BIOPSYCHOSOCIAL FACTORS IN THE SEXUAL DESIRE OF CONTRACEPTION-USING COUPLES AND TRANS PERSONS

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Biopsychosocial factors in the sexual desire of contraception-using couples and trans persons

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Els, 4 december 2014

CONTENTS

VERKLARENDE LIJST AFKORTINGEN

AR	androgen receptor
CAG	cytosine-adenine-guanine
CNS	central nervous system
ECP	emergency contraceptive pill
GCT	gender-confirming treatment
HC	hormonal contraception
HSDD	hypoactive sexual desire disorder
LH	luteinising hormone
OC	oral contraception
SHBG	sex hormone binding globulin
T	testosterone

CHAPTER 1

GENERAL INTRODUCTION

The overwhelming presence of 'lust', 'longing' or sexual desire both in media and in our society at large, combined with the observation of a rather limited body of scientific knowledge, underscores the continued need for a better understanding of this concept. The current doctoral dissertation presents a series of studies that have taken a closer look at a range of potential biopsychosocial factors affecting sexual desire in two populations: contraception-using couples, and trans persons who have concluded their gender-confirming treatment. Both of these groups have been described to experience an effect of contraception and treatment procedures, respectively, on their sexual desire levels, allowing us to study the relative contribution of hormones and psychosocial factors. First, we focus on potential biological (contraceptive product and genetically pre-disposing androgen sensitivity), psychological (self-esteem and affect) as well as social or dyadic (relationship and sexual satisfaction, sexual desire of the partner) correlates of sexual desire in the context of contraception-using couples. Next to examining those correlates of sexual desire throughout changing contraception use, we also look at some of those correlates within the contraceptive cycle. Second, we address the biological (treatment-induced changing hormone levels and genetic androgen sensitivity), psychological (mental functioning) as well as social or dyadic (relationship status, sexual orientation) correlates in trans persons who have concluded their gender-confirming treatment. In this introductory chapter, we start by outlining the concept of sexual desire as it has been proposed by contemporary theoretical models. Next, we provide an up-to-date overview of the empirical research on sexual desire in both the study populations of this dissertation. Finally, we conclude this chapter by stating the research objectives of the current doctoral dissertation and by providing an overview of the empirical chapters.

THE CONCEPTUALIZATION OF SEXUAL DESIRE

We start by defining the concept of sexual desire as it is defined by the authors of the Sexual Desire Inventory, the instrument used in most of the presented studies in this dissertation. We further differentiate sexual desire from the related concept of sexual arousal, and summarise the current diagnostic criteria for related sexual desire dysfunction, as presented in the latest version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5).

A definition of sexual desire...

In this doctoral dissertation, we adopt the definition of sexual desire as it was proposed by the authors of the Sexual Desire Inventory (Spector, Carey, & Steinberg, 1996). More specific, sexual desire "refers to interest in sexual activity. It is primarily a cognitive variable, which can be measured through the amount and strength of thought directed toward approaching or being responsive to sexual stimuli." The authors continue by stressing that "desire involves thought that may motivate an individual to seek out or be receptive to sexual opportunities." The Sexual Desire Inventory was found to be multidimensional, in the sense that factor analysis yielded "one general construct of sexual desire and four related constructs involving interest in masturbation, interest in using erotic materials, sexual dreams, and interpersonal attraction (Spector, Carey, & Steinberg, 1996, p. 178-179)."

... and its relation with and differentiation from sexual arousal

Scholars and academics have traditionally viewed both sexual desire and arousal to be relatively distinct though related phenomena with the first being a rather cognitive-motivational component of sexuality and the second the physical counterpart (indicated by penile tumescence in men and vasocongestion and lubrication in women). However, qualitative studies have shown that, at least a proportion of, (mostly sexually functional) women explicitly state they have difficulty differentiating "arousal" from "desire" (Brotto, Heiman, & Tolman, 2009; Graham, Sanders, Milhausen, & McBride, 2004). Also, a recent study on sexual difficulties and dysfunctions (i.e., sexual difficulties with associated significant distress) in a large convenience sample supported this overlap,

stating that the comorbidity of sexual desire and arousal dysfunctions in women was very high and varied between 25 and 62% (depending on the subcategory of specific dysfunction) (Hendrickx, Gijs, & Enzlin, 2014). However, this study also pointed out that the proportion of women classified as having desire difficulties/dysfunctions alone was higher than the proportion having a combination of desire and arousal difficulties/dysfunctions (Hendrickx, Gijs, & Enzlin, 2014, p. 10).

Further, it was assumed until recently that physiological or genital arousal, was automatically connected to the subjective experience of sexual feelings (Rellini, McCall, Randall, & Meston, 2005, p. 116). However, based on the earlier work of Laan and Everaerd (1995), a series of studies by Chivers and colleagues (Chivers, & Bailey, 2005; Chivers, Reiger, Latty, & Bailey, 2004; Chivers, Seto, & Blanchard, 2007) supported a discordance between genital reactions and subjective arousal (or feeling aroused) in women. In a recent meta-analysis (Chivers, Seto, Lalumière, Laan, & Grimbos, 2010), this concordance was quantified as higher in men (r = .66) than in women (r = .26).A more detailed conceptual differentiation between these interrelated concepts will be presented as a conclusion on the contemporary incentive motivation model of sexual desire (see further, p. 11).

DSM-5 and the Female Sexual Interest/Arousal Disorder

After considerable debate on the previous diagnoses of Hypoactive Sexual Desire Disorder and Female Sexual Arousal Disorder (DSM-IV-TR, APA, 2000) (e.g., Clayton, DeRogatis, Rosen, & Pyke, 2012a, 2012b; Derogatis et al., 2011), DSM-5 decided to merge both in the new entity of "Female Sexual Interest/Arousal Disorder (FSIAD)" (APA, 2013, p. 433). FSIAD is described as a polythetic complaint, of which possible manifestations can include: lack of sexual interest in sexual activity, reduced or absent erotic thoughts, lack of initiation and receptivity to sexual activity, reduced pleasure during sex, reduced or absent desire emerging during a sexual encounter, and a reduction in genital and non-genital sexual sensations (APA, 2013).

Further, DSM-5 is the first edition that has differentiated the aspects of "initiation" of sexual activity and being "(un)receptive" to a partner's advances in the context of female sexual desire dysfunctions. In the past two decades, there has been much

attention for the concept of “responsive” or “triggered” desire, which is considered more common in women than “spontaneous” desire (Basson, 2000).This approach in the pathological side of sexual desire makes clear that the concept is indeed in need of a theoretical model, integrating the above-mentioned processes.

SEXUAL DESIRE AND ITS THEORETICAL FRAMEWORK

Starting from this pre-defined concept of Spector and colleagues (1996), this doctoral dissertation places sexual desire within the more recent theoretical framework of incentive motivation models. Summarized, those models state that sexual desire is the result of the interplay between an adequately functioning sexual response system and sexually meaningful stimuli that activate it (Toates, 2009). This integrative framework provides a vision on sexual desire as elicited by the interaction of biological, psychological and contextual factors (Laan & Both, 2008). We first provide a short description of earlier drive models and their shortcomings, after which we elaborate on the incentive motivation model.

Models of sexual desire as a drive

Sigmund Freud (1953) preferred the term “libido”, which he conceptualized as a process fuelled by sexual instincts. “Since everyday language possesses no counterpart to the word ‘hunger’, science makes use of the word ‘libido’ for that purpose” (Freud, 1953, p.135). Freud (1964) stated that “its source is a state of excitation in the body, its aim is the removal of that excitation.”… “We picture it as a certain quota of energy which presses in a certain direction. It is from this pressing that it derives its name of “Trieb” (“drive”) (Freud, 1964, p. 96). The sexual drive was thus placed within a similar category as other drive states, such as hunger and thirst. “An instinct, then, is distinguished from a stimulus by the fact that it arises from sources of stimulation within the body, that it operates as a constant force and that the subject cannot avoid it by flight, as is possible with an external stimulus” (Freud, 1964, p. 96). The premise is the idea of homeostasis, in which the drive builds up within the body and, once the tension is relieved, an individual can continue until the tension starts to build again. Freud did

not explain what causes the building of this force in the body, resulting in the substrate for this drive remaining a black box.

After Freud's first conceptualization of sexual desire as a drive state, it took a several decennia before new models developed in the field. Based on numerous observations of the sexual functioning in the volunteers in their lab, psychophysiological pioneers Masters and Johnson (1966) developed the EPOR-model of the sexual response including excitement, plateau, orgasm and resolution. In the 1970's, sex therapist Helen Kaplan (1977) reported a rising number of patients who were able to become physically excited, but complained about a lack of desire towards sexual activity. Based on these clinical impressions, she elaborated on the original model of Master and Johnson by adding the phase of sexual desire (DEOR: desire, excitement, orgasm and resolution). However, just as Masters and Johnson, Kaplan believed sexual desire to be a biological instinct. She defined sexual desire as "specific sensations which move the individual to seek out or become receptive to sexual experiences". These sensations "are produced by the physical activation of a specific neural system in the brain" (Kaplan, 1979).

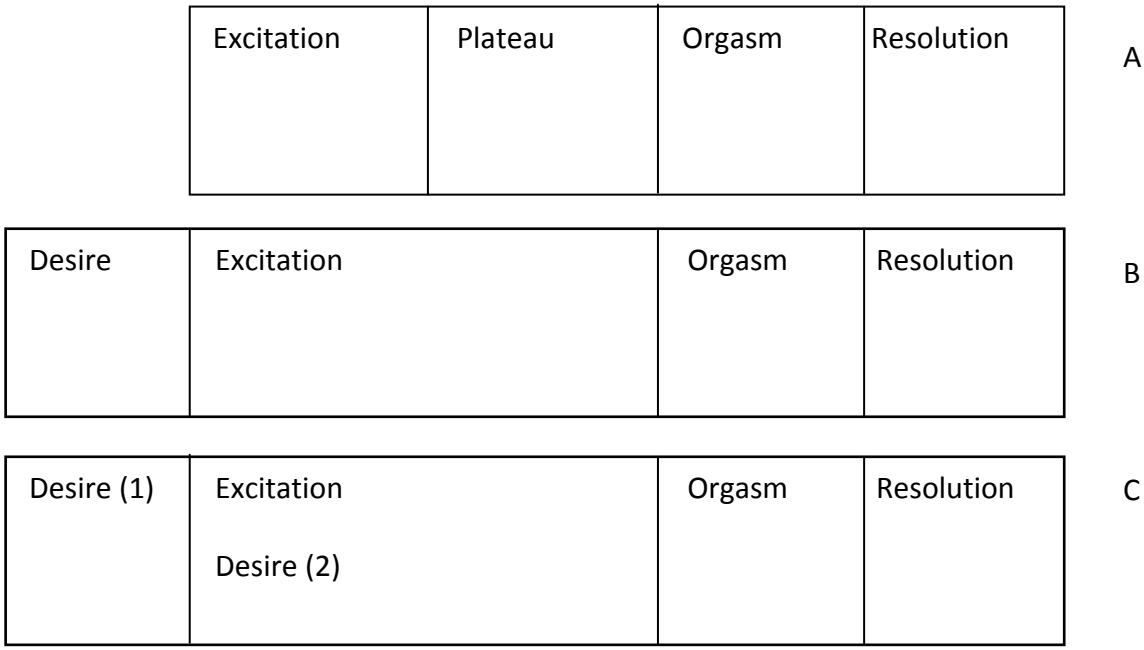

Figure 1. The development of the linear human sexual response model: from the original EPOR-model of Masters and Johnson (1966) (A), through the DEOR-model of Kaplan (1979) (B), to the proposed modification (C) of Levin (2001). *Based on Levin (2001, p. 66)*

Kaplan (1995) suspected these systems to be located in the hypothalamus, the organ in the brain where physiological deficits and the restoration of homeostasis are signalled. “Once again, we can learn from the similarities between eating and sex. More specifically, under normal circumstances, a state of starvation activates the ventromedial hypothalamic ‘appetite centres’. This neurophysiologic activity produces a subjective feeling of hunger” (Kaplan, 1995, p. 17). She considered the processes in those centres to be a black box, because it remains unknown how processes in the hypothalamus contribute to sexual desire.

These different versions of the drive model were the start of the idea that feeling sexual desire is a normal state and several proximal and distal factors can inhibit the desire to cause a lack thereof, constituting the disorder of “hypoactive sexual desire” (Kaplan, 1979). And although the term of hypoactive sexual desire was recognized by sex therapists since the 1970’s, it was not until the third edition of the DSM (DSM-III, APA, 1980) that desire problems were included as a separate entity “inhibited sexual desire disorder”.

Critiques on the drive models

Several critiques have been voiced on the presumptions behind the drive models. First, Levin (2001) has questioned the linear sequence of the DEOR-model. He states that “human sexual desire is complex and is not a simple entity, it can change during the sexual scenario experienced by a person” (p. 68). He states that sexual desire can precede sexual arousal, and vice versa; and that the difficulty lies in thinking there is only one type of activation of desire. In part C of Figure 1, he therefore proposes a distinction of “spontaneous desire” (desire 1), that is created endogenously, and a second phase of “responsive desire” created by exogenous stimuli (desire 2). The author himself however indicates that this is not to be understood as a statement that two independent mechanisms would act in the brain, but that the one mechanism of desire can be activated at different times of the sexual activity (Levin, 2001). The question what causes the “spontaneous” desire however remains in his proposed model.

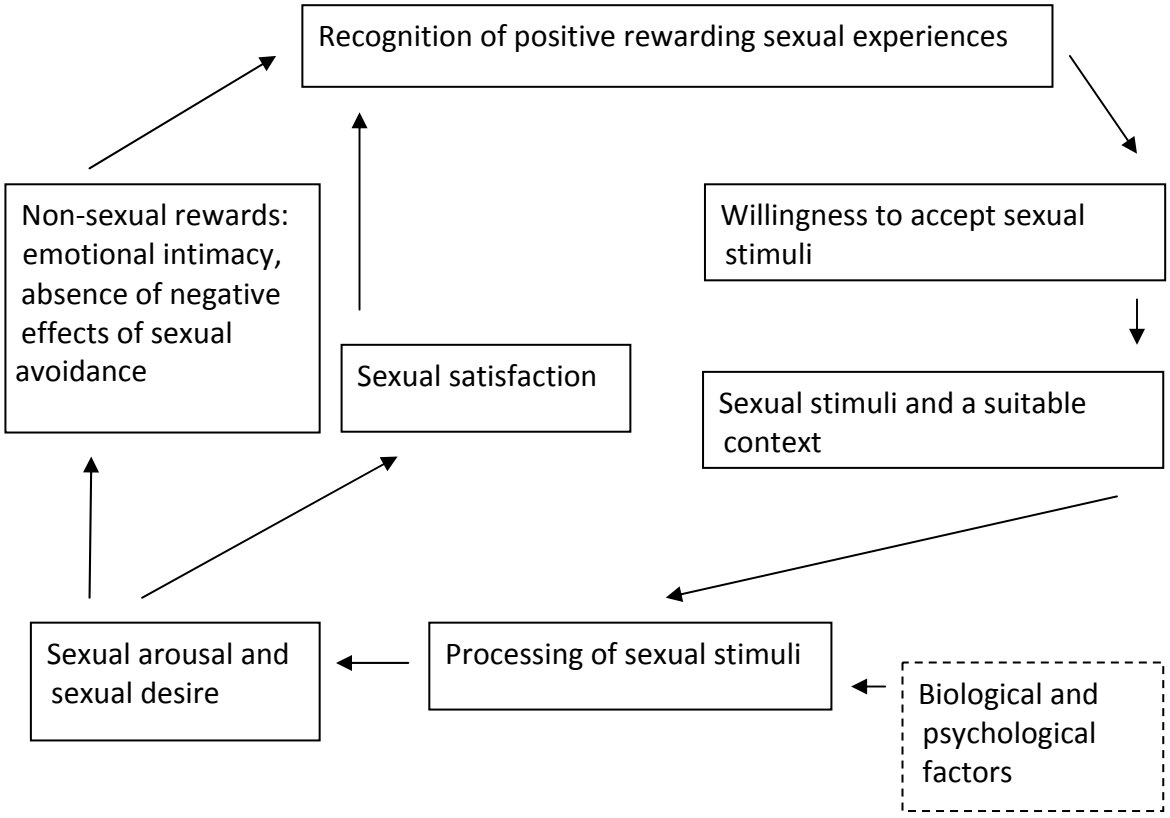

Figure 2. Intimacy-based model, by Both, Laan, & Weijmar Schultz (2010), based on Basson (2001a).

Second, Basson(2001a) observed how the classic linear sexual response cycle assumes a sexually neutral starting point, while in reality sexual as well as non-sexual factors can elicit the start of the sexual response. Basson especially pointed towards the importance of intimacy as a stimulus for the activation of the sexual response. Research by Meston and Buss (2007) has however shown that, apart from intimacy, a range of other motives can elicit sexual desire or arousal.

Third, other authors pointed out that not only the resolution phase of the sexual response has been neglected, but the importance of sexual (dis)satisfaction has been minimized. The presumption that orgasm is intrinsically associated with sexual satisfaction, could be problematic considering sexual behaviour can be driven by multiple motivations (Gijs, Laan, & Both, 2009).

Fourth, Both, Everaerd and Laan (2007) raised the issue of a lack of evidence that sexual abstinence would have any adverse effects. Moreover, no biological need seems

to be satisfied, as in the case of hunger and thirst. Beach (1956) stated that "what is commonly confused with a primary drive associated with sexual deprivation is in actuality sexual appetite, and this has little or no relation to biological or physiological needs" (p. 4).

Incentive motivation model of sexual desire

While drive models presume that we have sex because we feel like it, the incentive motivation model turns around that causality (we feel desire since we are having sex). Incentive motivation theory emphasizes how sexual desire is the result of the activation of an adequately functioning response system by sexually attractive stimuli (i.e. incentives) (e.g., Both, Everaerd, & Laan, 2007; Toates, 2009), and hence, sexual desire is elicited, through the expectation of reward.

Information processing model of the sexual response. The term "sexual system" refers to the psychobiological make-up of humans, giving them the capacity to respond sexually (Gijs, Laan, & Both, 2009). But what are the information processes that are implied in this term? As depicted in Figure 3 below, some authors have proposed a conceptual model of the generation of sexual response, dividing the process in two processing stages (Janssen, Everaerd, Spiering, & Janssen, 2000). On the automatic or preattentive route, the main process is first, *appraisal* (interpretation and evaluation) of sexual stimuli, and second, *response generation* (preparing and starting a sexual response), integrating meaning with response or motor plans, which may lead to subjective experience of sexual arousal and genital response. Both stages of appraisal and response generation are proposed to operate on an automatic or preattentive level, and form the central pathway of the model as those processes mediate between stimuli and responses. Further, the model also includes controlled or attentive processes (involving higher level regulation processes) that both affect and are affected by the earlier central pathway operations (Janssen, Everaerd, Spiering, & Janssen, 2000).

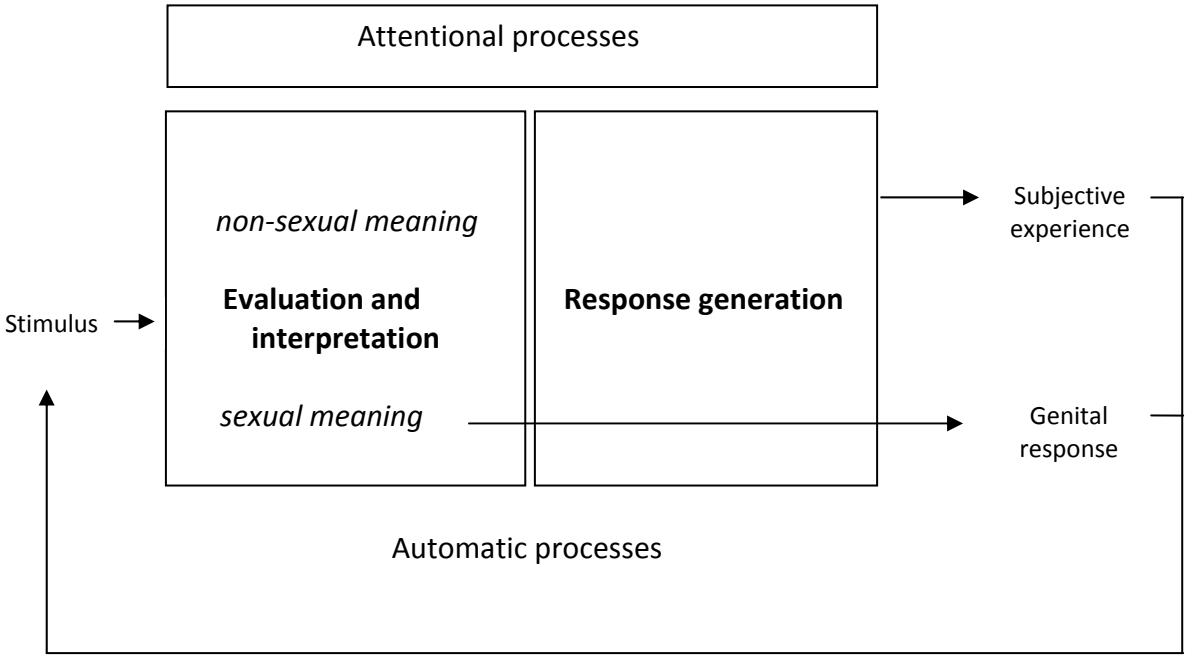

Figure 3. Information processing model of the sexual response by Both, Laan, & Weijmar Schultz, 2010, based on Janssen, Everaerd, Spiering, & Janssen, 2000.

