in sexuality and paraphilia—A neurobiological approach. Part II: Testosterone and paraphilia. J Sex Med 2011;8:3008–3029.**

**Key Words.** Paraphilia; Sex Offenders; Testosterone; Sexuality; Brain; Antiandrogen Therapy

### Introduction

According to the DSM-IV-TR criteria, the psychiatric disorder paraphilia is defined by the following symptoms: recurrent, intense sexually arousing fantasies, sexual urges or behaviors that occur over a period of at least 6 months and generally involve (i) nonhuman objects; (ii) the suffering or humiliation of oneself or one's

partner; or (iii) children or other non-consenting persons (Criterion A), and those which “cause clinically significant distress or impairment in social, occupational, or other important areas of functioning” (Criterion B); both criteria must be met ([1], for a discussion see [2]). Subtypes of paraphilia are pedophilia, exhibitionism, frotteurism, and voyeurism [1]. In the case of pedophilia, individuals who fantasize about are sexually

aroused by, or experience sexual urges toward prepubescent children (generally <13 years); it has to be mentioned that not all child molesters have pedophilia and vice versa (e.g., see [3]). On behalf of the persons concerned, as well as on behalf of society, an effective therapy is of great importance, especially if the person is suffering under extreme psychological distress or shows criminologically relevant behavior. Current therapeutic approaches include psychotherapy as well as pharmacological treatment. Androgen-lowering therapy is one of these. Antiandrogen drugs, such as cyproterone acetate, medroxyprogesterone acetate, or the more recently introduced gonadotropin-releasing hormone agonists (GnRH), are utilized to decrease drastically the testosterone (T) concentration in the patients, thereby reducing the risk of recidivism. Yet the therapeutic success of these agents is uncertain. Meta-analyses and reviews report only moderate and often mutually inconsistent effects [4–8]. Considering methodological quality, most of these studies do not reach level 4 or 5 of the Maryland Scale of Scientific Rigor [5]. Furthermore, these studies often only report criminologically relevant or subjective sexual parameters to measure therapeutic outcome, e.g., recidivism rate, subjective information about sexual urges, or penile plethysmography [9]. However, as shown in Part I of this review, current knowledge about T (based on fundamental research) suggests that T modulates almost every aspect of sexual behavior [10]. Furthermore, the complex relationship between T and its effect on sexual functions, as well as the high complexity of human sexual behavior itself, should be taken into account. Therefore, in the next three sections we present a survey of current knowledge about the association between T and paraphilia or sexual offences, and we include neurobiological and neurophysiological aspects of paraphilia. Furthermore, we discuss the impact of genetics on T and on forensically relevant disorders. In the following section, we examine the currently achieved success of androgen-lowering therapy in paraphilic patients and sexual offenders. In the studies cited here, different patient groups were examined, e.g., sex offenders, paraphilic patients, and child molesters. Where possible, we refer to the specific groups examined in order to differentiate clearly between them. Combining current knowledge about T from fundamental research and current knowledge about androgen-lowering therapies, we provide some new considerations to measure therapeutic outcome on a broader basis with the goal of under-

standing the high inter-individual variability between patients. This scientific proposal could lead to the development of criteria for choosing the appropriate therapy for the individual patient.

## Paraphilia

### *Neurobiology of Paraphilia*

To date, we have no thorough understanding of the neurobiology of paraphilia. Case studies of hypersexual and paraphilic behavior in neurological and psychiatric disorders have demonstrated that pedophilic and paraphilic behavior are predominantly related to dysfunctions in the frontal and/or in the temporal lobe (e.g., [11–14]). In a recent survey of eight patients with pedophilic behavior, Mendez and Shapira demonstrated that brain disorders may trigger a predisposition to sexual attraction toward children through disinhibition (in cases with frontal disease) and sexual preoccupation (in cases with right temporal disease). Hypersexuality was found to be associated with subcortical disease in nonmotor basal ganglia, hypothalamus, or septal nuclei [14]. Hypersexuality can also be observed in dementia, where frontal or cortical damage is associated with disinhibition as well as in temporal lobe epilepsy or the Tourette syndrome (where the hypersexuality seems to be caused by a disinhibition of the limbic system) and finally in patients with frontal lobotomy [15]. Moreover, hypersexuality and aberrant sexual behavior can also occur in Parkinson's disease in the course of a dopamine-replacement therapy [16,17].

There exist few models of the pathophysiology of paraphilia. These models are mainly derived from clinical observations and treatment effects in psychiatric and paraphilic disorders (see also next section) [18–20]. More specific neurobiological models have only been proposed for pedophilia and have been based on case studies and only a few structural and functional imaging data. A detailed overview of these four structural [21–24] and seven functional imaging studies [25–31], with a discussion of their potentials and especially their methodological problems, can be found in two articles from our group [32,33] (see also Table 1). In the first structural study Schiltz et al. found an enlargement of the anterior temporal horn of the lateral ventricle in four pedophilic patients [21]. In the second study, they found a decrease of grey matter in the right amygdala, the hypothalamus, the substantia innominata, and the stria terminalis in 15 pedophilic patients compared with 15 control persons [22]. Schiffer et al. found a volume reduction of grey matter in 18 pedophilic patients

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