Origin of sexual desire in Incentive motivation. In that context of information processing, a sexual stimulus is a stimulus that activates the sexual system or gives rise to a conscious sexual experience (Gijs, Laan, & Both, 2009). Most sexual stimuli will acquire their activating capacity by learning processes such as classical conditioning: pleasure that is elicited by genital stimulation and orgasm will get associated with certain stimuli, which later in itself can elicit sexual desire (Both et al., 2008). Therefore, we could state that sexual desire is the result of a layered and complex process, encompassing these steps: (1) the presence of a sexual stimulus that activates the sexual system, (2) causing, from within the working memory, appraisal aimed at processing that sexual stimulus, leading to (3) the activation of a conscious memory linking the meaning of that stimulus in the explicit memory, and (4) activating emotional arousal in the preattentive implicit memory. Finally, (5) activation of the sexual response system is associated with several evaluation processes, that make sure the response generation does or does not take place (Gijs, Laan, & Both, 2009).

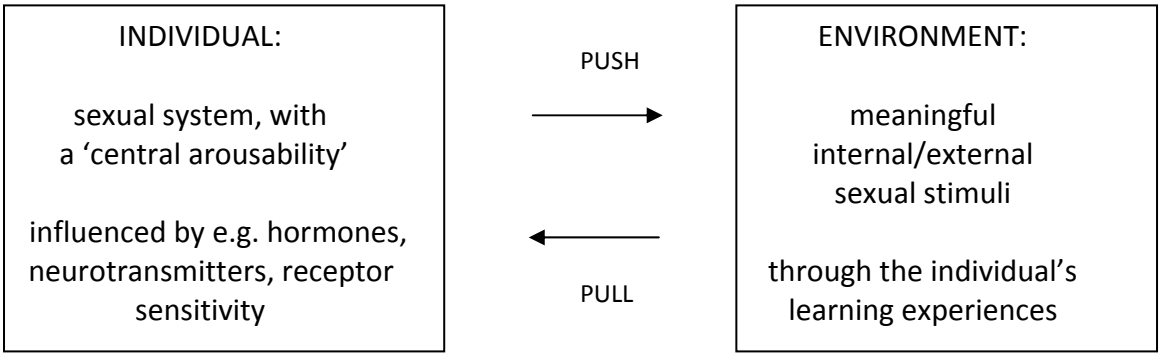

Figure 4. Non-exhaustive overview of factors influencing the activation of sexual desire. Based on Bindra, 1974; Singer & Toates, 1987; Both, Everaerd, & Laan, 2007.

Action tendency. The information processing model already implied the two energetic aspects in the activation of sexual desire: a 'push' and a 'pull' element. First, the sensitivity of one's sexual system *pushes* the individual towards sexual stimuli. This sensitivity or "central arousability" can be dependent on biological factors such as sex steroid levels, a genetically predisposed sex steroid receptors' sensitivity, neurotransmitters, etc. Second, the environment, with its sexual stimuli, *pulls* the individual towards sexual activity (Laan & Both, 2008). There, a connection is made with the "sexual memory", that is memory associated with sexual responding, and refers to recollections of sexual encounters, attitudes toward sex, sexual fantasies and knowledge on sexual rewards or costs (Spiering & Everaerd, 2007).

Therefore, sexual desire is not elicited merely by the potential rewarding (or neutral or aversive) value of the external or internal sexual stimulus, but also by biological factors that influence the sensibility of the sexual system (for a further elaboration on this, see p. 15-19). Finally, when sexual desire is activated as described above, a connection is made between the emotional-motivational circuit and the motor circuit when the action tendency can be expressed by approaching or starting sexual behaviour that encompasses the promise of reward. The expression of this action tendency is of course mediated by the use of reasoning, the ability of reflect and judge a situation (Everaerd, 2003). In the motivational process, the cortex and prefrontal areas of the brain contribute significantly in whether behaviour is actually proceeded with (Damasio, 1994; Fuster, 1997).

Desire and arousal concepts from an incentive motivation perspective. Based on assumptions of the incentive motivation theory and the observation of discordance of genital and subjective arousal, previous authors have attempted to define their intercorrelation as follows. Everaerd (2003) stated that *sexual arousal* (as an objective, genital sexual response) is elicited in the presence of sexually rewarding situations. When this arousal transcends a certain threshold and is perceived by the individual, sexual arousal is experienced as lust. *Lust* is the conscious experience of the physiological sexual response, which coincides with desire. *Sexual desire* is defined as a desire towards the rewards a sexual interaction will yield (Everaerd, 2003).

To conclude, the current doctoral dissertation defines sexual desire as the subjective experience of being attracted to or pushed towards objects or behaviours with potential rewarding effects. Sexual desire seems to incorporate the prospect of satisfaction through sexual behaviour, but it has as much to do with promise, hope, as with longing and craving (Everaerd, Laan, Both, & Spiering, 2001).

DOES HORMONAL CONTRACEPTION[1] AFFECT WOMEN'S SEXUAL DESIRE?

Over fifty years of "the pill": introduction and prevalence of its use

After ground-breaking work of Gregory Pincus and his colleagues (Pincus et al., 1959) on the development of the oral contraceptive pill, the Food and Drug Administration (FDA) approved its use for married women on May 9th, 1960. A Supreme Court ruling in 1972 also gave unmarried couples "the right to non-procreative sex" (Tone, 2001; Watkins, 1998). Especially the first few decades, both popular news and scientific papers reflected on both medical and sociological aspects of oral contraception (OC). In 1966, several American newspapers ran a story asking "Can its availability to all women of childbearing age lead to sexual anarchy?" (Burrows, Basha, & Goldstein,

[1] Hormonal contraception can differ in terms of constituents (types of oestrogen and progestin), dosage, ratio of progestin to oestrogen, mode of administration and temporal pattern of dosage (monophasic, biphasic, or triphasic). The current dissertation will use the term "oral contraception (OC)" when discussing studies on one or more types of the oral contraceptive pill. The term "hormonal contraception (HC)" will be used as a more broad, umbrella term for studies discussing both oral and/or other forms of hormonal contraception, such as the newer formulations such as the vaginal ring or the contraceptive patch.

2012). Scientific publications reported both pessimist ("Scholarship will languish, children will be neglected and the society will fall into decadence and decline, because no one fears pregnancy.") and optimist arguments on this revolutionary phenomenon ("...widespread use of family planning will strengthen the family structure, make every child a wanted child...") (p. 83) (Udry & Morris, 1969).

More than fifty years after its introduction, OC is the most popular contraceptive method in Western Europe, with 50 to 85% of women being current or former users (Skouby, 2004). In Belgium, the Health Interview Survey estimated that, currently, 57% of women of childbearing age rely on OC (Bayingana et al., 2006).

Overview of earlier research on HC and female sexual desire

Initially, there were very few concerns about negative effects on female sexual functioning, quite the opposite. Since OC separated the sexual from the contraceptive act (Zell & Crisp, 1964), most expected an improved sense of well-being and sexual desire when women no longer feared pregnancy (Glick, 1967). The earliest reports (Glick, 1967, Dennerstein & Burrows, 1976) stated that the majority of women did not experience negative sexual side effects, while it was mentioned that a small subset of women reported a decreased sexual desire.

Although today, the literature on- more broadly- hormonal contraception (HC) and its various possible side effects is extensive, it is surprising how little the specific effects on female sexuality are understood. In the late 1980s, the field received a boost after support from the Safety and Efficacy Task Force of the Human Reproduction Program at the World Health Organization (WHO), who first ordered a literature review on the effects of OC on well-being and sexuality (Bancroft & Sartorius, 1990), and based on that, a series of research studies (Bancroft, Sherwin, Alexander, Davidson, & Walker, 1991a, Bancroft, Sherwin, Alexander, Davidson, & Walker, 1991b, Graham & Sherwin, 1993; Graham, Ramos, Bancroft, Maglaya, & Farley, 1995; Graham et al., 2007; Sanders, Graham, Bass, & Bancroft, 2001; Graham, Bancroft, Doll, Greco, & Tanner, 2007; Greco, Graham, Bancroft, Tanner, & Doll, 2007).

Those studies, together with more recent additions, pointed out a number of results on the sexual life of HC-users: first, sexual and emotional effects are the most important

reasons for discontinuation, second, a negative effect on sexuality exists in a significant minority of HC-users, and three, a different cyclical pattern exists in HC-users compared to freely cycling women. Those three lines of research will be discussed more in depth.[2]

Sexual and emotional effects are the most important reasons for discontinuing HC. Several studies have reported that discontinuation (and switching) of OC is common (up to 47%, Hatcher & Nelson, 2004; Oddens, 1999; Sanders, Graham, Bass, & Bancroft, 2001), but most studies have not well explored the explanations. Sanders and colleagues (2001) measured the reasons for discontinuation of OC's in a group of women attending a family planning clinic, and this on two different levels. First, they collected the spontaneously reported reasons, which mainly were physical (37%) and emotional side effects (33%). Eight percent reported sexual side effects. Second, the study ran a logistic regression on which was the best predictor for discontinuation, and found very different results. It appeared that the best predictors turned out to be the frequency of sexual thoughts, decreased sexual arousability and emotional side effects. These divergent results illustrate that asking for reasons of discontinuation might elicit socially desirable responses(Sanders, Graham, Bass, & Bancroft, 2001). A systematic and prospective assessment of mood and sexuality is hence called for.

Negative effects on female sexuality exist. Considering the high discontinuation rate, cross-sectional studies comparing two or more groups of women using different HC-formulations are unable to reliably detect sexual effects, as women with negative sexual side effects in the past will have selected themselves out. Since the 1980s, only two placebo-controlled studies have been carried out, mostly due to the difficulty of avoiding unplanned pregnancy during placebo administration and the difficulty of finding funding in this field.

Graham and Sherwin (1993) reported a study in which triphasic OC was compared with placebo in the treatment of 45 women with premenstrual complaints. While premenstrual mood improved in both the OC and placebo group (for an elaboration on mood, see p. 20 and further), a significant reduction in sexual desire was seen in the OC group only. During the baseline cycle, sexual desire was strongest during the menstrual

[2] A discussion of studies on the effects of HC on female sexual desire before the 1980s are deemed as less relevant, since (a) the composition of the earliest HC was significantly different from the currently available preparations and (b) the discourse on HC in society today has changed considerably.

and the post-menstrual phase, while during the OC-cycles, those phases showed the lowest desire ratings. A later publication (Graham, Ramos, Bancroft, Maglaya, & Farley, 1995) studied 150 women (in two centres, Edinburgh and Manila) who had been sterilized or whose partners had been vasectomized. A parallel, double-blind group design with a combined OC, a progestin-only pill and a placebo demonstrated that half of the women who started an OC reported a decline in sexual desire and, to a lesser extent, in the frequency of sexual activities. Interestingly, this effect was observed only in one centre: only the Scottish women reported a decrease. The authors nuanced that the Scottish women were more positive regarding sexuality and hence, had a larger scope for negative change.

Further, a few studies also looked at newer forms of HC, such as the vaginal ring and formulations with the newer progestin, drospirenone. An Italian study compared a control group (no HC) with women starting on the vaginal ring or a classic combined OC. After three and six months, an increase in sexual desire was observed in both contraceptive groups, but the increase was highest in the vaginal ring group, compared to the control group (Guida et al., 2005). A similar study (without control group) confirmed a progressive increase in sexual desire among vaginal ring users, compared to OC-starters (Sabatini & Cagiano, 2006). A Thai study has compared a newer OC containing drospirenone (Yasmin®) versus a classic combined OC (Meliane®) and demonstrated a significant improvement in sexual desire after three months of use in both groups (Oranratanaphan & Taneepanichskul, 2006). An Italian study also started 106 women on this same product, but registered no changes in sexual desire (as measured by a single item of the Personal Experience Questionnaire), despite improvements in other aspects of sexual functioning (e.g., enjoyment, satisfaction) (Caruso et al., 2005).

A different within-cycle pattern of sexual desire in HC-users. Contrary to the relative large body of literature on within-cycle patterns of sexual desire (and behaviour) in freely cycling women (for a review, see Hedricks, 1994), similar information on potential within-cycle changes in HC-users is almost non-existent. The research in freely cycling women is not completely consistent, but in summary points towards an increased sexual desire at mid-cycle (and possibly again prior to menses) (Bullivant et al., 2004, Roney & Simmons, 2013). Studies on the menstrual cyclicity of sexual behaviour in

freely cycling women are less consistent (Brewis & Meyer, 2005, Bullivant et al., 2004, Roney & Simmons, 2013, Wilcox et al., 2004).

Only two studies have reported on potential cyclical patterns of sexual desire in OC-users. A large, retrospective study in 4112 readers of a women's magazine (both OC-users and non-users) (Warner & Bancroft, 1988) asked for an indication, amongst other things, on highs and lows in sexual desire during their last menstrual cycle. While non-users were more often reporting a high in sexual desire during or after menses, in OC-users a 'flattening out' of sexual desire could be observed: OC-users were less likely to report either highs or lows, and reported a greater spread across the cycle. A later, prospective study in three groups of women (triphasic OC, monophasic OC and non-users) stood out due to the remarkable similarity of cycle patterns in all three groups: similar tendencies that had shown significance in the retrospective study did not reach statistical significance in the prospective study (Walker & Bancroft, 1990).

BIOPSYCHOSOCIAL FACTORS IN THE RELATION BETWEEN SEXUAL DESIRE AND HC

After this overview of the earlier research on the relation between female sexual desire and HC, the following part will look at several mechanisms that could be underlying those effects. The possible factors have been ordered by their biological, psychological, or social/relational nature.

Biological factors

Sex steroids and female sexuality. As previously discussed, steroid hormones affect the "central arousability" of the human sexual system by priming the mediobasal hypothalamus and limbic system to be selectively responsive to sexual incentives (Pfaff,1980, 1999).While studies, e.g. in surgically and naturally menopausal women (Nathorst-Böös, Wilkund, Mattson, Sandin, & von Schoultz, 1993; Sherwin, 1991) have clearly shown that oestrogens are necessary for normal vaginal lubrication and avoiding dyspareunia, the direct effect of oestrogens on sexual desire and arousability are less clear. Weak correlations between levels of estradiol and sexual desire have been found by some studies (Freeman, Sammel, Lin, Gracia, & Pien, 2007; Guthrie, Dennerstein,

Taffe, Lehert, & Burger, 2004), but not by others (Avis, Stellato, Crawford, Johannes, & Longcope, 2000). So to what extent the more general improvements in sexual function and enjoyment associated with e.g. menopausal oestrogen replacement, are secondary to the specific effect on vaginal lubrication, or involve direct effects in the brain, remains uncertain (Bancroft, 2009).

Women have circulating levels of testosterone (T) on average about a tenth of those found in men, with these lower physiological ranges making the finding of correlations more difficult. Studies on administration of exogenous androgens, leading to supra-physiological T levels e.g. in surgically menopausal women, showed a relation with sexual desire (Sherwin & Gelfand, 1985a, 1985b). These studies have led to the hypothesis that T may enhance the 'cognitive-motivational' aspects of female sexual behaviour (Sherwin & Gelfand, 1985a, 1985b). More recent, (pharmaceutically sponsored) studies on a T patch for menopausal women have been published (Buster et al., 2005; Braunstein et al., 2005; Shifren et al., 2000). However, therapeutic responses were presented as mean change per treatment group, making it impossible to differentiate between those women who would and would not respond. Further, population-based studies have found minimal or no correlation between T and sexual desire (Davis, Davison, Donath, & Bell, 2005; Guthrie, Dennerstein, Taffe, Lehert, & Burger, 2004).

HC-induced decrease in serum free testosterone. In the context of HC-use, serum levels of T, mostly free or biologically available T, have received quite some attention. It has been known for some time that HC reduces free T (Jung-Hoffman & Kuhl, 1987; Van der Vange, Blankenstein, Kloosterboer, Haspels, & Thijssen, 1990; Janaud, Rouffy, Upmalis, & Dain, 1992; Darney, 1995; Thorneycroft et al., 1999; Boyd, Zegarac, Posvar, & Flack, 2001). This reduction is probably the most common iatrogenic cause for lowered T in women (Bancroft, 2009). HC has a potential effect on T levels by two major mechanisms: (1) blockage of the mid-cycle T rise by suppression of ovulation and the associated pattern of ovarian androgen production, and (2) estrogen-induced increase of plasma proteins with sex steroid-binding properties, such as Sex Hormone Binding Globulin (SHBG), reducing free T (Coenen, Thomas, Borm, Hollanders, & Rolland, 1996; Graham et al., 2007). Coenen and colleagues (1996) further speculated that even if differential progestins exert an intrinsic androgen action, this is negligible compared to this state of "iatrogenic hypo-androgenism".

This mechanism of HC-induced reduction in free T and its relation to sexual desire is very poorly understood and has yielded complex study results. So far, three studies have established a relation between T and sexual desire in OC-users, whose levels are in the lower physiological range (Alexander & Sherwin, 1993; Bancroft, Davidson, Warner & Tyrer, 1980; Bancroft, Sherwin, Alexander, Davidson, & Walker, 1991b). In the earliest study (Bancroft, Davidson, Warner, & Tyrer, 1980), two groups of OC-users were studied: one with and without sexual problems. Interestingly, only the no problem group showed this correlation with sexual desire. It appears as if once a sexual problem has installed itself, other inter- and intrapersonal mechanisms might obscure the relation between T and sexual desire. This lack of correlation between free T and sexual desire has further led to the hypothesis, first suggested by Alexander and Sherwin (1993), that the effect of varying T levels on women's sexual desire will only become apparent when they are close to or below a certain "threshold". This would be similar to the mechanism of the threshold mechanism in men, where T effects are only apparent within a normal T range (e.g., Buena et al., 1993).

Graham and colleagues (2007) published the first study in which the change in free T, mood and sexuality were prospectively measured in women starting on OCs. They found no direct relation between adverse changes in sexual desire and the degree of reduction in free T. However, a correlation between the degree of free T change and sexual desire after three months of use was present. The authors specifically pointed out that a large group of women also experienced a substantial free T reduction without reporting adverse effects on sexual desire, or even experiencing an increase.

Desensitization hypothesis. This last study of Graham and colleagues (2007) confirms the desensitization hypothesis that had been postulated earlier (Bancroft, 2002, 2005). This hypothesis is a theoretical attempt to explain some unanswered questions in relation to androgen effects on sexuality in general.

First, the conflicting study results point to a greater variability in the sensitivity of women to androgens, which could result from a greater genetic variability in women compared to men. So, the genetically determined androgen sensitivity appears to be expressed differently in men and women. Second, men need more T to achieve and maintain peripheral masculinisation (e.g., body hair growth, voice change, muscle bulk). It has been postulated that if men were as sensitive to the central nervous system (CNS) effects of T as females, then the behavioural effects of these masculinising levels would

be maladaptive. Hence, there is a need for 'desensitization' of the brain to behavioural T effects during early male development (prenatally and during post-natal T surge).While the precise mechanisms of this desensitization are not established, a consequence would be that it would flatten out the genetically determined variations in CNS receptor responsiveness to T. Much higher T levels from puberty onwards can then be allowed without hyperstimulation of CNS mechanisms.

Third, with no such desensitization occurring in females, this genetic variability would be more evident at lower T levels and would be manifested as greater variability in behavioural responsiveness. This is supported by studies in women with congenital adrenal hyperplasia, which is associated with higher levels of T during foetal development and some degree of masculinised behaviour, but low levels of sexual desire and activity as well as low fertility (Meyer-Bahlburg, 1999). Although a number of other factors could impair normal sexual development in such context, this evidence is consistent with some degree of desensitization of high foetal T levels, falling to normal after birth and remaining low.

Further, the question remains whether such desensitization is restricted to early developmental critical phases, or whether it could occur in any life cycle. For instance, evidence of tolerance to supra-physiological levels of T in women with repeated exposure has been reported in a number studies in menopausal women on hormone replacement (e.g., Burger et al., 1984; Brincat et al., 1984; Sherwin & Gelfand, 1987; Davis, McCloud, Strauss, & Burger, 1995).This suggests that such desensitization might also occur in women later in life, or at least to some extent.

Finally, this hypothesis predicts that women are not only sensitive to much lower amounts of T than are men, but also show considerable inter-individual variability in their responsiveness to T. The main approach for exploring this would be to look for markers of T sensitivity (Bancroft, 2009).

Measuring androgen sensitivity: the androgen receptor CAG repeat length. As suggested by e.g. the desensitization hypothesis, pre-existing hormonal differences between women might account for different responses to HC-use. In addition to circulating hormone levels (and the distinction between bound and free hormone), women also differ in terms of prenatal hormone exposure (and the accompanying brain organization effects), hormone receptor numbers and hormone receptor sensitivity

(Oinonen, 2009). Considering this, it might be useful to determine hormone sensitivity in looking at sexual effects of HC.

Only one study has examined anthropometric indicators of androgen exposure, more specific the 2D:4D ratio, an anthropometric indicator of androgen exposure, referring to the length of the index and ring finger. That study found OC-users with a lower 2D:4D ratio (usually found in men) to suffer more often from negative emotional and sexual side effects (Oinonen, 2009). Amongst the speculative explanations the authors proposed, there was the 'prenatal organizational effect' hypothesis, consistent with the desensitization hypothesis above. The authors stated that a low 2D:4D ratio may reflect high prenatal T exposure in utero, causing the *androgen receptor* (*AR)* to become either less sensitive (i.e. require higher androgen levels to maintain a correct functioning; down-regulation), or more sensitive (i.e. up-regulation). Considering that OC decreases androgen levels, such women could indeed be more at risk of experiencing androgen-related effects.

Androgen sensitivity is further mediated by variation in the *AR* gene, located on the X chromosome at Xq11-12. The aminoterminal transactivating domain of the *AR* contains a highly polymorphic cytosine-adenine-guanine (CAG) trinucleotide repeat sequence and regulates androgen signalling in steroid hormone-sensitive cells (Brown, et al., 1989; Lundin, Giwercman, Richthoff, Abrahamsson, & Giwercman, 2003). In women, the CAG repeat has thus far mainly been studied in those with polycystic ovaries (e.g., Diaz, Lopez-Bermejo, Petry, de Zegher, & Ibanez, 2010; Kim et al, 2008; Van Nieuwerburgh et al., 2008) and in breast cancer patients (Gonzalez, Javier, Rodriguez et al., 2007). The inhibitory effect of the CAG repeat length on T levels (more CAG repeats associated with weaker *AR* activity and hence higher T levels) in men has not been confirmed in women. Studies have reported that fewer CAG repeats are associated with higher levels of androgens, suggesting a stimulatory effect (more CAG repeats lead to stronger *AR* activity) in women (Westberg et al., 2001).

Psychological factors

Research on the mechanisms that could be underlying the relation between HC and sexual desire has primarily focused on biological factors, and far less on psychological and social factors. Previous studies have mainly looked at the effects of, or co-variation

with, mood. Although sexual self-esteem has received some attention as a mediator of the relation between attachment anxiety and general sexual functioning (e.g., Brassard, Dupuy, Bergeron, & Shaver, 2013), this potential factor of self-esteem –studied in the current dissertation- has not yet been studied in the context of sexual desire of HC users.

A co-varying mood[3] and sexual desire? It is well-recognized that negative mood, whether experienced as anger, depression or anxiety, has a negative impact on sexual desire. Since the experience of sexual desire, in the context of an incentive motivational theory, can appropriately be considered as an emotion, it is interesting to examine the extent to which the processing of both emotions interacts. Several lines of research have tried to explain the sometimes paradoxical relationship between negative mood and sexual desire.

First, there is abundant literature showing that men and women with clinical depression most often show a decreased sexual desire. The association between a depressive mood and sexual desire is not always one of a negative correlation, as older clinical literature has shown. For instance, Angst (1998) showed that among a male depressed sample, 26% reported decreased, but 23% reported increased sexual desire. Surprisingly, there is a decreased tendency to assess increased sexual desire when studying clinical depression, which limits the available evidence. Further, evidence that mood disorders are the most frequent co-morbidity in "sexual addiction" (or compulsive sexual behaviour) (Black, Kehrberg, Flumerfelt, & Schlosser, 1997), is an additional indication that the relation between depression and sexuality is not always unidirectional.

Second, experimental studies have provided limited evidence that the induction of negative mood states might inhibit a following sexual response. A study by Kuffel and Heiman (2006) compared two groups of women, one group mildly to moderately depressed and another with a normal mood. They asked the women to watch erotic films, after instructing them to adopt a positive ("you like your sexuality a lot") or negative ("you do not like your sexuality") sexual schema script, using one of these scripts with each film. The positive script was associated with feeling more aroused then the negative script. Interestingly, the scripts yielded similar effects in all women,

[3] Mood and affect are often used interchangeably in the literature. DSM-IV-TR (2000) defined mood as "a more pervasive and sustained emotional climate'' while affect involves "more fluctuating changes in emotional weather" (p.819).

depressed or not. Evidence of lab-induced mood states on measure of sexual desire is not available to the knowledge of the author.

Third, studies into non-clinical variations in affect and their relationship to sexual desire have also added to this body of literature. A recent study from the Kinsey Institute in 663 female college students and 399 college-aged men showed that the majority of women indeed reported a decreased sexual desire when feeling depressed or anxious (50% and 34% respectively). A minority of both genders (about 10%), however, reported increased sexual desire during those mood states, and more frequent in relation to anxiety than depression (Lykins, Janssen, & Graham, 2006).

The relationship with mood in HC-users. The topic of mood change due to HC remains controversial, despite it is one of the most common reasons reported for discontinuation of usage (Goldzieher & Zamah, 1995; Sanders, Graham, Bass, & Bancroft, 2001). Two approaches have been adopted in research: an earlier, categorical approach assessing the risk of developing a mood disorder, and a more recent, dimensional approach reporting on affect.

The earlier studies were quite concerned that the prevalence of mood disorders might increase due to OC use, due to the relatively high oestrogen levels that were used (Kay, 1984). In this context, those studies mostly compared groups of never-users, past-users and present OC-users, over the course of several months. Studies reported on both increases and decreases of depression rates in OC-users (e.g., Herzberg, Draper, Hohnson, & Nicol, 1971), without reaching a firm conclusion. An early review can be found in Cullberg (1972).

More recent studies have relied on self-rating scales, filled out across the contraceptive cycle or repeatedly for several cycles, which can show trends in mood changes between non-users and OC users. Studies that focused on variability in mood tend to conclude that starting OCs does provide a stabilizing effect on mood. Several studies have found that OC-users showed less variability across the cycle in affect levels compared to non-users (Walker & Bancroft, 1990; Graham & Sherwin, 1993). Interestingly, no researchers have examined group differences in positive affect variability across the cycle. When looking at what trends exist in this variability, most available studies demonstrated that OC users experience less negative affect than non-

users during the menstrual[4] phase (e.g., Wilcoxon, Shrader, & Sherif, 1976, Sutker, Libet, Allain, & Randall, 1983; Boyle & Grant, 1992). Studies are yet to establish whether lower levels of physical symptomatology on OC-users might be the reason behind this decreased negative affect.

Effects on mood or sexual desire in HC-users? Or both? A recurring theme in the earlier literature that looks at both sexual desire and mood in users, is that negative sexual effects could be attributed or are secondary to negative mood changes (e.g., Cullberg, 1972). Considering the evidence above on the link between sexual desire and mood, one should not automatically assume that when HC-use results in a worsening of mood, that a reduction in sexual interest can be expected. Two studies have shown that decreases of sexual desire during OC use can occur without negative mood change. First, Graham and Sherwin (1993), also mentioned above, compared a triphasic OC and placebo as a treatment for premenstrual complaints. Pre-menstrual mood improved in both the OC as the placebo group, while there was a significant decrease in sexual desire only in the OC-group. Second, a placebo-controlled, double-blind study of Graham and colleagues (1995) in 150 women from two different centres (Edinburgh and Manila) demonstrated a subtle worsening of mood in monophasic OC starters, compared to progestin-only-pill starters or the placebo group. This worsening of mood was less marked than the changes in sexual interest, was evident in both centres, and appeared later on in the placebo period. Interestingly, a reduction in depression was found in the progestin-only pill group, while the monophasic OC and placebo group showed a progressing increase. In conclusion, it appears important that both mood/affect are carefully and prospectively assessed in HC research, preferably with negative and positive mood as separate measures.

Social, dyadic and partner factors

The link between relationship well-being and sexual functioning has been repeatedly confirmed in research. Moreover, a specific link was confirmed between sexual desire and relationship functioning, in both men and women (e.g., Brezsnyak &

[4] Technically speaking, OC-users experience a withdrawal bleeding as opposed to menstruation. It is common in literature to also refer to this part of the contraceptive cycle as the "menstrual" phase, as in freely cycling women.

Whisman, 2004). We will now look into several social, dyadic and partner correlates of sexual desire in the context of heterosexual partnerships.

The 'relational' natureof female sexual desire? Inherently contented in the concept of women's sexual desire is the idea that it would primarily be relationally driven and dependent (Meana, 2010). The circular desire model of Basson -although in its original description written in reference to both men and women (Basson, 2001b), but with later focus mainly on the model's applicability to women (Basson, 2000, 2001a, 2002, 2003a, 2003b)- even proposes emotional intimacy to be a crucial, maintaining factor in the experience of women's sexual desire. Unquestionably, sexual desire almost necessarily, but not exclusively, implies the intrinsic yearning for *another* (with the exception of autoeroticism and certain paraphilias, for a review, see Lawrence, 2009). Research into sexual fantasies have demonstrated women's fantasies to be, more often than men's, romantically driven (e.g., Zurbriggen & Yost, 2004), Also, qualitative studies have pointed to the importance of relationship factors in women's desire: feeling desired (Brotto, Heiman, & Tolman, 2009), as well as the feeling of being accepted (Graham, Sanders, Milhausen, & McBride, 2004), is very arousing to women.

However, men and women might not always fit into those strict gender-differentiated narratives when it comes to sexual desire. Meston and Buss's (2007) study could not establish a gender difference in the importance of two categories in reasons for having sex: "love and commitment" and "expression". When it came to the item "I desired emotional closeness", as many men as women endorsed this item.

Sexual desire in a committed partnership. Although the "relational" aspect in female sexual desire has received quite some attention, research has also pointed to a "dampening" of sexual desire in long-term, committed relationships (e.g., Laumann, Gagnon, Michael, & Michaels, 1994; Sprecher, 2002). One could contemplate to reduce this to a mere intertwining of longevity and relationship duration. Of course, as a partnership matures, the partners' ages increase, and research has shown women's sexual desire to decline with age (for a review, see Hayes & Dennerstein, 2005). However, a German study demonstrated that even in the relatively young partnerships of college students, sexual desire declines in the female partner only (Klusmann, 2002). A qualitative study of Sims and Meana (2009) discovered three main themes in women's causal attributions for this decline: (1) the institutionalization of the relationship, as

women blamed the formalization of their union making sex an obligation, (2) overfamiliarity, or the gradual loss of individuality, and, (3) de-sexualized roles, or the incompatibility of the daily roles as mother, professional, and homemaker with the sexual role expected in the bedroom. This was again confirmed by McCall and Meston (2006): formalization of the partnership obviously impacts sexual desire: feelings of love, security, partner support, commitment, and emotional closeness are less likely to lead to sexual desire in married women than in single women.

This relation between sexual desire and the duration of a partnership has not only been approached in research, but from the beginning until today, also received attention from clinical theory. Sex and relationship therapist Esther Perel (2006) states that by cultivating security, stability, love, and commitment, a couple is at risk of losing the very ingredients that fuel their eroticism (e.g., passion, danger, the unknown).

Relationship satisfaction. Since the early studies on sexual desire, it was assumed that marital distress, or conflicts in the non-sexual aspects of a partnership, is reflected in the partners' sexual desire (Verhulst & Heiman, 1988). Relationship dissatisfaction can be a causal factor, as well as an outcome of, lowering sexual desire. The reciprocal cycle of increasing marital distress, reducing sexual intimacy and sexual desire is thought to regularly lead couples into an escalating pattern of sexual dysfunction (LoPiccolo& Friedman, 1988). To the authors' knowledge, very little research has taken into account a couples' perspective on sexual desire, let alone looked at hypotheses pertaining sexual desire and relationship satisfaction in HC users.

Sexual functioning. Close to the relation between sexual desire and relationship satisfaction or functioning, of course also general sexual functioning is related to the experience of sexual desire. Only one study has specifically looked into the importance of sexual functioning with regards to the relation between HC use and sexual desire. An early study of Bancroft and colleagues (1980) compared two small groups of OC users, one group complaining of impaired sexual function, and another group without sexual problems. The observation that a relation between sexual desire and serum T levels could only be found in the no problem group, led the authors to conclude that confounding psychological factors, causal or secondary to the sexual impairment, probably obscured this correlation in that group. At the same time, these results call for an awareness not to overstate the hormonal determinants of OCuse on female sexual

functioning, and definitely accounting for the sexual (dys)functional status of the women participating in such studies.

Partner-related attributes. Apart from the relationship and sexual dynamics itself, the influence of several partner-related attributes on female desire has been studied. In a large, population-based Finnish sample, Witting and colleagues (2008) identified following partner-related attributes to affect female sexual desire: having a partner with a stronger sexual desire, having a partner with inadequate sexual skills, the women refusing to satisfy sexual needs of her partner, and a partner to whom the woman is not attracted. Although in the different context of menopausal transition, an Australian longitudinal, controlled study established that a woman's feelings for her partner and increasing sexual problems in that partner, were major determinants of her sexual desire, above and beyond any hormonal processes that can occur in life (Dennerstein, Dudley, & Burger, 2001).

Clinicians have further reported that, in the context of a heterosexual partnership, his sexual dysfunction can also adversely affect her desire for sex, and improvement can simultaneously increase hers (Brotto& Luria, 2014). From the perspective of an incentive motivation model, partner-related factors that influence the range and intensity of stimuli used and the woman's response to those cues become an important focus. In this context, it is also important to point out that the lower sexual desire (more often the woman's) rather than the higher desire (more often the man's) is identified as a cause in case of interpersonal difficulties in a relationship (Clement, 2002). Consequently, women often experience a discrepancy as their problem (Davis, Katz, & Jackson, 1999; Wood, Mansfield, & Koch, 2007).

In summary, the field studying sexual desire and HC use has been lacking an interpersonal or couples perspective, with mostly taking into account user-characteristics. Future research should better take into account relational-sexual dynamics, partner characteristics, as well as distinguish those factors from the woman's arousability.

HOW DOES GENDER-CONFIRMING TREATMENT AFFECT SEXUAL DESIRE?

Apart from the context of HC use, this dissertation also looked at sexual desire and its correlates in the context of gender dysphoric individuals having received (partial or full) gender confirming treatment (GCT)[5]. Not only have both populations been reported to experience an effect of contraception and treatment, respectively. Both populations further provide a unique opportunity to examine the relative contribution of hormones and psychosocial correlating factors in the relation with sexual desire.

GCT is associated with acquiring primary and/or secondary cross-sex characteristics, through first, administration of cross-sex hormone therapy and, second, surgical intervention(s). Considering this context, the population of gender dysphoric individuals provides us with an interesting paradigm to study both the changes of sexual desire as an iatrogenic effect of GCT, and its correlates. Before we discuss the currently available results on sexual desire in the context of GCT, we will first present a brief overview of the concept of gender dysphoria and the current treatment possibilities.

The history and conceptualization of gender dysphoria

The foundation of the conceptualization of 'transsexualism' was laid by Magnus Hirschfeld (1868-1935), a German physician who was one of the first sexologists of his time and a strong advocate of the first gay rights movement, aiming at decriminalizing *inversion* or homosexual behaviour. Since he feared that this movement risked being divided by effeminate and cross-dressing homosexuals, he differentiated intersexuality, homosexuality, transvestism and transsexualism as natural sexual variations with a biological basis (Hirschfeld, 1910). It was however Stoller, together with Ralph R. Greenson, who introduced the term "gender identity" (Greenson, 1964, Stoller, 1964). Stoller (1968) wrote of a "core gender identity (e.g., I am male)... derived from three sources: the anatomy and physiology of the genitalia; the attitudes of parents, siblings and peers toward the child's gender role; and a biological force that may more or less modify the attitudinal (environmental) forces" (p. 40).

[5] The current doctoral dissertation prefers the use of the broader term "Gender Confirming Treatment", contrary to the older term "Sex Reassignment Surgery". This choice is founded in the current view of the World Association of Transgender Health (WPATH) and its Standards of Care, promoting a view more aimed at gender expression, compared to the previous focus on genital surgery as a prerequisite for treatment.

Together with an increasing endocrinological knowledge in the 1920s, it was discovered that both men and women have male and female sex steroids. It was in the light of the emerging medical knowledge, that a 22-year old American soldier, George Jorgensen, travelled to Denmark in 1952 to receive hormonal treatment and sex reassignment surgery to become Christine Jorgensen. She became the first well-known post-operative trans woman[6] as her story received significant media attention (Jorgensen, 1967). As a consequence, increasing numbers of individuals started seeking treatment. The Danish professionals were supported by Harry Benjamin, a German endocrinologist, skeptical of psychoanalysis' ability to relieve patients' gender dysphoria. He was one of the first to treat individuals in New York and San Francisco in the 1950s and 1960s (Benjamin, 1966). In memory of his pioneering clinical and research work, the "Harry Benjamin International Gender Dysphoria Association (HBIGDA)" (now the "World Professional Association of Transgender Health" or WPATH) was founded.

Transsexualism first became a psychiatric diagnosis in 1980, when DSM-III categorized it as the most extreme subtype of "Gender Identity Disorder", and defined it as "a sense of discomfort and inappropriateness about one's anatomic sex, the wish to be rid of one's own genitals, and to live as a member of the other sex for at least two years" (APA, 1980). During the years, DSM used different conceptualizations, leading up to the current diagnosis in DSM-5 describing the actual symptom, gender dysphoria (DSM-5, p 451). This term, with a long history in clinical sexology, has always captured the distress, due to the profound disconnection between one's biological sex (as assigned at birth) and one's gender identity (or subjective experience of being male, female or other) (Fisk, 1963; Zucker & Brown, 2014).

Today, the term 'transgender' is also frequently used (Ekins & Kind, 2006). This concept is used both as an umbrella term for a variety of gender non-conforming or gender-variant individuals (transsexuals, cross-dressers, gender benders), as well as a description for individuals presenting with a mix of male and female traits (Stryker,

[6] The earliest literature in the 1960s and 1970s used the terminology "transsexual man" and "transsexual women" (e.g., Benjamin, 1966), referring to the birth sex of the individual consulting for CGT. In the 1980s and 1990s the terms "male-to-female (MF) transsexual" and "female-to-male (FM) transsexual" were introduced. Today, as the term transsexualism in general is felt to have negative associations, literature uses the terms "trans men and women", this time referring to the experienced gender identity. For clarity, the abbreviations FM and MF are sometimes added.

1998). The increased popularity of this term represents a moving away from the gender binary, not only in activist circles but also in progressive gender clinics (Nieder, 2011).

Gender Confirming Treatment

Since the story of Christine Jorgensen, much has changed in the field of health care for gender dysphoric individuals. Several reviews have shown consistently that the outcome of GCT is one of significant improvement, for both trans men and women (Green & Fleming, 1990; Pfäfflin & Junge, 1998). We will briefly summarize the current treatment protocol, as it is currently available in the Centre for Sexology and Gender Problems of the Ghent University Hospital (cfr. T'Sjoen, van Trotsenburg, & Gijs, 2013). This CGT-protocol is based on the recommendations as stated in the 7th edition of the Standards of Care (Coleman et al., 2011) of the World Professional Organization of Transgender Health (WPATH).

First diagnostic phase. Most gender dysphoric individuals enter the health care system by contacting a mental health professional with a clear "self-diagnosis" and immediately request GCT. Others may be unsure about their gender identity and seek guidance and advice. Due to the subjective nature of gender dysphoria, a thorough diagnostic phase is recommended.

In this first phase, three clinical goals are paramount. First, a (confirmation of the) diagnosis is obtained. Therefore, the gender dysphoric complaint is thoroughly explored with (next to many other topics) special attention going to psychosexual and gender development, subjective meaning of cross-dressing, sexual behaviour, self-image and sexual orientation[7]. Second, psychiatric co-morbidity is assessed to obtain a diagnostic profile. Recent literature has shown that special attention should be paid to mood and anxiety disorders as the most prevalent Axis I problems (Heylens et al., 2014). Personality disorders (Axis II) and Autism Spectrum Disorders are no formal contra-indication for treatment, but remain a focus during the entire counselling process. Other substantial psychiatric diagnoses are rare (Heylens et al., 2014). Third, thorough

[7] Contrary to early treatment protocols, sexual orientation is currently no longer a decisive factor in the diagnostic phase. However, considering the potential social consequences of becoming part of not one minority group (the transgender community) but two (the gay, lesbian, bisexual community), and the need to assess the individuals skills in dealing with minority stress, the sexual identity remains a topic that receives attention during diagnosis and treatment, when applicable.

psycho-education is needed on the irreversible effects of GCT, in order to obtain realistic expectations concerning both hormonal substitution and surgical intervention (De Cuypere, Heylens, & Elaut, 2013).

Second diagnostic phase. In a second phase, the diagnosis is evaluated on its consistency and feasibility to live in the desired gender role ("real life experience"). Contrary to previous editions of the Standards of Care, a real life experience of at least three months is no longer a necessary step to indicate treatment. Both the first and second diagnostic phase can take up to twelve months, although there is considerable variation in individual trajectories (De Cuypere, Heylens, & Elaut, 2013).

Hormonal substitution. Although many effects are reversible, the step towards hormonal substitution should be carefully considered. In trans women estrogen treatment (oral, e.g., Progynova®, or transdermal, e.g., Oestrogel®, Estraderm®) with anti-androgens (e.g., Androcur®) is used to start feminization of the body (for endocrine guidelines, see Hembree et al., 2009). The effects are difficult to predict with certainty but include breast development, redistribution of fat in a more feminine pattern, softening of the skin, decreased muscle mass and strength, decreasing fertility and lower sexual desire. For trans men, the appropriate treatment is testosterone therapy (e.g., Nebido® or Sustanon®), which can be expected to increase facial and body hair, increased muscle mass and strength, deepening of the voice and clitoral enlargement. Especially after orchiectomy in the trans women, and ovariectomy in the trans man, hormone substitution should be continued lifelong (van Trotsenburg & T'Sjoen, 2013a, 2013b).

Surgical intervention. In trans women, gender confirming surgery consists of a vaginoplasty, or the creation of a vagina (usually out of penile skin, using the penile inversion technique). In the same surgery, an orchiectomy, labiaplasty and clitoroplasty are performed (Monstrey, Weyers, Hoebeke, Buncamper, & Bouman, 2013).In trans men, gender confirming surgeries consist of both breast surgery and genital surgery, mostly performed in three stages: (1) a subcutaneous mastectomy (breast removal), combined with a hysterectomy and ovariectomy (removal of uterus and ovaries), (2) a phalloplasty, or the genital transformation, including the lengthening of the urethra and vaginectomy, scrotoplasty and construction of the penis, (3) implantation of testicle and/or erection prosthesis. It must be stressed that not all individuals choose to undergo all stages (Bouman, Monstrey, & Meijerink, 2013).

Overview of earlier research of GCT, sexual desire and correlating factors

Most of the earlier research in health care for gender dysphoric individuals was aimed at attaining a better understanding of the risks and techniques of surgery (e.g., Monstrey et al., 2009; Lawrence, 2006), the presence of post-surgical regret (e.g., Olsson, & Möller, 2006), and the reduction of the dysphoria (e.g., Smith, van Goozen, Kuiper, & Cohen-Kettenis, 2005). While both hormone substitution and genital surgery can be assumed to have great sexual consequences, it is astonishing how little clinical and research attention has been given to sexual functioning before, during and after receiving GCT. Studies addressing sexual desire are especially scarce. This situation is probably due to the assumption of early literature that gender dysphoria was a hyposexual condition (Person, & Ovesey, 1974a, 1974b; Pomeroy, 1969) and the fear of gender dysphoric individuals to be seen as having merely sexual goals when desiring treatment. Currently, sexual functioning following GCT is seen as an important outcome for most individuals (Klein & Gorzalka, 2009).

GCT and sexual desire in trans women. An early, controlled prospective study compared two groups of trans women in a two-year follow-up: one going through routine procedure (who were still on the waiting list for vaginoplasty) (group R) and one "advanced" group (who had surgery one year and nine months preceding the follow-up assessment)(group A) (Mate-Kole, Freschi, & Robin, 1990). While the authors did not elaborate on that result, they listed a significantly higher sexual desire at follow-up in group A, while desire had not changed in group R.

Rehman and colleagues (1999) published that out of 28 post-surgical trans women, two reported a loss of sexual desire over time. Unfortunately, the authors do not specify whether the decrease preceded the treatment. The study of Schroder and Carroll (1999) also assessed sexual desire directly in a group of 17 post-surgical trans women and reported on its frequency. Sexual desire occurred on a daily basis in two participants (12%), from one to four times of a two-week period for six participants (36%), and once a month or less for another six women (36%). The remaining three women reported no desire for sexual activity (18%). Considering the nature of the assessed information, it is difficult to interpret these percentages as within or beneath a "dysfunctional" range.

A study by Weyers and colleagues (2009) demonstrated that sexual desire (as measured by a subscale of the Female Sexual Function Index) was significantly lower in a

sample of 50 post-surgical trans women, compared to a group of cisgender (or non trans) women without sexual complaints. Further analysis revealed that the subgroup of women in a heterosexual partnership reported similar desire levels as the comparison group. However, this subgroup more often experienced complaints with regards to sexual arousal, lubrication and pain. Finally, a Dutch survey study into the sexual health of lesbian, homosexual, bisexual and transgender individuals selected a subsample of 325 individuals in the male-to-female spectrum, which was a diverse group with regards to treatment status (pre- and post- treatment) but also to treatment wish (*n* = 183 trans women desiring no/partial/full CGT and *n* = 142 transgenderists, "identifying as either partly female, partly male, as something in-between, or as neither" desiring no/partial/full treatment). It was reported that a quarter of trans women experienced weak or absent sexual desire, while only 5% experienced this as a problem. These numbers were significantly lower in the group of MF transgenderists (5% and 0.7%, respectively). Further, none of the trans women and 5% of MF transgenderists experienced an excessive sexual desire (de Graaf, Bakker, & Wijsen, 2014).

GCT and sexual desire in trans men. To the author's knowledge, only two studies have looked into the experience of sexual desire by trans men. A first Italian publication (Costantino et al., 2013) prospectively studied several domains of the sexual functioning in 50 trans men, with data collection starting before hormone substitution, continuing after twelve months of hormone substitution, and finally, after at least six months of surgery (mastectomy, ovariectomy and hysterectomy, no phalloplasty). After one year of T administration, a significant increase was seen in the frequency of masturbation, sexual desire, arousal and sexual fantasies. Since most parameters (with the exception of sexual desire) in the post-surgical assessment returned to baseline, the authors stated that different results might be found in subjects prescribed another treatment regimen (higher T dose), and when sexual functioning would be measured using and a validated scale (instead of one single item). Further, the previously mentioned Dutch study also inquired for the sexual health in 251 individuals in the female-to-male spectrum (*n* = 148 trans men and *n* = 103 transgenderists). In this group, 12% of trans men and 13% of FM transgenderists reported a weak to absent sexual desire, while excessive sexual desire was experienced by 2% of trans men and 1% of FM transgenderists (de Graaf, Bakker, & Wijsen, 2014).

Conclusion. As so very little has been formally studied and published on the relationship between GCT and sexual desire in both trans women and trans men, it cannot be a surprise that the information on which correlates might influence this relation is completely non-existent. Based on the knowledge of sex steroids in both men and women and the significant changes those hormones are subjected to during hormonal substitution, we would expect an impact of both the hormonal and surgical treatment in gender dysphoric individuals. This information is not only relevant to health care providers trying to assess the post-treatment situation in their patients, but also for treatment applicants, who are contemplating whether or not to continue with certain aspects of treatment.

RESEARCH OBJECTIVES OF THE DOCTORAL DISSERTATION

The present doctoral dissertation presents with the main objective to gain more insight into sexual desire and its biopsychosocial correlating factors in two different study populations. First, the majority of women has experience with using one or more forms of HC, but little information is available on its potential sexual effects. To date, research has mainly focused on studying the potential sexual side effects in women starting on OCs, next to adopting an approach comparing several groups of HC users. If we want to broaden this picture, we need to prospectively monitor biopsychosocial correlating factors of sexual desire in women changing between several contraceptive products. Considering previous research has shown the responses of women to be highly variable, it will be useful to use the woman as her own control in this design. Further, we set out to include the partners' sexual desire. In addition to this prospective cross-over design, the current dissertation aimed at increasing our knowledge on similar processes within the contraceptive and menstrual cycle. Previous research has either studied freely cycling women, while very little information on potential cyclical patterns of sexual desire within the contraceptive cycle exists. Moreover, no study has included the partners' perspective. Therefore, prospective diary studies in HC-using couples are needed.

The second aspiration was to gain more insight in the domain of sexual desire in the context of GCT. As research today is lacking the most basic information on the number

of individuals experiencing an impact of GCT on their sexual desire levels, we aimed at quantifying the increases or decreases in individuals who have received GCT in the past. Further, we wanted to start a first exploration of biopsychosocial correlates that could be of importance in this specific population.

Research Questions and Hypotheses

Based on the two main research objectives stated above, the following research questions and hypotheses were tested within the different chapters of this doctoral dissertation.

Estimates of sexual desire changes. In both the study domains of this dissertation, the first research question was aimed at trying to test and/or quantify the changes in sexual desire, both in the context of HC use and GCT treatment. More specifically, we aimed to explore whether women changing between different contraceptive preparations would experience a change in their level of sexual desire, with the expectation that mainly women using combined preparations would report decreasing sexual desire levels. Further, a similar hypothesis was formulated in the context of within-cycle changes of sexual desire in OC users and a control group of freely cycling women. More specifically, we expected a rather stable level of female sexual desire within the cycle of OC users, while a mid-cycle increase was expected in freely cycling women. Finally, the last few chapters aspired to capture the number of individuals who have experienced sexual desire changes throughout the GCT. Based on the knowledge on sex steroids and sexual functioning in other sexological study domains, we hypothesized a decrease in sexual desire in trans women, and an increased sexual desire in trans men.

Biopsychosocial correlating factors of sexual desire. When examining these potential changes in sexual desire, several correlating factors have been tested on their co-variation with sexual desire. First, in the context of HC users, we looked at the biological predictors of contraceptive product and genetic androgen sensitivity. Consistent with the desensitization hypothesis, we especially expected women with a lower androgen sensitivity (shorter *AR* CAG repeat length) to experience decreases in sexual desire. With regards to psychological correlating factors, we expected to find women with a better self-esteem, less depressive symptoms and a higher relationship

satisfaction, to report a stronger sexual desire. We also expected women whose partner had a lower dyadic sexual desire to experience lower levels of sexual desire. In the study on within-cycle patterns, we hypothesized to find a different pattern for negative affect and sexual desire in the female partners, emphasizing the different cyclical pattern of both processes. Second, in the domain of GCT-treatment, we hypothesized that both androgen sensitivity and sex steroid levels would help explain the iatrogenic effects of hormone substitution and surgical intervention on sexual desire. More specifically, we hypothesises a relationship between free T in both trans men and trans women. Further, we expected the treatment satisfaction to correlate with sexual desire.

Chapter Overview

In the first empirical study, *Chapter 2*, we provide a first exploration of the field of contraception in Flanders by mapping the contraceptive profiles, and factors affecting them, in two samples from the SEXPERT- survey 'Sexual health in Flanders'. First, the study aimed at assessing the knowledge and use of emergency contraception in both a population- based sample of 723 women and a probability sample of 216 women of Turkish descent (all aged 14-60 years). Second, the prevalence of current contraceptive use was calculated in a subset of heterosexual, sexually active women of childbearing age (14-49 years). Based on those prevalence rates, the percentage of women risking an unplanned pregnancy could be determined. Third, the role of socio-economic status (income and educational level) and ethnicity in the knowledge of emergency contraception as well as contraceptive use were examined. Results are compared to the epidemiological data from the Health Interview Survey and implications for clinicians and policy makers are discussed.

Chapter 3 extends the previous chapter by applying the biopsychosocial approach in a prospective, within-subject design in contraception-using heterosexual couples consecutively using several contraceptive preparations. Research on the sexuality of contraception-users primarily focused on changes in sexual desire after starting on HC (Graham, Bancroft, Doll, Greco & Tanner, 2007; Greco, Graham, Bancroft, Tanner & Doll, 2007). Staying within that focus on circulating free T levels and psychosexual dynamics, we additionally aimed at exploring the influence of a genetic marker of androgen sensitivity, the *AR* CAG repeat length. First, the potential role of androgen sensitivity in

the effect of contraceptive product on female serum hormone levels was studied. Second, the influence of androgen sensitivity and contraceptive product on female sexual desire was assessed on two levels: solitary and dyadic sexual desire, or the desire to behave sexually by oneself respectively towards a partner. Third, mixed models looked at the potential role of several psychosexual processes (e.g., female sexual dysfunction, depressive symptoms, self-esteem, sexual and relationship satisfaction, sexual desire of the partner) in female sexual desire.

While Chapter 3 looked at which correlating factors affect female sexual desire in the light of different and changing contraceptive products, *Chapter 4* aimed at studying sexual desire within the contraceptive cycle. Although research in freely cycling women repeatedly has shown a mid-cycle peak (around ovulation) in female sexual desire, information on potential cycle shifts in the sexual desire of OC users is lacking. A diary study was designed with 55 heterosexual, OC-using couples, who were current users of one of four contraceptive groups, of which one a control group using non-hormonal contraception (e.g., intra-uterine devices, sterilisation). Both solitary and dyadic sexual desire, frequency of sexual activity, positive, and negative affectwere assessed prospectively.

To further our understanding of factors associated with sexual desire, Chapters 5 to 7 discuss the sexual desire in trans persons, or people with gender dysphoria who have received gender-confirming treatment. The context of gender-confirming treatment, consisting of cross-sex hormone substitution and sex-reassignment surgery, provides an interesting paradigm in which biopsychosocial factors influencing sexual desire can be studied. *Chapter 5* explored the clinical complaints of low sexual desire in trans women (male-to-female individuals after hormonal and surgical gender-confirming treatment). A group of 62 trans women and a control group of 30 freely cycling women (not using hormonal contraception) was studied in a cross-sectional design. First, the prevalence of hypoactive sexual desire disorder was determined. Second, we assessed the association between serum androgen levels and sexual desire in both groups.

Chapter 6 extends on the previous results by exploring whether androgen sensitivity could be a modulating factor in the relationship between serum androgen levels and sexual desire in a subset of the trans women discussed in Chapter 5.

Chapter 7 summarizes two cross-sectional studies on the relation between gender-confirming treatment and sexual desire. A first study explored the role of T substitution

in both the solitary and dyadic sexual desire of 45 trans men (female-to-male individuals after hormone and surgical gender-confirming treatment). A second study extended on the results of Chapter 5 by addressing the association of gender-confirming treatment and sexual desire in 214 trans women and 138 trans men. Both studies looked into the changes in sexual desire during treatment, based on retrospective data.

Finally, *Chapter 8* presents a general discussion of the most important findings of the above-mentioned studies. Both limitations and strengths of the studies are stated. Methodological and clinical implications, as well as a focus for future research in the field of sexual desire, are presented.

Table 1. Overview of different studies examining sexual desire and its bio-psycho-social correlates

	Chapter 2	**Chapter 3**	**Chapter 4**	**Chapter 5**	**Chapter 6**	**Chapter7**
Main goal	contraceptive prevalence	sexual desire change switching HC	cycle-related change in HC-users and non-users	HSDD after GCT and relation to T	interaction CAG and T on sexual desire/HSDD	sexual desire after GCT ; relation with T and GCT
Biological factors		total & free testosterone CAG repeat length	bleeding days	total & free testosterone	total & free testosterone CAG repeat length	total & free testosterone, LH treatment status physical functioning
Psychological factors		mood psychological well-being self-esteem	mood weekend preference			mental functioning
Social/dyadic factors	income educational level	relationship satisfaction sexual functioning	relationship satisfaction sexual satisfaction sexual activity	relationship satisfaction sexual satisfaction		relationship status relationship duration
n	723 women general population (sample I) 216 women Turkish minority (sample II)	55 heterosexual couples	89 hetero couples (63 COC, 26 NHC)	62 trans women 30 freely cycling women	34 trans women	46 trans men (study I) 138 trans men and 214 trans women (study II)
Design	population survey	randomised within-subject cross-over	diary study	cross-sectional	cross-sectional	cross-sectional follow-up

Note. GCT: gender-confirming treatment, HSDD: hypoactive sexual desire, T: testosterone, CAG: androgen sensitivity, COC: combined oral contraception, NHC: non-hormonal contraception

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CHAPTER 2

CONTRACEPTIVE USE IN FLANDERS (BELGIUM): A COMPARISON BETWEEN A GENERAL POPULATION AND A TURKISH ETHNIC MINORITY SAMPLE[1]

ABSTRACT

The goal of the present study was to identify contraceptive profiles, and factors affecting these, among women of childbearing age, living in Flanders. The prevalence of knowledge and use of the emergency contraceptive pill (ECP) and contraceptive use is assessed in two samples from the SEXPERT-survey 'Sexual health in Flanders': (1) a population-based sample (*n* = 1832, aged 14-80 years), and, (2) a probability sample of respondents of Turkish descent (*n* = 432, aged 14-60 years). Knowledge, but not use, of the ECP is significantly lower amongst women from the ethnic minority sample, even after correction for income and educational background. A lower educational level is associated with less knowledge of the ECP in *both* samples. In the general population sample, 16% of sexually active women of childbearing age are at risk of an unplanned pregnancy, compared to 14% of their peers of Turkish origin. Those rates are comparable, even after controlling for the different socio-economic status (income and educational level) in both samples. Contraceptive profiles of sexually active women of Turkish descent residing in Flanders are mostly similar to those of their counterparts in the general population. Further research is required to develop strategies to improve ECP-knowledge amongst women with lower educational achievement.

[1] Based on Elaut, E., Buysse, A., Caen, M., Vandamme, J., Vermeire, K., & T'Sjoen, G. Contraceptive use in Flanders (Belgium): a comparison between a general population and a Turkish ethnic minority sample. Provisionally accepted by the *European Journal of Contraception and Reproductive Health.*

INTRODUCTION

Policy makers involved in contraception and reproductive health care in Flanders currently lack information on the number of women at risk of an unplanned pregnancy, and on the factors potentially influencing that risk. Reliable data on the prevalence of current contraceptive use, in the general population as well as in ethnic minorities, are needed to calculate that number. In Belgium, the Health Interview Survey (HIS) is conducted throughout the different regions every four years. The most recent epidemiological data on contraceptive use (HIS-edition from 2004) (Bayingana et al., 2006), showed that 75% of sexually active women aged 14-49 years (or their partners) living in Flanders (the northern, Flemish-speaking part of Belgium, which has about 6 million inhabitants) had used contraception during the twelve months preceding the survey. Most of the women using contraception reported that they had relied on oral contraception (57%) or sterilisation (15%), with 0.7% stating they used the emergency contraceptive pill (ECP) (Bayingana et al., 2006).

Although the HIS provides epidemiological data on contraceptive use for the general Belgian and regional population, use in the Turkish and Moroccan ethnic minorities, the largest ethnic minority groups in Flanders, has rarely been studied. Research from the 1990s showed that of 20- to -39- years- old, married women of Turkish and Moroccan descent, 75% and 72%, respectively, reported current contraceptive use (Lodewijckx, 1996), a figure similar to that pertaining to their Belgian peers (Bayingana et al., 2006). In the nineties, women of Turkish and Moroccan descent living in Belgium used more modern contraceptives than those living in their country of origin (contraceptive use 10% and 30% lower in Turkey and Morocco, respectively) (Lodewijckx, 1996).

To obtain a larger sample of Flanders' largest ethnic minorities, Levecque and colleagues (2006) grouped the data concerning contraceptive use from three consecutive HIS-editions (figures from the 1997, 2001 and 2004 surveys). Unfortunately, because of their small size, the data from both ethnic minorities were analysed together. Based on a definition taking into account both country of origin and current nationality, it was found that 2.4% of the sample was of Turkish or Moroccan descent, and that both ethnic minorities were the largest in Belgium (Levecque, Lodewyckx, & van den Eeden,

2006). Women of Turkish or Moroccan origin used far less contraception than their Flemish peers (39% vs 75%) (Levecque, Lodewyckx, & van den Eeden, 2006). That seems to contradict the results of the 1990s analysis by Lodewijckx (1996).

Although the percentage of pregnancies ending in an induced abortion in Belgium is low according to Eurostat-data (in 2011, 13% of pregnancies ended in an abortion, compared to 20% in both Spain and the United Kingdom), recent data collected amongst women consulting Flemish abortion clinics suggest that contraceptive use is lower amongst women of Turkish and Moroccan descent than amongst their native Belgian peers (Neefs & Vissers, 2005). Women of the first and second generation (with at least one parent born abroad) were very much overrepresented (compared to their relative number in the general population), as they accounted for 39% of the sample. The authors reported that 71% of the women of Turkish descent and 64% those of Moroccan descent had been using contraception in the year preceding the consultation at the clinic, compared to 79% of the women of Flemish origin. In the sample studied by Neefs and Vissers (2005), the women of Turkish descent were more often married (63%) than those of Flemish origin (25%); women of Turkish descent also were of higher parity than the women of Flemish origin (two or more children: 50% vs. 31% and nulliparous: 34% vs. 47%).

While the epidemiologic data of the HIS (Bayingana et al., 2006; Levecque, Lodewyckx & van den Eeden, 2006) can shed a light on contraceptive practices of the general population and the largest ethnic minorities in Flanders, they do not allow us to estimate the number of sexually active women not using contraception. The prevalence of women at risk of unplanned, and potentially unwanted, pregnancies in Flanders remains unknown. The current study quantifies the knowledge and use of the ECP, as well as the prevalence of contraceptive use amongst women drawn from a population-based sample and others drawn from a probability sample of respondents of Turkish descent (second generation immigrants) in Flanders. The study also aims to examine the role of socio-economical factors in the knowledge of the ECP and contraceptive use.

METHODS

Survey method: general population and Turkish ethnic minority sample

This study is based on data from two surveys conducted in Flanders. The first one, 'SEXPERT I: Sexual health in Flanders' (Buysse et al., 2013), was a large-scale representative survey on sexuality, sexual health and relations in Flanders. That survey contains extensive information on sexual health characteristics and bio-medical, psychological, demographic and socio-cultural correlates. Because sexuality is an aspect of life which concerns both young and older people, respondents aged 14 to 80 years were included. Data were collected between February 2011 and February 2012. The final database consists of 1832 respondents (response rate: 39% of the eligible subjects). Respondents were randomly drawn from the Belgian National Register. To enhance statistical power every third of the sample consisted of people belonging to one of three predefined age categories (14 to 25, 26 to 49 and 50 to 80 years). After data were collected, the final sample of women and men was weighted by gender, age, and schooling level so that they would be representative of the Flemish population aged 14–80. All data were gathered via face-to-face interviews, with a combination of computer-assisted personal interviewing (CAPI) and computer-assisted self-interviewing (CASI). In addition, all sensitive information, i.e. a wide range of sexual health characteristics, was gathered in a CASI setup, so that respondents never had to share private information about their sexual health with the interviewer. Detailed study design and recruitment information have been previously described (Buysse et al., 2013).

The second survey 'SEXPERT II: Sexual health of ethnic minorities in Flanders' refers to a similar study conducted amongst the largest ethnic minority groups in Flanders. That study used a similar methodology (mixed CAPI/CASI- design) as the SEXPERT I study and took place between December 2011 and February 2013. Data were gathered in a population-based probability sample drawn from the two largest, non-Western, ethnic minorities in Flanders: people of Turkish or Moroccan descent. The first stage in the sampling method consisted of selecting Primary Sampling Units, i.e. the Flemish municipalities. By ordering and systematic sampling, it was ensured that the chance of a municipality being selected was proportional to the number of inhabitants meeting the criteria for eligibility (between 14 and 60 years of age, of Belgian nationality, with at

least one parent born with the Turkish or Moroccan nationality). Secondly, respondents were randomly selected from the Belgian National Register. Since the subsample of Moroccan descent yielded a very low response rate (26%), it was decided to only take into account the subsample of Turkish descent (*n* = 432, response rate: 57% of eligible respondents) for further analyses. The data from the final total sample of women and men of Turkish origin were weighted by gender and age in order to make them representative of the population of Flemish residents of Turkish descent, aged 14-60 years.

Data definition

Sexual activity. All study participants were asked if they ever had sex and if they ever had sexual intercourse. Sex was defined as *'several ways of making love during which there is genital contact, i.e. the touching of someone's genitals'*. Sexual intercourse was defined as *'penetration of the penis into the vagina or anus*'. Throughout the questionnaire, those definitions were repeated to maximise the chance of all participants having a similar understanding of these operational definitions. Respondents were assessed as sexually active when they responded that they had having had sex (as defined above) in the last six months preceding the survey.

Contraceptive use. In women who were pre-menopausal, information was gathered on their current contraceptive method. That question listed 13 of the most prevalent contraceptive methods and an open answer category. For further analyses, those methods were divided into four categories: (i) long acting methods (intraterine system [IUS], intrauterine device [IUD], hormonal implant, contraceptive injection and female or male sterilisation); (ii) pills (both combined oral contraceptives [COCs] and progestin-only pills), vaginal ring and patch; (iii) barrier methods (condom), coitus interruptus and rhythm methods; and (iv) no method. While coitus interruptus and rhythm methods are not barrier methods, they were added to the third category as the numbers were not high enough to justify a five way split of the contraceptive methods. Women were also assessed on the perceived difficulty of employing their current method. All women in the survey were asked about their knowledge and use of the ECP and, for those who had resorted to it, on the frequency of its use.

Indicators of socio-economic status. These consisted of subjective income, educational level and profession. The first indicator, income level, captures the extent to which respondents dispose of sufficient resources to meet their daily needs. We turned that indicator into a variable with three categories, distinguishing people who have difficulties living comfortably (answers 1-3), people who do not find it really hard to live comfortably (answers 4-5) and people who find it very easy to live comfortably (answers 6-7). The second indicator measured the educational level; respondents selected -with the help of an answer card listing all possible diplomas in the Belgian education system- the highest attained educational level. Apart from those socio-economic indicators, information was gathered on both marital and relationship status. Finally, the importance of religion was assessed. The answer categories of the variables listed above are all listed in Table 1.

Data analysis

SPSS version 20 was used. As described in the Methods above and depicted in Figure 1, the current study used data from two surveys. Both the general population and the probability sample from the Turkish ethnic minority were merged into one file. Chi-square tests were performed to test the differences between categorical variables (e.g., experience with sex and sexual intercourse). Since the age distributions in the general population sample differed from that in the ethnic minority sample (general population sample: 14-80 vs. ethnic minority sample: 14-60 years), analyses for the general population data were performed on the smaller, 14-60 years, subset of the data.

Figure 1 further illustrates how the analysis of knowledge and use of the ECP was performed on the total sample of women, aged 14-60 (n = 940, socio-demographic characteristics in left part of Table 1). For the analysis of contraceptive use and risk of unplanned pregnancy, a subset of heterosexual women of childbearing age (between 14 and 49 years), sexually active (in the last six months), not pregnant or without desire to become pregnant and not (post-) menopausal, was used (n = 501, right part of Table 1).

Finally, two stepwise logistic regressions were carried out to assess the role of different socio-economic indicators on knowledge of the ECP and contraceptive use.

Table 1. Socio-demographic characteristics and sexual activity of women in the general population and the Turkish ethnic minority sample

Women aged 14-60					*Sexually active women aged 14-49*			
General population		Turkish minority			General population		Turkish minority	
n = 724		*n* = 216			*n* = 389		*n* = 112	
n	%	n	%		n	%	n	%
				****Age, years****				
63	9	19	9	14-17	24	6	1	0.9
181	25	72	33	18-29	128	33	30	27
140	19	64	30	30-39	120	31	51	46
160	22	41	19	40-49	116	30	30	27
180	25	20	9	50-60				
724		216		Valid n	388		112	
				****Marital status≠ ****				
205	28	62	29	Nevermarried/cohabited	121	31	10	9
321	45	129	60	Married	160	41	95	86
19	3	3	1	Widowed	1	0.3	0	0
59	8	17	8	Divorced	24	6	3	3
8	1	3	1	Separated	2	0.5	1	0.9
102	14	2	0.9	Cohabiting	74	19	2	2
8	1	0	0	Other	6	2	0	0
722		216		Valid n	388		111	
				****Steady partner*				
575	79	144	67	Yes	341	88	104	94
724		216		Valid n	388		112	

Women aged 14-60					*Sexually active women aged 14-49*			
General population *n* = 724		Turkish minority *n* = 216			General population *n* = 389		Turkish minority *n* = 112	
n	%	n	%		n	%	n	%
				****Parity‡***				
212	31	33	25	Nulliparous	148	38	19	21
291	43	99	75	One or two children	156	41	73	79
172	25	0	0	Three or more children	85	22	0	0
675		132		Valid n	389		92	
				****Educational level‡ *****				
107	15	48	23	Currently still in school	56	14	6	6
98	14	57	27	Lower education	34	9	35	33
132	18	67	32	Lower secundary scholing	68	18	45	42
155	21	26	13	Higher secundary scholing	88	23	15	14
232	32	10	5	Higher education	143	37	6	6
724		208		Valid n	389		107	
				****Importance of religion‡ *****				
140	20	3	1	Very unimportant	88	23	0	0
196	27	3	1	Quite unimportant	114	30	3	3
194	27	15	7	Neither important, nor unimportant	108	28	7	6
151	21	61	28	Quite important	55	14	35	32
38	5	133	62	Very important	21	5	65	59
719		215		Valid n	386		110	

Women aged 14-60					*Sexually active women aged 14-49*			
General population *n* = 724		Turkish minority *n* = 216			General population *n* = 389		Turkish minority *n* = 112	
n	%	n	%		n	%	n	%
				******Subjective income≠******				
96	13	85	39	Difficult living comfortably	38	10	46	41
294	41	97	45	Not really difficult living comfortably	158	41	50	45
331	46	34	16	Very easy living comfortably	192	50	15	14
721		216		Valid n	388		111	
				Sexual activity				
669	93	160	74	***Ever had sex	/	/	/	/
723		216		Valid n				
642	98	152	96	Ever had sexual intercourse≠	373	98	104	95
656		159		Valid n	381		109	
567	85	133	84	Sexually active last six months≠	/	/	/	/
668		159		Valid n				

Note. Sum of subsections (valid n) might differ slightly from the total n due to the application of a weighing factor.
≠ Percentages for these variables were calculated on the valid n (in subsection of the table) and not on total n (above the table), due to missing values (number of missing values = total n minus valid n).
**p*<.05, ** *p*<.01, ****p*<.001

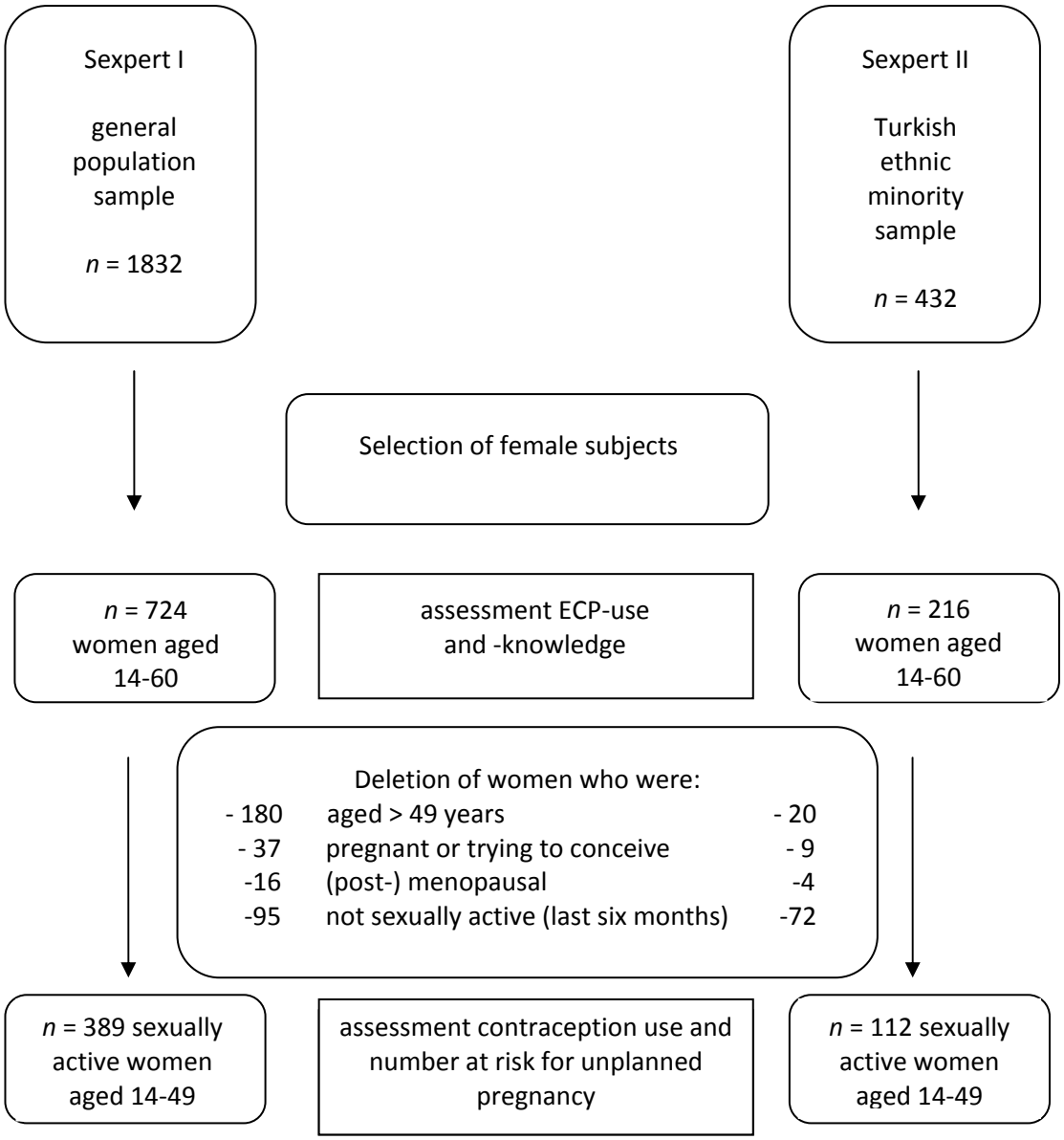

Figure 1. Overview of study datasets and analyses

RESULTS

Socio-demographic characteristics

Table 1 lists the socio-demographic characteristics of both groups as they will be used for further analysis. Those mentioned on the left side of the table refer to the total sample of subjects aged 14 - 60 years which was used for the analysis on the knowledge and use of the ECP. Within that first group, the women of Turkish origin are younger, more often married (instead of cohabiting), more religious and less wealthy than their native Belgian peers. No difference was found with regard to being in a steady relationship. The second sample of sexually active women aged 14-49 years, used for the analysis on contraceptive use (right side of Table 1), largely depicts the same differences between the general population and the Turkish ethnic minority. In that second sample, the difference in being in a stable relationship disappeared.

Table 1 also contains some information on the sexual activity of the study samples. The first sample, aged 14-60 years, presents with a lower lifetime prevalence of sex but a similar lifetime prevalence of sexual intercourse (according to above-mentioned definitions) for the women of Turkish origin.

Knowledge and use of the emergency contraceptive pill

This analysis uses the first sample of female subjects aged 14-60 years (n = 940, see Table 1). All women in that sample were assessed on their knowledge of the ECP. In the general population, 94% (n = 674) of women have knowledge of the ECP; that percentage is lower (51% or n = 109) in the Turkish ethnic minority sample ($\chi^2(1) = 221.683$, $p < .001$).

Only women who knew about the ECP, were asked about the frequency of their use of it. The left hand column of Table 2 depicts the frequency of use in all women with knowledge of the ECP whereas the right column divulges the frequency of use in women who used it at least once. There is no significant difference ($\chi^2(1) = 1.370$, $p = .242$) between the two populations with regards to the numbers having used the ECP at least once, amongst women who knew about it. So while the knowledge of the ECP differs

between the women from the general population and those of the Turkish minority, there was no significant difference in the use of emergency contraception.

Table 2. Frequency of use of the emergency contraceptive pill (ECP) in the general population and the Turkish minority sample, aged 14-60 (*n* =783)

	Frequency ECP-use (in women with knowledge)		Frequency ECP-use (in women with user experience)	
General population sample	*n* = 674		*n* = 127	
	n	*%*	*n*	*%*
Never	474	79	/	/
At least once	127	21	/	/
Valid n	601		127	
Once	/	/	79	62
Twice	/	/	25	20
Three times	/	/	12	9
Four times or more	/	/	11	9
Turkish minority sample	*n* = 109		*n* = 11	
	n	*%*	*n*	*%*
Never	57	84	/	/
At least once	11	16	/	/
Valid n	68		11	
Once	/	/	5	/
Twice	/	/	3	/
Three times	/	/	0	/
Four times or more	/	/	3	/

Note. To avoid repetition, the left side omits percentages of multiple ECP-use. Similarly, the right side omits percentages on having used the ECP at least once.Percentages of the frequency of ECP-use in women of Turkish origin with user experience have been omitted due to low numbers.
≠ Percentages for these variables were calculated on the valid n (in subsection of the table) and not on total n (above the table), due to missing values (number of missing values = total n minus valid n).

Current contraceptive use

The analysis of contraceptive use was carried out in the second sample of women (*n* = 501, see Table 3). In the *general population sample,* 84% of the women reported having used at least one contraceptive method. The most popular method (38%) was the COC, followed by the levonorgestrel releasing-intrauterine system (LNG-IUS) (14%) and female sterilisation (10%; Table 3). In the *Turkish ethnic minority sample*, 86% of the women stated they had used at least one contraceptive method. Again, the COC was the most popular method (37%), followed by female sterilisation (19%) and the LNG-IUS (11%; Table 3).

Since the use of the most popular methods did not differ between both samples ($\chi^2[3] = 7.121$, $p = .068$), the analysis shown in Table 4 is carried out on both the general population and Turkish minority sample together. In this sample, women most commonly relied on contraceptive pills, the ring or the patch, while barrier methods were less often resorted to.

The age groups differed in the frequency they chose a certain method (Table 4). Combined hormonal contraception (COCs, the vaginal ring and the patch) is the most popular in the youngest age groups (14-17 and 18- 29 years), whereas women aged 30-39 and 40-49 years mostly rely on long-acting methods (mostly an IUS). Furthermore, the women at risk are not the youngest age group, but the women in their thirties and forties (Table 4).

The difficulty of use of contraception is shown in Table 5. A small minority reported the current contraceptive method as being very difficult to use. The long-acting methods were generally experienced as very easy in use, whilst a minority of the women found using COCs and barrier methods quite difficult. The difficulty of use was very similar in both samples (data not shown).

Table 3. Current contraceptive use in the sexually active general population sample and Turkish minority sample (*n* = 501)

General population sample *n* = 377 [#]			Turkish minority sample *n* = 105 [#]	
n	*%*		*n*	*%*
60	*16*	*No contraceptive method*	*14*	*13*
106	*28*	*Long-acting methods*	*37*	*35*
54	14	LNG-IUS*	11	11
36	10	Sterilisation (female)	20	19
2	0.5	Sterilisation (male)	0	0
6	2	Copper intrauterine device	5	5
4	1	Contraceptive injection	0	0
3	0.8	Hormonal implant	1	1
1	0.3	LNG-IUS* and CI*	0	0
188	*50*	*Pills, ring and patch*	*42*	*40*
143	38	COC*	39	37
15	4	Contraceptive ring	1	1
9	2	Progestin-only pill	1	1
14	4	Condom and hormonal method	0	0
1	0.3	Contraceptive patch	1	1
3	0.8	COC and CI	0	0
1	0.3	COC, CI and condom	0	0
2	0.5	COC, periodic abstinence, condom	0	0
23	*6*	*Barrier methods ǂ*	*12*	*11*
17	5	Condom	6	6
0	0	CI*	3	2
2	0.5	Periodic abstinence/ rhythm	2	2
3	0.8	CI* and condom	1	1
1	0.3	CI and periodic abstinence	0	0

Note. The sum of subsections might differ slightly from the total n due to the application of a weighing factor and due to rounding percentages to the nearest unit.

[#] Eleven women in the general population sample and8 women in the Turkish minority sample did not provideinformation on contraceptive use.

* LNG-IUS,levonorgestrel releasing-intrauterine system; COC, combined oral contraceptive; CI, coitus interruptus.

ǂ While coitus interruptus and rhythm methods are not barrier methods, these were added to this category since numbers were not high enough to justify a more stratified split.

Table 4. Contraceptive methods in the general population and Turkish minority sample (*n* = 501)

	Total sample	14-17-years	18-29-years	30-39-years	40-49-years
	%	*%*	*%*	*%*	*%*
No method	15	4	13	15	22
Long-acting methods	29	0	8	37	46
Pills, ring and patch	48	83	76	39	24
Barrier methods≠	8	13	3	9	9

Note. ≠ While coitus interruptus and rhythm methods are not barrier methods, these were added to this category since numbers were not high enough to justify a more stratified split.
[#] Eighteen women did not provide information on contraceptive use.
Relationship contraceptive and age groups: $\chi^2(9)=109.407$, $p<.001$

Table 5. Experienced difficulty of use in the general population and Turkish minority sample (*n* = 409)

	Very difficult	Quite difficult	Not easy not difficult	Quite easy	Very easy
	%	*%*	*%*	*%*	*%*
Long-acting method	0	0	1	4	95
Pills, ring and patch	0.4	8	8	23	60
Barrier methods≠	0.3	6	20	34	40

Note. [#] Of the 409 women using contraception (see Table 3), information on the difficulty of use was missing in 60.
≠ While coitus interruptus and rhythm methods are no barrier methods, these were added to this category since numbers were not high enough to justify a more stratified split.
Relationship experienced difficulty of use and contraceptive groups: $\chi^2(8) = 50.729$, $p < .001$

The role of socio-economic status in contraceptive profiles

One might argue that the observed difference in knowledge of the ECP between the samples is due to discrepancies in socio-economic status. Furthermore, although the frequency and method of contraceptive use are comparable in both samples (see above), it is possible that the socio-economic status of the women at risk of an unplanned pregnancy (in both samples) differs from that among women not at risk. Those hypotheses were tested by two stepwise binomial logistic regressions, (i) with knowledge of the ECP (yes/no) in the women aged 14-60 years as a dichotomous outcome variable, and (ii) with contraceptive use (yes/no) in the women aged 14-49 years as a dichotomous outcome variable.

The first step of those two separate binomial logistic regression analyses takes into account the (bivariate) effect of the sample (general population vs. Turkish minority sample) on the knowledge of the ECP or contraceptive use. The second and third steps of the analyses once again assess the effect of the sample, but this time controlling for educational level and income (second step) and including a two-way interaction between the sample and educational level (third step). Educational level is included since that indicator might be related to knowledge (e.g., on contraception); while income is chosen as the most relevant indicator for the means available for a woman to spend on contraceptives. The potential additional indicator, (profession), was not included since that would lead to multi-collinearity (intercorrelation between the predictors in a multiple regression).

When looking at the first hypothesis on the difference in ECP-knowledge, the bivariate model shows that women from the general population are 14 times more likely to know of ECPs (*B* = 2.647; *Exp(B)* = 14.112) (with a 95% confidence interval [*CI*] for the odds ratio [*OR*] of 9.5- 21.1). This difference persists, even after controlling for socio-economic status (Table 6).

Women with a lower overall educational attainment are less likely to know of ECPs (*B* = -1.766; *Exp(B)* = 0.171) (95% *CI* for the *OR*: 0.1-0.3). Comparably, women with a lower secondary educational level are half as likely than higher educated women to know about ECP (*B* = -0.618; *Exp(B)* = 0.539) (95% *CI* for the *OR*: 0.3-1.0). The only significant interaction effect between sample and educational level is found in step 3: the difference in ECP-knowledge between samples is smaller when only students are

compared (*B* = 2.953 - 1.365 = 1.588). This means that the difference in ECP-knowledge between both samples is similar in all groups, except for the students. When only the group of students is considered, the difference between samples in ECP-knowledge is smaller compared with the overall difference between samples (Table 6).

Table 6. Effect of sample, educational level and (subjective evaluation of) income on knowledge of the emergency contraceptive pill (ECP)

Knowledge of the ECP (yes versus no) *Reference: no*			
	Step 1 *B*	Step 2 *B*	Step 3 *B*
Constant	0.033	1.162	0.798
1. Ethnic background of the sample *Reference: Turkish ethnic minority*	2.647***	2.312***	2.953***
2. Educational level *Reference: higher secondary/ higher education*			
student (still in school)		-0.469	0.181
no/lower education		-1.766***	-1.425**
lower secondary		-0.618*	-0.200
3. Income *Reference: very easy living comfortably*			
Not really difficult living comfortably		-0.500	-0.516
Difficult living comfortably		-0.245	-0.274
4. Sample*educational level° *Reference: higher secondary or higher education/Turkish ethnic minority*			
Student (still in school)/general population survey°			-1.365*
Explained variance (Nagelkerke R^2)		0.370	0.376

Note. °Only significant two-way interaction effects are included in the table, step 3.
*p < .05. ** p < .01. ***p < .001

When looking at the second hypothesis, both groups are just as likely to avoid risking an unplanned pregnancy (*B* = 10.149; *Exp(B)* = 0.861) (95% *CI* for the *OR*: 0.5-1.6). This similarity between both samples remains unchanged when controlling for income and educational level. Furthermore, step two reveals that the odds of students (still at school) using contraception are four times higher than the odds of women who finished their higher education (*B* = 1.455; *Exp(B)* = 4.285) (95% *CI* for the *OR*: 1.3-14.1). The interaction effect, as shown in step three, indicates how that effect is a lot stronger in the general population sample (*B* = 1.455 + 3.394 = 4.849) compared to that of the Turkish ethnic minority (Table 7).

Table 7. Effect of sample, educational level and (subjective evaluation of) income on contraceptive use

Contraceptive use (yes versus no) *Reference: no*	Step 1 *B*	Step 2 *B*	Step 3 *B*
Constant	1.821	1.505	2.239
1. Ethnic background of the sample *Reference: Turkish ethnic minority*	-0.149	-0.089	-0.877
2. Educational level *Reference: higher secondary/ higher education*			
student (still in school)		1.455*	-1.316
no/lower education		0.915	-0.386
lower secondary		0.281	-0.212
3. Income *Reference: very easy living comfortably*			
Not really difficult living comfortably		-0.225	-0.184
Difficult living comfortably		0.068	0.068
4. Sample*educational level° *Reference: higher secondary or higher education/Turkish ethnic minority*			
Student (still in school)/general population survey°			3.394*
Explained variance (Nagelkerke R^2)		0.049	0.086

Note. °Only significant two-way interaction effects are included in the table, step 3.
*$p < .05$. ** $p < .01$. ***$p < .001$

DISCUSSION

Findings and interpretation

As part of a population survey on sexual health (SEXPERT: Sexual health in Flanders) (Buysse et al., 2013), the current study brings to light a lower prevalence of knowledge, but a similar frequency of use, of the ECP in a probability sample of women of Turkish descent (second generation), compared to a population-based sample of women from the general population. The prevalence of contraceptive use, and therefore the number of women at risk of an unplanned pregnancy, is very similar in both groups.

Knowledge about the ECP (after controlling for educational background and income) is considerably lower among women of Turkish descent. Women acculturated within a Turkish community, are embedded in a quite different value system when it comes to contraception and motherhood (Callaerts, 1996; Schoenmaeckers, Lodewijckx, & Gadeyne, 1999). The difference in ECP-knowledge might be due to the virginity standard and the greater emphasis on founding a family soon after marriage in that group. Since ECP-knowledge does not fit well into those cultural values, it is possible that the information on the ECP, as provided in relationship and sexual education at school, is less often picked up amongst women of Turkish descent. In *both* groups, women with a lower educational background are less informed than higher educated women.

Again, after controlling for socio-economic status (educational background and income), women of Turkish descent appear to be using contraception at rates comparable to those of the general population, and have a similar prevalence of risk of unplanned pregnancy. This is supported by results from related analyses of the SEXPERT-data (Vandamme et al., unpublished), which show that the frequency of unplanned pregnancies is the same in both the Turkish and the general population sample. Furthermore, the current study's percentage of women in the oldest group (40-49 years) risking unplanned pregnancy (22%), is in line with the Flemish abortion percentage in this age group (23%) (M. De Wilde, personal communication, 2013). These results can help to dispel the myth that *only* young women are at risk of unplanned pregnancies.

Finally, in both the general population and the Turkish ethnic minority, there is no difference in contraceptive use between women with a lower (secondary) educational background and those with higher educational achievements. However, women still in school are four times more likely to use contraception and appear to postpone having their first child, possibly until after they finish their training.

Both groups list a very similar top three most commonly used contraceptive methods: COC, LNG-IUS and female sterilisation. Moreover, the division of different contraceptive methods (long-acting, barrier, pills) as well as the age distribution of those methods is also similar: younger women mostly rely on oral contraception while long-acting methods are preferred when fertility declines or when childbearing is thought to be over. Despite the great emphasis on motherhood for women of Turkish origin (Callaerts, 1996), it appears that that group has adopted the Western standard of family planning by using modern forms of contraception.

Strengths and weaknesses of the study

'Sexual health in Flanders' is the first population-based survey on sexual health in Flanders. Its strength lies in its large representative sample and the use of CAPI/CASI interviewing techniques, which improve the quality of the data by reducing social desirability in responses. The current study describes the results of a population-based sample and a probability sample of Turkish descent. A weight factor is applied for age to make the samples representative of the general population and the Turkish ethnic minority in Flanders.

Socio-demographic differences (e.g., income, educational level) between both samples persist, despite weighting the datasets for age. By controlling for this in two stepwise binomial logistic regressions, the possibility is ruled out that the existing differences in socio-economic status are the underlying causes for the remaining differences in contraceptive profiles.

Unfortunately, due to a very low response rate in the Moroccan sample, it is impossible to present any results for the second, large, ethnic minority in Flanders.

Differences in results and conclusions in relation to other studies

The present results point towards 16% and 14% of women in the general population and women of Turkish descent, respectively, risking an unplanned pregnancy. A lower percentage (9%) was recently reported by Dutch investigators analysing data of a population survey (Picavet, 2012). The latter also brought to light two trends confirmed by our study: firstly, COCs, the IUS and female sterilisation are the most popular contraceptive methods, while relatively new methods (such as the vaginal ring and contraceptive patch) are rarely used; and, secondly, the use of long acting methods, mainly the LNG-IUS and female sterilisation, increases with age.

A similar range of contraceptive use for women of Turkish descent and their Flemish peers (86% and 84%, respectively) is clearly observed. The authors of an older study had already highlighted the similarity in contraceptive use between those groups (both 75%) in Flanders (Lodewijckx, 1996). Considering that it was conducted twenty years ago, one would expect to currently find a greater acculturation and dissemination of contraceptive knowledge within the Turkish ethnic minority. However, since that study did not correct the prevalence rate for pregnant, (post-) menopausal or sexually active women, the comparison is limited. In conclusion, it seems plausible that the contraceptive use has increased in this ethnic minority in Flanders.

The current contraceptive prevalence in the Turkish ethnic minority is, however, much higher than calculated by Levecque and colleagues (2006) (39%). Moreover, the contraceptive use in women from the general population is higher in the SEXPERT-study than that reported in the last HIS-edition (Bayingana et al., 2006). It still remains difficult to compare prevalence rates due to a mixed sample from women of Turkish *and* Moroccan descent, and due to methodological differences in the calculation (contraceptive use during the last year in the HIS versus current use in SEXPERT).

Relevance of the findings: implications for clinicians and policymakers

The more limited ECP-knowledge in both lower educated groups and women of Turkish descent, emphasize how Flemish policy makers should continue to sufficiently, address the topic of emergency contraception. In addition, the similarity in

contraceptive prevalence negates the need for ethnic group-specific interventions, which is often seen in prevention strategies and government policies.

Unanswered questions and future research

Future research should aim to clarify why women of Turkish descent report being less aware of emergency contraception than their Flemish counterparts. Qualitative research could focus on the potential role of a different value system for contraception. Considering the clear relation between not knowing about emergency contraception and both a lower educational achievement and ethnic descent, future research should explore strategies to increase sexuality education in those less educated groups.

CONCLUSION

Even after controlling for socio-economic background, the Turkish ethnic minority in Flanders is less often informed on the existence of emergency contraception. However, after controlling for those factors, the use of contraception in that group is quite similar to usage among their peers from the general population. Therefore, the number of women at risk of an unplanned pregnancy in both groups is comparable.

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CHAPTER 3

RELATION OF ANDROGEN RECEPTOR SENSITIVITY AND MOOD TO SEXUAL DESIRE IN HORMONAL CONTRACEPTION USERS[1]

ABSTRACT

Since very little research in this field is available, this study aims to assess the role of psychosexual, relationship, hormonal and genetic measures in the sexual desire of users of three hormonal contraceptive products [low-dose combined oral contraceptive (20 mcg ethinylestradiol/150 mcg desogestrel), progestin only pill (75 mcg desogestrel), and vaginal ring (daily dose of 15 mcg ethinylestradiol/120 mcg etonogestrel)]. Fifty-five couples were randomized over three groups in which the women consecutively used each product during three months. Both partners repeatedly filled out questionnaires on solitary and dyadic sexual desire (desire to behave sexually by oneself or towards a partner). Total and free testosterone, Sex Hormone Binding Globulin, and a genetic marker of androgen receptor sensitivity [Cytosine-Adenine-Guanine (CAG) repeat length] were assessed on blood samples of the female partners. Sexual desire was higher in women with either short or long CAG repeats (solitary, p = .004; dyadic, p = .008). Desire levels were higher during vaginal ring use (solitary, p = .018; dyadic, p = .007). The woman's mood was found to impact her dyadic sexual desire (p < .001); this scale was also strongly associated with the male partner's dyadic sexual desire (p < .001). The current study found evidence for a role of androgen receptor sensitivity and mood in the sexual desire of hormonal contraceptive users.

[1] Based on Elaut, E., Buysse, A., De Sutter, P., De Cuypere, G., Gerris, J., Deschepper, E., & T'Sjoen, G. (2012). Relation of androgen receptor sensitivity and mood to sexual desire in hormonal contraception users. *Contraception, 85*, 470-479.

INTRODUCTION

With over one hundred million women worldwide using oral contraception, one would expect a substantial number of publications on contraception and sexual functioning in reproductive-aged women. Surprisingly, available evidence is scarce as well as inconclusive with a number of studies suggesting some effect on female sexuality (Graham, Bancroft, Doll, Greco, & Tanner, 2007; Sabatini, & Ciagano, 2006; Strufaldi et al., 2010) and other publications unable to confirm these effects (Ott, Shew, Ofner, Tu, & Fortenberry, 2008; Schaffir, Isley, & Woodward, 2010). This field of research has also been hampered by various methodological difficulties, such as single-item or very different sexuality measures, high discontinuation rates and cross-sectional designs. Furthermore, the field remains hindered by the lack of a true bio-psycho-sexual approach, which could lead to a clearer view on the probably complex interplay between genetics, hormones, psychosocial, relationship and sexual functioning. It has been suggested that the hormonal contraception-induced reduction in free testosterone (T) could have an impact on women more sensitive to free T's behavioral effects (Graham, Bancroft, Doll, Greco, & Tanner, 2007) hormonal contraception could be lowering testosterone levels below some women's threshold, but not below the threshold of other women (Bancroft, 2002; Oinonen, 2009). A recent Canadian study (Oinonen, 2009) has reported on the 2D:4D ratio (an anthropometric indicator of androgen exposure, referring to the length of the index and ring finger) in hormonal contraception users, underlining the need to identify genetic markers for androgen sensitivity. Oionen (2009) found users with a lower 2D:4D ratio (usually found in men) to suffer more often from negative emotional and sexual side effects of hormonal contraception. Androgen sensitivity is further mediated by variation in the *androgen receptor* (*AR*) gene, located on the X chromosome at Xq11-12. The aminoterminal transactivating domain of the *AR* contains a highly polymorphic cytosine-adenine-guanine (CAG) trinucleotide repeat sequence and regulates androgen signalling in steroid hormone-sensitive cells (Brown et al., 1989; Lundin, Giwercman, Richthoff, Amrahamsson, & Giwercman, 2003). In women, the CAG repeat has so far mainly been studied in women with polycystic ovaries (Kim et al., 2008; Diaz, Lopez-Bermejo, Petry,

de Zegher, & Ibanez, 2010; Shah, Antoine, Pall, Taylor, Azziz, & Goodarzi, 2008; Van Nieuwerburgh et al., 2008) and breast cancer patients (Gonzalez et al., 2007). The inhibitory effect of the CAG repeat length on testosterone levels (more CAG repeats associated with weaker receptor activity and hence higher testosterone levels) in men has not been confirmed in women. Studies have reported fewer CAG repeats are associated with higher levels of androgens, suggesting a stimulatory effect (more CAG repeats lead to stronger receptor activity) in women (Westberg et al., 2001).

This study set out to test whether serum testosterone levels in contraceptive users are not only influenced by the contraceptive product but also by genetic variation in the AR gene; and, whether female sexual desire is associated with an interaction between variants in the *AR* gene coding and contraceptive product. Finally, it was hypothesized that psycho-relational processes of self-esteem, depressive symptoms, relationship and sexual satisfaction would directly influence female desire levels.

METHOD

Participants

Through advertising in local newspapers, the Ghent University Hospital, the Ghent University and on several websites, 55 heterosexual couples were recruited. Included were pre-menopausal women between 18 and 45 years of age in a good, general health who had been in a stable, heterosexual relationship for at least nine months. Routine eligibility criteria for hormonal contraception use were applied. Candidates with polycystic ovarian syndrome, liver problems or hereditary thrombotic disease were not included. Although women using any drug with possible effects on sexual function were excluded, no criterion was set concerning sexual functioning of the women/man/couple, as this was set out to be an extra layer in our analysis. Women already using hormonal contraception were not refused participation in order to assemble a group of participants representative for the general female, pre-menopausal population. The study was approved by the local Ethical Committee and is in accordance with the Helsinki Declaration. All procedures were carried out with the adequate understanding and written consent of the participants.

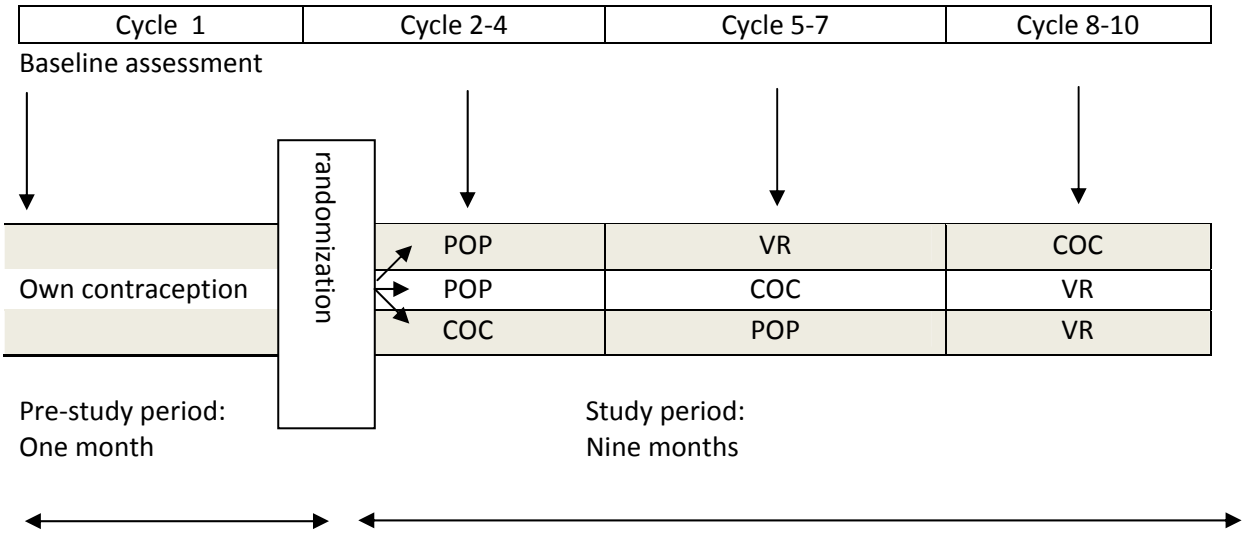

Figure 1. Study timeline.

Study Design

A within-subject, crossover study with three methods of hormonal contraception was designed. After selection upon a baseline assessment, all couples were randomly assigned (participants drew a number which referred to one of the groups) to one of three groups in which only the sequence of the contraceptive products differed; all female partners consecutively used all three contraceptive methods for a period of three months, resulting in a 10-month study duration (see Figure 1 for a study timeline). No wash-out period was foreseen before randomization or between study contraceptive products. The provided contraceptives were a low-dose combined oral contraceptive (COC) containing 20 mcg ethinylestradiol (EE) and 150 mcg desogestrel, a progestin only pill (POP) containing 75 mcg desogestrel and the vaginal ring (VR) in a daily dose of 15 mcg EE and 120 mcg etonogestrel. This not only allows the design for evaluating the route of administration (COC versus VR), but also the effect of the absence/presence of EE (COC versus POP). Both partners were asked to fill out psychosexual questionnaires at baseline (assessment time 1) and during the use of each product (assessment times 2-10). Female partners were asked to provide blood samples at baseline and after the first week of the third contraceptive cycle of each contraceptive method. Serum levels of

androgens (total and free T) and sex hormone binding globulin (SHBG) were assessed. The *AR* CAG repeat length was assessed as a measure of androgen sensitivity.

Statistical methods

Oneway ANOVAs were used for continuous, normally distributed variables, and χ^2-tests or Kruskal Wallis tests for continuous, respectively categorical skewed variables to compare baseline characteristics. Data on the *AR* CAG repeat length were assessed in 42 out of 55 women. Both alleles were divided into two equal-sized groups (median values were 20 for the first allele and 23 for the second allele); those with 20/23 or fewer repeats were defined as short (S), whereas those with more than 20 or 23 repeats were defined as long (L). The female participants could thus be grouped as: homozygous SS, heterozygous SL and homozygous LL. Hypotheses were tested with mixed model analyses with subjects fitted as random to account for dependencies within subjects. This procedure allowed us to use all available data points, and not only those of women who completed the study protocol. Since all women used all study contraceptives, this was a *within-subject analysis* on all assessment times (Brown & Prescott, 2006).

Models all adjusted for baseline values of participant age, relationship duration and BMI. Considering the heterogeneity of the contraceptive background of the participants, baseline contraceptive method and relevant baseline endocrine measures were included in the models. As no wash-out was included in the study design and endocrine data were only available for assessment times 1, 4, 7 and 10, it was decided only to enter the psychosexual data from these data points to minimize the influence of a potential carry-over effect. (Assessment time 1 refers to the baseline assessment time; assessment time 4 refers to the third cycle of the first contraceptive method, assessment time 7 refers to the third cycle of the second method and assessment time 10 to the third cycle of the third method used [as depicted in Figure 1]).

Predictive Analytics Soft Ware (PASW18) and Statistical Analysis System (SAS 9.2) were used for statistical analysis. Statistical significance was set at the 5% level throughout all analyses. To correct for the multiplicity caused by multiple pairwise comparisons, a Bonferroni-correction (reducing the significance level to 0.017) was consistently applied in these comparisons.

Materials

Sexual desire measures. The Flemish version of the 14-item Sexual Desire Inventory (SDI) (Spector, Carey, & Steinberg, 1996) as used to measure sexual desire of all participants, defined as 'an interest in sexual activity'. The scale measures the frequency and strength of thoughts in seeking out or being receptive to sexual stimuli. For the frequency-items, participants chose one of seven options. For the strength-items, participants scored their sexual desire on a nine-point Likertscale. Participants were asked to take the previous month as a referent. Adding up the items of the questionnaire resulted in a score for *dyadic sexual desire* (interest in behaving sexually with a partner) and *solitary sexual desire* (interest in behaving sexually by oneself). On both subscales, a higher score indicated a stronger sexual desire. The original SDI has good reliability and validity (Spector, Carey, & Steinberg, 1996). The internal consistency of the Flemish version used in this study was acceptable for both subscales (solitary sexual desire: Cronbach's alpha (α) = .76; dyadic sexual desire: α = .83).

Relationship and sexual satisfaction. The Dutch version of the 20-item Maudsley Marital Questionnaire (Arrindell, & Schaap, 1983; Arrindell, Boelens, & Lambert, 1983) was used to measure relationship, sexual and general life satisfaction in both male and female partners. Items are scored on a Likert scale from 0 to 8. We adapted the original questionnaire's time format: participants were asked to take the previous month as a referent instead of the last two weeks. Higher scores reflect stronger *dis*satisfaction. Internal consistency in the present sample was high (α = .87).

General sexual functioning. The Flemish version of the Female Sexual Function Index (FSFI) (Rosen et al., 2000; Wiegel, Meston, & Rosen, 2005) was used to assess the general sexual functioning of the female partners. The FSFI assesses the domains of sexual desire, arousal, lubrication, orgasm, satisfaction and pain. Adding these subscales further results in a total score which can be used as an indication of sexual (dys)function: women with a total score below the cut-off of 26.55 are very likely to report one or more sexual dysfunctions (Wiegel, Meston, & Rosen, 2005). The internal consistency of the scale in the present sample was high (α = .86)

Psychological functioning. The Dutch version of the Symptom Checklist (SCL-90) (Derogatis, Lipman, & Covi, 1973) is a 90-item inventory inquiring about the presence of various psychological and physical complaints the week prior to the assessment, scored

on a five-point scale. We adapted the original time format: participants were asked to take the previous month as a referent. The SCL-90 reports on the subscales agoraphobia, anxiety, depression, somatisation, obsession/compulsion, suspicion and interpersonal sensitivity, hostility and sleeping problems. A total score of the subscales and the extra items results in the total score on 'psychoneuroticism', an indicator of overall psychopathology. The reliability and validity of the SCL-90 is good. The internal consistency in our study sample was very high (α = .96).

Self-esteem. The Dutch version of the Rosenberg Self-Esteem Scale (Franck & De Raedt, 2008; Rosenberg, 1989) was chosen as a measure for self-esteem in both male and female participants. The Likert-scaled items range from 0 (strongly agree) to 3 (strongly disagree). Higher scores reflect a higher self-esteem. The original scale has good reliability (Rosenberg, 1989); internal consistency of the current sample was high (α =.89).

Hormone levels. Serum testosterone was assayed in serum samples with LC-MSMS (liquid chromatography-mass spectrometry) (validated against ID-GC-MS, isotopic dilution gas chromatography-mass spectrometry); the intra- and inter-assay coefficients of variation for this assay were 9.1% and 16%, respectively, at a concentration of 16 ng/dL; 2.9% and 5.8% at a concentration of 300 ng/dL. The lower limit of quantification was 2.3 ng/dL. A commercial kit was used to determine the serum concentrations of SHBG (Roche E170 modular, ECLIA); intra- and inter-assay coefficients of variation were 0.8% (at a concentration of 44 nmol/L) and 1.6%, respectively. For all measurements, samples were assayed in the same assay run. Serum FT was calculated from TT, serum SHBG and albumin, using a validated equation from the mass action law (Vermeulen, Verdonck, & Kaufman, 1999).

Determination of AR CAG repeat length. Genomic DNA was extracted from EDTA-treated blood using a commercial kit (Purgene Kit; Gentra Systems, Minneapolis, MN). The *AR* exon 1 region encoding the CAG repeat was amplified using PCR (polymerase chain reaction) with forward primer 5'-GAATCTGTTCCAGAGCGTGC3', fluorescently labeled with FAM (fluorescein amidite) and reverse primer 5'-TTCCTCATCCAGGACCAGGTA-3'. Each PCR was initiated with a 5-min denaturation step at 95° C and terminated with a 20-min extension step at 72° C, in-between reaction profiles were as follows: denaturation at 95° C for 60 s, annealing at 62° C for 60 s, and extension at 72° C for 90 s, for 35 cycles. The PCR products were mixed with a Genescan

400HD ROX size standard and deionised formamide and electrophoresed on a 96-capillary 3730 *xl* Genetic analyzer (ABI Prism®, Perkin-Elmer Applied Biosystems, CA, USA).

RESULTS

Of the 55 couples entering the study, 39 (70.9%) completed the entire study protocol. Of the 16 couples who left the study prematurely, nine couples ended their relationship and therefore no longer fulfilled inclusion criteria. Five women reported side effects of the contraceptive products as a reason for discontinuation (fluid retention and mood swings with the COC, twice for vaginal irritation with the VR, and continuing heavy bleeding with the POP). Two women became pregnant during the study: one was a user failure (accidently prolonging of the prescribed ring-free week) and the other a product failure (pregnancy despite a perfect adherence to the COC-intake instructions).

Descriptive characteristics at baseline

Couples were randomized to one of three groups (COC-POP-VR; POP-COC-VR and POP-VR-COC). Participants were mainly students, resulting in a young mean age of the study sample (women: M = 23.05 years, SD = 4.28; male partners: M = 25.25, SD = 5.32). Baseline characteristics are shown in Table 1: in Group 2, a significantly lower relationship duration could be observed (p = .020). This may be due to an underrepresentation of older couples in this group. A correction for this baseline difference was included in all relevant models. Mean sexual desire scores (as the central variable in the present study) were similar in all three groups at assessment time 1 (solitary sexual desire of women: p = .577 and men: p = .419; dyadic sexual desire of women: p = .122 and men: p = .661). No differences in female sexual desire could be found between users of different baseline contraceptive methods (one POP-user and three CPA-users were excluded from this analysis due to the low numbers in these groups) (solitary: COC: 7.59 ± 5.86, VR: 6.83 ± 4.31, condoms: 11.38 ± 5.90, p = .213; dyadic sexual desire: COC: 37.41 ± 11.38, VR: 40.17 ± 2.64; condoms: 37.63 ± 5.01, p = .824). While these differences are not statistically significant, they were deemed clinically relevant; thus, an adjustment for baseline female sexual desire and

contraceptive product was included in all relevant models. As no specific criteria were set for sexual dysfunction, it appeared that, at baseline, 10 women (18.2%) had a total FSFI-score of 26.55 or less, indicative of a possible female sexual dysfunction. Based on this rather substantial number, we maintained the (categorical) variable female sexual dysfunction in further models. The endocrine measures of the female partners showed some baseline differences: TT (p = .004) and SHBG (p = .006) were both higher in Group 2. This was due to higher serum levels in two women who were COC-users at baseline. However, they could not be considered as outliers nor did they exceed the ranges often reported in contraception literature (Elkind-Hirsch, Darensbourg, Ogden, Ogden, & Hindelang, 2007; Wiegratz et al., 2003). The serum levels of total and free T and SHBG were further explored by baseline contraceptive method. Figure 2 depicts a higher free T, and inversely a lower SHBG, in condom users in comparison to baseline COC-users (both p = .001); a similar pattern is observed between condom and VR-users (free T: p = .020 and SHBG: p = .010) (Kruskal-Wallis tests). To allow our models to correct for these baseline differences, baseline free T levels were included in all relevant models. *AR* CAG repeat length varied between 15 and 31. Prompted by previous studies (Westberg et al., 2001; Hietala, Sandberg, Borg, Olsson, & Jernstrom, 2007) and as described above, the *AR* CAG repeat length results are reported in three groups: homozygous SS (n = 18 or 32.7%), heterozygous SL (n = 12 or 21.8% of the women) and homozygous LL (n = 12 or 21.8%). Androgen sensitivity did not differ between female participants in different groups ($\chi^2(4) = 4.67$, p = .323).

Table 1. Characteristics at assessment time 1 by group (results are mean ± *SD*)

	Group 1 (*n* = 20) POP-VR-COC[1]	Group 2 (*n* = 16) POP-COC-VR	Group 3 (*n* = 19) COC-POP-VR	p^2
Relationship duration (months)	32.75 ± 22.14	21.06 ± 16.64	41.21 ± 21.67	.020
Age (years)				
Women	23.00 ± 3.60	22.00 ± 3.58	24.00 ± 5.36	.394
Men	24.10 ± 4.38	25.00 ± 3.76	26.68 ± 7.02	.314
BMI[3]	21.13 ± 2.07	21.76 ± 1.88	21.27 ± 3.00	.720
Baseline contraception				
POP	0.00%	0.00%	5.30%	.533
COC	80.00%	75.00%	63.10%	
VR	0.00%	12.50%	21.10%	
Condoms	20.00%	12.50%	10.50%	
Sexual Desire Inventory				
-Solitary sexual desire				
Women	8.90 ± 5.40	7.44 ± 6.55	7.05 ± 5.40	.577
Men	12.31 ± 3.01	12.19 ± 4.96	10.73 ± 5.65	.419
-Dyadic sexual desire				
Women	35.60 ± 10.25	41.88 ± 7.72	36.42 ± 10.08	.122
Men	42.00 ± 9.65	42.37 ± 6.01	40.05 ± 8.26	.661
Total testosterone (ng/dl) [3,4]	24.36 ± 8.91	37.31 ± 13.11	27.98 ± 11.97	.004
Free testosterone (pg/ml) [3,4]	1.92 ± 1.38	1.67 ± 0.83	1.81 ± 1.40	.843
SHBG (nmol/l) [3]	142.19 ± 77.76	220.74 ± 59.40	164.77 ± 72.86	.006
AR CAG repeat length[3]				
Homozygous SS	60.00%	35.7%	30.8%	.323
Heterozygous SL	26.7%	35.7%	23.1%	
Homozygous LL	13.3%	28.6%	43.2%	

Note. [1] POP= progestin only pill; VR = vaginal ring; COC = combined oral contraceptive.

[2] Oneway ANOVA for continuous, normally distributed variables; χ^2 for categorical variables.

[3] Data from female participants.

[4] Conversion factors to SI unit: 3.467.

Hypothesis 1: serum hormone levels are not only related to study contraceptive method but also to androgen sensitivity based on AR CAG repeats

A mixed model (random intercept for subject, correction for age, BMI, assessment time and study contraceptive) was constructed to test the interaction between contraceptive and *AR* CAG repeat length on total T serum levels. The model indicated no significant interaction (p = .867). While no effect of contraceptive product on total T was found, the model came close to demonstrating an effect of *AR* CAG repeat length on total T (p=.476 and p=.053). Women in the SS-group showed elevated total T level during the study in comparison to women in the LL-group (SS: 34.77 ± 11.22 ng/dL; SL: 30.79 ± 10.84 ng/dL; LL: 27.32 ± 9.81 ng/dL) (SS > LL, p = .023; SS = SL, p = .111; SL = LL, p = .299) (model not shown).

In a similar model for free T, the interaction between *AR* CAG repeat length and study contraceptive was significant (p=.009) (see Mixed model 1 in Table 2). SS-women showed higher free T levels than LL-women during POP- (SS: 5.17 ± 2.21 pg/mL; SL: 4.66 ± 1.69 pg/mL; LL: 3.53 ± 1.02 pg/mL) (SS > LL: p = .008; SS = SL: p = .289 and SL > LL: p = .030), COC (SS: 1.89 ± 0.64 pg/mL; SL: 1.63 ± 0.70 pg/mL; LL: 1.39 ± 0.51 pg/mL) (SS > LL: p < .0001; SS > SL: p = .025 and SL = LL: p = .089) and VR use (SS: 2.07 ± 1.04 pg/mL; SL: 1.74 ± 0.65 pg/mL; LL: 1.48 ± 0.58 pg/mL) (SS > LL: p = .011; SS = SL; p = .544 and SL > LL: p = .016). This effect is visualized in Figure 3. Furthermore, an interaction between SHBG and contraceptive product on free T was found, confirming the known effect of a product-dependent SHBG-effect on FT (p = .014). Also, free T throughout the study was not only determined by baseline contraceptive method, but also by the free T levels while using a certain baseline method (p = .024 and p < .001, respectively). Looking at the least square means, the only significant difference in FT was found between baseline POP and COC users (p = .002). However, since only one woman was a POP-user at baseline, this effect can be discarded. A measure for the increase or decrease in serum androgen levels during the study in comparison to baseline levels could not be provided, due to the heterogeneity of baseline contraceptive methods.

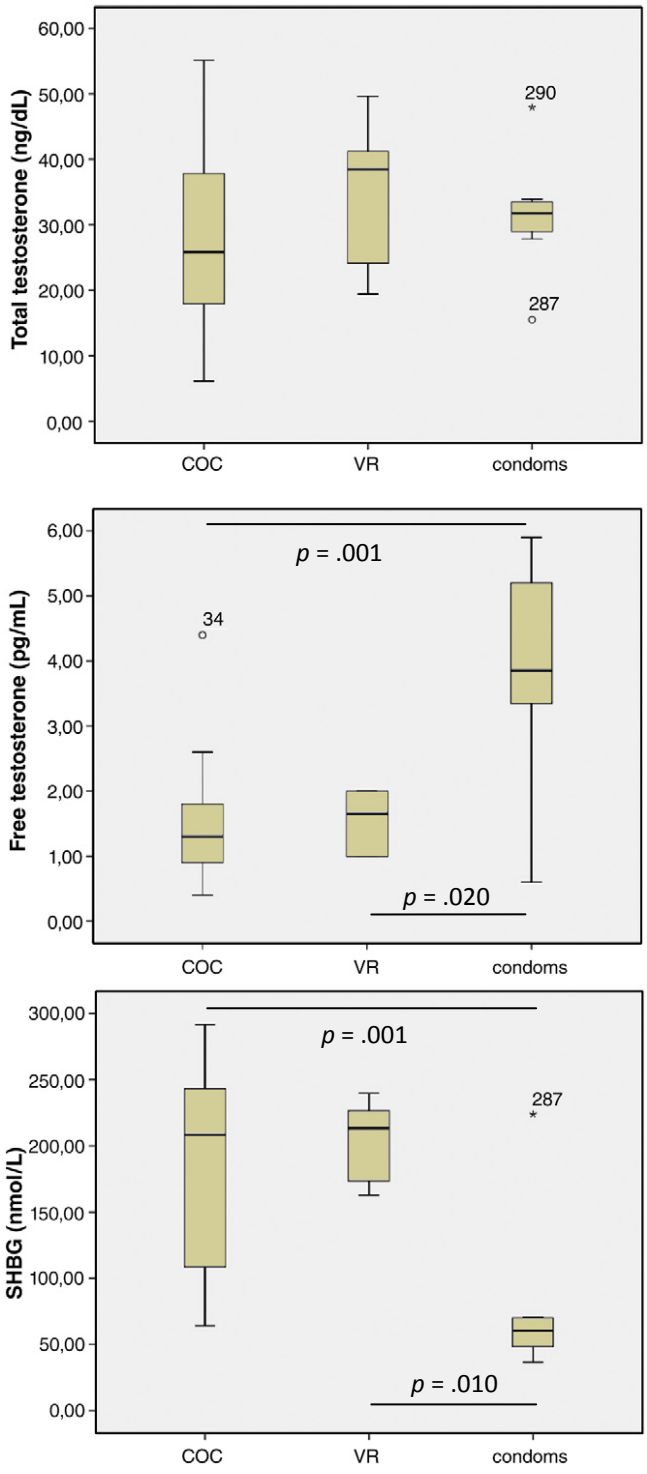

Figure 2. Serum hormone levels by baseline contraceptive method.

COC = combined oral contraceptive (*n* = 37); VR = vaginal ring (*n* = 6); condoms (*n* = 8) Data from women using COC with cyproterone acetate (*n* = 3) and POP (*n* = 1) are not presented due to small numbers. In these boxplots, half of the data (percentile 25 to 75) is represented by the boxes. Dark lines in the boxes indicate the median. T-bars from the boxes extend to the minimal and maximum value. Points and stars are outliers, defined as values more than three times the height of the box.

Table 2. Mixed model 1: interaction *AR* CAG repeat length and product on free T levels

Effect	*df1*	*df2*	*F value*	*p*
Free T (baseline)	1	29	18.58	.006
Age	1	29	0.58	.454
BMI	1	29	11.68	.002
Assessment time	2	29	1.16	.327
Group	2	29	2.39	.109
Product (baseline)	4	29	1.96	.127
Product (study)	2	29	15.95	<.0001
CAG repeat length	2	29	11.63	<.001
Product (study) x CAG repeat length	4	29	4.12	.002
SHBG (study)	1	29	28.58	<.0001
SHBG (study) X Product (study)	2	29	4.94	.014

Note. T = testosterone

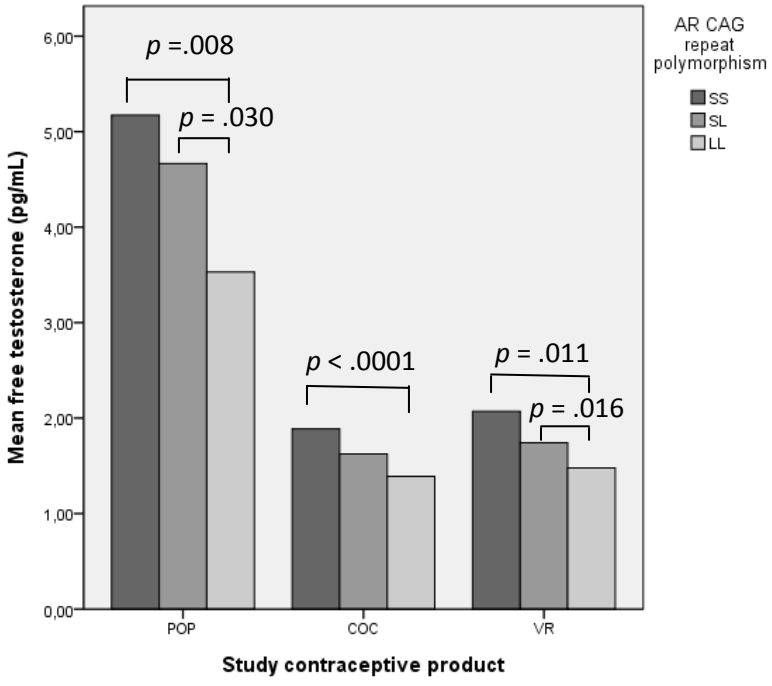

Figure 3. Interaction between *AR* CAG repeat length and study contraceptive on FT

SS = homozygous SS, SL = heterozygous SL, LL = homozygous LL

POP = progestin only pill, COC = combined oral contraceptive, VR = vaginal ring

Hypothesis 2: female sexual desire is associated with androgen sensitivity and study contraceptive

Mixed models were constructed to assess the interaction between study contraceptive (POP, COC and VR) and the *AR* CAG repeat lengths (SS, SL and LL) on solitary and dyadic female sexual desire. Since all women used all study contraceptives, this consisted of a *within-subject* comparison. These effects were also assessed by general linear models (GLM) at only one assessment time (assessment time 7), leading to a *between-subject* comparison. Both mixed and GLM models adjusted for age, relationship duration, BMI, baseline contraceptive method, baseline FT levels, baseline sexual desire and baseline female sexual dysfunction (as addressed above). Free T levels during the study were not included as a predictor in either models since the free T-model above pointed to a significant interaction between study contraceptive and *AR* CAG repeat length on this variable. Only the determinants of free T levels, *AR* CAG repeat length and study contraceptive were included. Nevertheless, a model *with* the inclusion of those free T levels was highly similar to the models without this inclusion (not shown).

Mixed model 2: solitary sexual desire or the desire to behave sexually by oneself. The model for solitary desire showed no interaction between study contraceptive and *AR* CAG repeat length (p = .549). However, significant effects of *AR* CAG repeat length and study contraceptive method were shown (p = .004 and p = .018, respectively) (Table 3). After applying a Bonferroni correction for multiple comparisons, women in the LL-group reported a stronger solitary sexual desire (SS > SL, p = .042; SS = LL, p = .386; SL < LL, p = .002). After adjustment for the effects of androgen sensitivity, the effect of contraceptive method pointed to a stronger solitary sexual desire during VR use in comparison to COC and POP use (COC = POP, p = .920; VR > COC, p = .006; VR > POP, p = .013). However, the factor that was most significantly associated with solitary sexual desire in the study was the level of the woman's own baseline score (p < .0001). The contraceptive method used at baseline did not have any relation with solitary sexual desire (p = .738). Finally, effects of group and assessment time must be pointed out. Solitary desire was not similar amongst women in different study groups or on all assessment times (p = .048 and p = .008, respectively): desire seemed to decrease as the

study progressed (assessment time 4 > 7, p = .004; assessment time 4 > 10, p = .005; assessment time 7 = 10, p = .124).

Table 3. Mixed and GLM model for solitary and dyadic sexual desire

Mixed model solitary sexual desire Effect	*df1*	*df2*	*F value*	*p*
Free T (baseline)	1	26	1.19	.285
Age	1	26	1.61	.216
BMI	1	26	6.55	.017
Assessment time	2	26	5.89	.008
Group	2	26	3.43	.048
Product (baseline)	3	26	0.42	.738
Product (study)	2	26	4.69	.018
AR CAG repeat length	2	26	7.05	.004
Relationship duration	1	26	0.56	.461
Solitary desire (baseline)	1	26	96.91	<.0001
FSD (baseline)	1	26	6.51	.017
FSD (study)	1	26	0.18	.670
SCL90_depression (study)	1	26	0.72	.404
Mixed model dyadic sexual desire Effect	*df1*	*df2*	*F value*	*p*
Free T (baseline)	1	26	0.01	.913
Age	1	26	5.12	.032
BMI	1	26	1.43	.242
Assessment time	2	26	5.13	.013
Group	2	26	0.89	.423
Product (baseline)	3	26	3.50	.030
Product (study)	1	26	5.96	.007
AR CAG repeat length	2	26	5.94	.008
Relationship duration	1	26	0.62	.438
Dyadic desire (baseline)	1	26	56.59	<.0001
Dyadic desire partner (study)	1	26	22.90	<.0001
FSD (baseline)	1	26	1.00	.327
FSD (study)	1	26	4.53	.043
SCL90_depression (study)	1	26	20.04	<.001
MMQ_relationship satisfaction (study)	1	26	0.00	.963
MMQ_sexual satisfaction (study)	1	26	0.37	.546
Self esteem (study)	1	26	1.67	.208

Note. df = degrees of freedom; F value = observed test statistic value of the F test for fixed effects parameters. *AR* = androgen receptor; T = testosterone; SHBG = sex hormone binding globuline; FSD = Female sexual dysfunction; SCL = Symptom check list; MMQ = Maudsley marital questionnaire. Baseline = baseline measure; study = measure during study contraceptive intake.

In order to perform a similar analysis without potential time (test-retest) effects, effects were also assessed by general linear models at only one assessment time (assessment time 7), leading to a *between-subject* comparison. Results from the GLM for solitary sexual desire all pointed in the same direction as the mixed model above, confirming the robustness of the findings (model not shown).

Mixed model 3: dyadic sexual desire or the desire to behave sexually with a partner. A similar mixed model was constructed for dyadic sexual desire; the factors self-esteem, relationship and sexual satisfaction were added due to their potential relevance for this subscale. No significant interaction between study contraceptive and *AR* CAG repeat length was found (p = .203). An effect of the *AR* CAG repeat length was shown (p = .008): again, the LL-group reported a stronger dyadic sexual desire after application of a Bonferroni correction for multiple comparisons (SS > SL, p = .052; SS = LL, p = .221; SL < LL, p = .007). After adjustment for androgen sensitivity, the effect of contraceptive product pointed towards a stronger desire during VR use (p = .007); the lowest desire scores were reported during POP use (VR > COC, p = .088, VR > POP, p = .004 and COC > POP, p = .015). An effect of baseline contraceptive could be observed: baseline VR users reported a stronger dyadic desire throughout the study in comparison to baseline COC users (p = .010). The most significant relation with a woman's sexual desire towards her partner was her baseline score (p < .0001). Another highly significant factor was found in the dyadic desire of the male partner: a stronger dyadic sexual desire in the male partner was associated with a stronger desire in the female partner (p < .001). In this mixed model, no effect of group could be detected (p = .423). A similar effect of assessment time as in mixed model 1 however remained (p = .013) (assessment time 4 > 7, p = .015; assessment time 4 > 10, p = .007 and assessment time 7 = 10, p = .202) (Table 3).

In the GLM model for dyadic sexual desire, the results above could not all be repeated. No effect of the *AR* CAG repeat length or contraceptive method was established (p = .227 and p = .161). Only associations with the women's baseline desire score and the male partners dyadic desire score could be confirmed (p = .002 and p = .026) (model not shown).

Hypothesis 3: female sexual dysfunction, depressive symptoms, self-esteem, sexual and relationship satisfaction will affect female sexual desire directly

Apart from the effects of study contraceptive product and a modulator of androgen sensitivity, a number of psychological and relational characteristics of these women and their partnerships were included in model 2 and 3 (Table3). Interactions between biological (FT levels and *AR* CAG repeat length) and psycho-relational (female sexual dysfunction, depressive symptoms, self-esteem, sexual and relationship satisfaction) predictors on sexual desire were tested, but none proved to be significant. Interaction terms between study contraceptive method and psycho-relational predictors also did not result in significant effects on female (solitary or dyadic) sexual desire (models not shown).

In the solitary sexual desire model, *baseline* female sexual dysfunction appeared to affect the dependent variable of desire directly: sexually functional women reported a stronger solitary sexual desire throughout the study (p = .017). *During the study*, depressive symptoms or female sexual dysfunction were not related to solitary sexual desire during the study (p = .404 and p = .670, respectively). In the dyadic sexual desire model, *baseline* female sexual dysfunction did not affect desire directly: functional and dysfunctional women reported similar desire during the study (p = .327). *During the study*, sexually functional women and women with less depressive symptoms reported a stronger dyadic sexual desire (p = .043 and $p < .001$). Further, women with a higher self-esteem, a better relationship and sexual satisfaction *during the study* did not report a stronger dyadic sexual desire (p = .208, p = .963 and p = .436, respectively) (Table 3). Since female sexual desire is a component of female sexual dysfunction, it was tested whether inclusion of this factor might prove to be an over-adjustment. However, all results remained highly similar without this factor (model not shown).

DISCUSSION

Summary and interpretation of the findings

The results presented in this paper point to higher levels of total and free T in contraceptive users with shorter CAG polymorphisms. The length of the polymorphism was further directly associated with women's sexual desire: women with longer, and thus highly active, androgen receptors reported stronger sexual desire. Sexual desire was also higher when participants were using the vaginal ring, in comparison to when they were using the combined oral contraceptive or the progestin-only pill.

At baseline, the women were a fairly heterogeneous group with respect to contraceptive methods. Nevertheless, female sexual desire was very similar, not only between contraceptive methods used at baseline, but also between study groups. We found a fairly high number of women (18.2%) who were potentially sexually dysfunctional, and therefore this factor was taken into consideration in all relevant analyses.

The observation that serum free T is not only influenced by contraceptive method, but also by the *AR* CAG polymorphism, has not previously been reported in female contraception users. This result partly contradicts an earlier publication by Hietala and colleagues (2007), where no association could be observed between total T and the polymorphism in users *and* non-users of oral contraception. However, the Hietala study did not measure free T. The present results point to a marked similar trend in serum levels of total *and* free T, with less active androgen receptors (SS-group) being associated with the highest testosterone levels, thus confirming the positive, stimulatory trend of the polymorphism in women as reported by Westberg and colleagues (2001).

The primary aim of this study however was to assess whether a number of genetic, hormonal, psychosexual and relationship measures would impact the sexual desire of the female participants. It was consistently found that the baseline level of solitary and dyadic sexual desire was most strongly related to female sexual desire. This finding reminds us how female sexual desire might sometimes be a rather stable intrapersonal characteristic, with a stronger impact than any other change measured.

Both solitary and dyadic sexual desire were associated with the transcriptional activity in the *AR* CAG polymorphism, with more active receptors being associated with

stronger sexual desire. Possibly, the sexual desire of this subgroup of women (LL-group), is not impacted by a contraception-induced free T-reduction due to their low threshold for testosterone effects. For both concepts, a more frequent and more intense sexual desire was further observed during vaginal ring use. This confirms the results published by an Italian group (Sabatini & Cagiano, 2006); however, the effect of study contraceptive on both desire scales in the present study was minimal. It must also be noted that while dyadic desire at baseline did not differ between women using different baseline contraceptive methods, it appeared dyadic sexual desire *during the study* was higher in those women who were ring users at baseline in comparison to women who at baseline used oral contraception. Although a similar effect of baseline contraceptive method could not be found for solitary sexual desire, the heterogeneity of baseline contraceptive methods may still have affected results.

With respect to the psychosexual and relationship factors, effects differed between solitary and dyadic sexual desire. First, it appeared that general sexual functioning of the woman at baseline only affected solitary sexual desire, or the desire to behave sexually by oneself. If women were sexually functional before the start of the study, they were more likely to report stronger solitary sexual desire throughout the study. This effect of general sexual functioning was *not* established for dyadic sexual desire, or the desire to behave sexually with a partner. Dyadic desire of the woman was, however, very much affected by the desire of the male partner, confirming the importance of interpersonal processes in a woman's desire for her partner. Second, distinctive effects of mood were observed for solitary and dyadic sexual desire. Women's desire to behave sexually by oneself was not in any way affected by mood; while their desire to behave sexually with their partner was positively influenced by a better mood. These findings shed new light onto the discussion that changes in sexual desire in contraceptive users would only be due to mood effects. In the present study, after models had been adjusted for the impact of hormonal contraception and androgen sensitivity, women with a more positive mood still reported a more frequent and stronger desire to behave sexually, but only towards their partner. This partly contradicts earlier findings of Graham and Sherwin (1993), who reported very little evidence for the co-variation of mood and sexual interest in contraceptive users. However, this earlier study assessed the effects of a triphasic contraceptive or placebo on women's mood and sexual interest; while the

present study examined the effect of mood on female sexual desire, after correction for a number of study variables.

Strengths, limitations and future research

Recently, a number of studies have chosen cross-sectional designs (Enzlin et al., 2011; Schaffir, Isley, & Woodward, 2010; Wallwiener et al., 2010); to study the relationship between sexual functioning and contraception. While practical or financial reasons often limit us to using such cross-sectional designs, the current study specifically chose to report on a sample of women using three different contraceptive methods consecutively. While the study sample is relatively small, this is partly compensated by the within-subject analyses where female participants served as their own control in all measures. Earlier research has also studied the topic from a single point of view, be it psychological (Graham, Ramos, Bancroft, Maglaya, & Farley, 1995) or more medical. The current study elaborates on the existing contraception and sexuality literature by monitoring a broad range of biological, psychological and relationship processes, and the specific interplay between them. Furthermore, a very accurate measure of FT, the LC-MSMS- method, was used.

It should be noted that the conclusions of this paper should be interpreted with caution. First, due to the small simple size, couples were randomized in three groups while theoretically, a much higher number of study groups was possible. As a consequence, not all study contraceptive products held all positions (e.g., the POP was never the last product women used), which hampered the robustness of the mixed model results. The small sample size could not guarantee a completely successful randomization; and, with the number of variables included in the models, we cannot exclude the possibility that significance at the 5% level could have occurred by chance. Second, considering the already complex design, it was decided not to include wash-out periods between the study contraceptive products or before the study began. Since female participants were all in their reproductive ages, and recruitment was not aimed at sterilized couples, a wash-out period with only condom use was anticipated to create another obstacle in an already difficult recruitment. Third, multiple comparisons can cause multiplicity and a Bonferroni correction needed to be applied consequently. Finally, due to the influx of a young, mainly student population and an

underrepresentation of older couples with longer relationship duration, generalization to the general population is limited.

Ideally, future research should be attentive to using multidisciplinary approaches and adopt a more broad approach on processes in contraceptive users. Also, new research following large number of starters on diverse forms of contraception is still very much needed; as well as the assessment of who is at risk for experiencing side effects and who will benefit sexually.

In conclusion, the current study found evidence for a role of the *AR* CAG repeat length and mood on the sexual desire of contraceptive users. However, in the field of contraception and sexuality, the answer is never only genetics, hormones or mood, relationship or personality, but specifically the interactions between all of these.

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CHAPTER 4

CYCLE-RELATED CHANGES IN MOOD, SEXUAL DESIRE, AND SEXUAL ACTIVITY IN ORAL CONTRACEPTION-USING AND NONHORMONAL-CONTRACEPTION-USING COUPLES[1]

ABSTRACT

Findings on women's sexuality across the menstrual cycle are inconsistent. One relatively consistent finding is a midcycle and premenstrual peak in sexual desire in freely cycling women. Results on the cycle-related effects of sexual behaviour are less clear. Large proportions of reproductive-aged women use combined oral contraception (COC), but studies on potential cycle-related shifts in sexual desire and behaviour are sparse. A prospective diary study assessed sexual desire, sexual behaviour and mood in 89 heterosexual couples. Women were using one of four contraceptive methods: (1) nonhormonal contraception, (2) low-dose COC containing 20 mcg ethinylestradiol and 75 mcg gestoden or desogestrel, (3) COC containing 35 mcg ethinylestradiol and 2 mg cyproteronacetate, and (4) COC containing 30 mcg ethinylestradiol and 3 mg drospirenone. No cycle effects of sexual desire were established in the COC group, but frequency of sexual intercourse declined in the last days of active pill-taking. These results were similar in both partners. Negative affect did not covary with sexual desire.

[1] Based on Elaut, E., Buysse, A., De Sutter, P., Gerris, J., De Cuypere, G., & T'Sjoen, G. (In press). Cycle-related changes in mood, sexual desire, and sexual activity in oral contraception-using and nonhormonal-contraception-using couples. *Journal of Sex Research.*

INTRODUCTION

Research findings on women's sexuality across the menstrual cycle have been quite inconsistent (Brown, Calibuso & Roedl, 2011). Some studies have reported an increase in *sexual desire* prior to the onset of the luteinizing hormone (LH) surge, and again prior to menses, in women not using hormonal contraception (Bullivant et al., 2004). A recent study assessing daily changes in ovarian hormones and daily ratings of female sexual desire partly replicated this, finding a mid-cycle increase in sexual desire, followed by a postovulatory decrease (Roney & Simmons, 2013). This study showed estradiol and progesterone to have an excitatory and inhibitory effect, respectively, on female sexual desire. Their results did not support a role for testosterone. The findings of Roney and Simmons (2013) confirmed previous findings in female rhesus monkeys, who share neuroendocrine patterns and mechanisms of ovarian function, with human females (Wallen, 1990, 2000, 2001).

Other studies have examined the covariation between menstrual cycle phases and *sexual activity* (Brewis & Meyer, 2005; Bullivant et al., 2004; Roney & Simmons, 2013; Wilcox et al., 2004). Concordant with their results for sexual desire, Bullivant et al. (2004) also found a clear rise in female-initiated sexual activity three to four days prior to the LH surge, and a second rise prior to menses, both in single and partnered women who were not trying to conceive and were using barrier methods of contraception. Male-initiated sexual activity did not vary across the menstrual cycle. Wilcox et al. (2004) looked at cycle effects in freely cycling women using effective nonhormonal contraception (intrauterine device or sterilisation by tubal ligation) and found a clear rise in the frequency of sexual intercourse within the fertile window (the six days ending at or shortly after ovulation). A large-scale international study also assessed the relationship between menstrual phase and sexual activity: Brewis and Meyer (2005) assessed the connection between intercourse and menstrual phase in over 20,000 sexually active, partnered women not using hormonal contraception or rhythm methods but without a desire for pregnancy. There were no significant differences in the occurrence of intercourse between the preovulatory, ovulatory and postovulatory

phases, but frequency of intercourse was lower during menses compared to other phases (Brewis & Meyer, 2005).

It appears that while studies point in the direction of ovarian hormones, such as estradiol and progesterone, predicting female sexual desire across the menstrual cycle, the evidence on menstrual cycle effects on sexual behaviour is less clear. In an attempt to clarify this, some studies also have included external, social predictors in their designs that potentially overwrite the hormonal influence on behaviour. For instance, Brewis and Meyer (2005) showed how the avoidance of sex during menses is widespread across the world. Hence, some authors argued that this avoidance can lead to a "heaping" of sexual activity postmenses without there being any hormonal influence (Dobbins, 1980). Furthermore, Roney and Simmons (2013) included a weekend variable in their regression analyses, which appeared to be a very strong predictor in all models on sexual activity. Harris and Vitzthum (2013) concluded that the combination of menses-associated avoidance of, and weekend-associated preferences for, intercourse, and potentially associated changes in behaviours (such as sleep, stress etc.), may overrride hormonal influences to create "heaping" - independent of ovulation.

While further research in freely cycling women is needed to increase our knowledge of the predictors of female sexual desire and activity, similar research on cycle effects in contraceptive women is even more scarce. Recent population-based data in Flanders (Belgium) showed that 50% of sexually active, reproductively aged women (without a desire for pregnancy) were currently using hormonal contraception (Elaut et al., 2014). A few studies have reported changes across the cycle in preferences for photographic sexual representations. One study showed how ratings of implicit erotic art differed between freely cycling women and women using combined oral contraception (COC): freely cycling women in the first half of their cycle reported seeing sexual themes more often, while no cycle shifts in the ratings of women using COCs occurred (Rudski, Bernstein, & Mitchell, 2011). Also, COC users were more interested in erotic art than freely cycling women if they were first exposed to these sexual visual stimuli during their pill-free week (Wallen & Rupp, 2010).

Research on the sexuality of COC users has primarily focused on changes in sexual desire after starting on or switching to hormonal contraception (Graham, Bancroft, Doll, Greco, & Tanner, 2007; Greco, Graham, Bancroft, Tanner & Doll, 2007), as COCs are known to lower the endogenous levels of free or bio-available testosterone (Coenen,

Thomas, Borm, Hollanders, & Rolland, 1996). This observation has led to the hypothesis that COCs might –at least in a subgroup of testosterone-dependent women- be lowering the levels of free testosterone below the critical threshold for some women, potentially leading to complaints of decreased sexual desire (Bancroft, 2002, 2005). Clear evidence supporting or refuting this "desensitization hypothesis" is currently lacking (Bancroft, 2003).

Rationale for the current study

To address the gap in the literature on potential cycle-related shifts in sexual desire and behaviour in users of COC, the current study assessed several aspects of sexuality across the cycle in both partners of heterosexual COC-using couples.

Sexual desire. COCs differ greatly in pharmacokinetics due to a broad variability in available dosages and compositions (e.g., ethinylestradiol dosage and different androgenic properties of the progestin used). The androgen environment of COC users depends on (1) the androgenic effect of the progestin used, (2) the anti-gonadotropic effect of the estrogen-progestin combination altering ovarian androgen production, and (3) the effect of the COC on plasma proteins (such as sex hormone binding globulin) with sex steroid-binding properties (Coenen et al., 1996). For instance, the third generation progestins of desogestrel and gestoden have androgenic effects (Darney, 1995; Elger et al., 2003), while drospirenone has an anti-androgenic effect (Jung-Hoffman & Kuhl, 1989). Apart from progestin, cyproterone acetate is also used in COCs specifically developed for the treatment of androgen-dependent conditions such as acne or hirsutism in women, even though very little is known about the sexual effects of this even stronger anti-androgenic compound. An earlier German study reported that up to 44% of women starting on COCs containing cyproterone acetate experienced sexual side effects (lack of sexual desire, arousal and orgasm problems) (Appelt & Strauβ, 1986), but, to the authors' knowledge, no recent studies on the sexual effects of COCs with this compound are available. Considering these differential pharmacokinetic effects, we cannot exclude that different COC compositions might lead to specific cycle-related patterns of sexual desire in women.

With regard to the nature of cycle-related changes in sexual desire in COC users, research is scarce. One study (Alexander, Sherwin, Bancroft, & Davidson, 1990) reported

a pattern of lower, but more stable, levels of free testosterone and sexual desire in COC users in comparison to non users. A prospective study using COCs or a placebo as a treatment for premenstrual symptoms reported a "levelling off" of sexual desire after three COC cycles (Graham & Sherwin, 1993).

Frequency of sexual activity. Compared to female sexual desire levels, the frequency of sexual activity within a couple is probably even more related to partner and contextual factors, such as the amount of time that can be spent with the partner (e.g., more time in weekends) and the avoidance of sexual activity during the withdrawal bleeding (see the widespread decrease during the menstrual phase as reported by Brewis and Meyer, 2005). Therefore, we included both psychosocial factors (weekend days and bleeding days), next to the previously mentioned potential effects of contraceptive cycle and COC group, in the models on frequency of sexual activity. Nonhormonal factors such as menses-avoidance and weekend-preference have only been studied in the context of potential cycle-effects on the sexual behaviour of freely cycling women (e.g., Roney & Simmons, 2013).

Mood. It is well recognized that negative emotion, whether experienced as anger, depression or anxiety, has a negative impact on sexual desire (Bancroft, 2009). A study of Lykins, Janssen & Graham (2006) into non-clinical variations in both mood and sexual desire, reported that the association between both is not always one of a negative correlation. The previously mentioned study of Graham and Sherwin (1993) suggested differential changes in mood and sexual desire in response to treatment with COC or placebo in women with premenstrual symptoms. To increase our knowledge on the cycle-related patterns of both sexual desire and mood in established COC users, the current study also included the factors positive and negative affect.

Current study design

We used several linear mixed effects models investigating potential predictors (cycle-effect, contraceptive group, affect, bleeding and weekend days) of sexual desire and sexual behaviour during the contraceptive cycle in all COC groups, separately for the male and female partners. Due to the potential pharmacokinetics of different COCs, the current study recruited couples in which the female partner used one of three different COCs, each with a potentially different androgenic profile. Due to the large

discontinuation rate in COC-starters during the first year of use (Hatcher & Nelson, 2004), and, to a reported decrease of sexual desire in a minority of COC-starters (Graham, Ramos, Bancroft, Maglaya, & Farley, 1995), women established on COCs were recruited.

We also included a control group of freely cycling women and their partners who were assessed in the same way as the COC groups. To avoid a behavioural bias around the time of ovulation, we included couples using effective nonhormonal contraception (sterilisation, intrauterine device or condoms). Finally, we decided to include the partners' perspective by assessing all psychosexual measures also in the male partner of all couples. Very few previous studies have examined both the female and male perspective on both sexual desire and frequency of sexual activity (e.g., Willoughby & Vitas, 2001).

Hypotheses

The current study first hypothesized that, (1a) levels of solitary sexual desire (or the desire to behave sexually by oneself) and dyadic sexual desire (or the desire to behave sexually with a partner) in all COC users would remain stable across the cycle; and that, (1b) sexual desire in the NHC group would follow the pattern, established in previous studies, of a mid-cycle and/or premenstrual increase. Second, it was hypothesized that, (2) negative affect would not predict sexual desire levels during the cycle in the COC or NHC groups. Third, the study hypothesized that (3) nonhormonal variables such as menses-avoidance and weekend preference would not covary with sexual desire in COC or NHC groups. However, those variables were hypothesized to covary with sexual activity patterns, resulting in an increased frequency of sexual activity (or "heaping") (4a) in the week after the withdrawal bleeding in all COC groups, or (4b) postmenses in the NHC group. Finally, it was hypothesized that (5) negative affect would not predict sexual activity patterns in the COC or NHC groups.

METHOD

Participants

Through advertising in local newspapers, the Ghent University Hospital, the Ghent University and on several websites, 89 heterosexual couples were recruited to participate in a diary study concerning sexual desire and behaviour across the menstrual cycle. All couples were current users of one of four contraceptive methods: (1) nonhormonal contraception (male sterilization, condoms, or nonhormonal intrauterine device) (*n* = 26, NHC); (2) low-dose COC containing 20 mcg ethinylestradiol and 75 mcg gestoden or desogestrel (*n* = 30, 20EE); (3) COC containing 35 mcg ethinylestradiol and 2 mg cyproteroneacetate (*n* = 12, 35EE/CPA); (4) COC containing 30 mcg ethinylestradiol and 3 mg drospirenone (*n* = 21, 30EE/DRSP). No minimal contraceptive duration was set as an inclusion criterion. In all three COC groups, the minimal contraceptive duration was nine months.

Couples needed to be in a stable, heterosexual relationship for at least one year. All couples were living together or spent at least 50% of their free time together. Additional inclusion criteria for the female partners were: being pre-menopausal, between 18 and 45 years of age, and in good general health. Women using medication with potential effects on sexual function and women with Polycystic Ovarian Syndrome were excluded. For women in the NHC group (nonhormonal contraception), having a regular cycle of approximately 28 days was an inclusion criterion. Taking the contraceptive pill in a regular, 21/7 scheme was an inclusion criterion for the women in the COC groups (20EE, 35EE/CPA and 30EE/DRSP). All procedures were carried out with the adequate understanding and written consent of the participants, and with approval by the local Ethics Committee.

Table 1. Study timeline and relation of menstrual and contraceptive phases to assessment times

	baseline	repeated assessments						
	T1	T2	T3	T4	T5	T6	T7	T8
NHC	1st day of menses	menstrual	mid-follicular	late-follicular	ovulation	mid-luteal	late-luteal	1st day of menses
20EE	pill free day 1	pill free day 5	pillday 2	pillday 6	pillday 10	pillday 14	pillday 18	pill free day 1
35EE/CPA	pill free day 1	pill free day 5	pillday 2	pillday 6	pillday 10	pillday 14	pillday 18	pill free day 1
30EE/DRSP	pill free day 1	pill free day 5	pillday 2	pillday 6	pillday 10	pillday 14	pillday 18	pill free day 1

Note. Repeated assessments T2-T8 asked participants for their experience of the day of assessment and the three days preceding assessment. NHC: group using nonhormonal contraception; 20EE: group using oral contraception with 20 mcg ethinylestradiol and 75 mcg gestoden/desogestrel; 35EE/CPA: group using oral contraception with 35 mcg ethinylestradiol and 2 mg cyproterone acetate; 30EE/DRSP: group using oral contraception with 30 mcg ethinylestradiol and 3 mg drosprirenone

Procedure

An online survey tool (Limesurvey©) was used to design a diary study with a comprehensive baseline assessment (assessment time one or T1) and seven consecutive, briefer, repeated measures (T2 - T8). The study timeline and the relation of the menstrual and contraceptive phases to the different assessment times are shown in Table 1. At T1, couples were asked about current medication use and relationship duration. Standardised measures were used to assess relationship, sexual and general life satisfaction (Maudsley Marital Questionnaire, MMQ) (Arrindell, Boelens, & Lambert, 1983; Arrindell & Schaap, 1985), sexual desire (Sexual Desire Inventory, SDI) (Spector, Carey, & Steinberg, 1996), and affect (Positive And Negative Affect Schedule, PANAS) (Engelen, De Peuter, Victoir, Van Diest, & Van den Bergh, 2006; Watson, Clark, & Tellegen, 1988).

During the T2-T8 session, both partners filled out questions on sexual desire (one question from the SDI: "How strong was your sexual desire to engage in sexual activity with your partner?"), affect (PANAS), and two questions, developed for the study, on the frequency of intercourse. Finally, all women completed the Calendar of Premenstrual Experience (COPE) (Mortola, Girton, Beck, & Yen, 1990).

Couples in the NHC group completed the baseline assessment on the first day of the female partner's menstruation. Couples in the COC groups (20EE, 35EE/CPA and 30EE/DRSP) completed the baseline assessment on the first pill-free day. After the baseline assessment, both partners completed repeated assessments every four days. Sessions T2 to T8 assessed participants' experiences of sexual desire, frequency of intercourse and affect for the day of assessment and the three days preceding assessment. All women in the NHC group completed the last assessment on the first day of their next menstruation (assessing the premenstrual period). Women in the COC groups completed the last assessment on the first day of their next pill-free week. Couples were paid 80 Euros for every cycle that contained no missing data. Couples were informed that one or more missed sessions would lead to a progressive reduction of this amount.

Menstrual phases were calculated from the first day of menstruation and a backward count method. A recent study (Brown et al., 2011) compared results of the

backward count method to results of cycles with a known LH surge to determine ovulation. The authors concluded that, while statistical power might be compromised in cycles with a less accurate timing of ovulation, few differences could be found between the two analyses. Harris and Vitzthum (2013) more recently explained how even the detection of an LH surge in itself is not a marker of the occurrence of ovulation. Notwithstanding the limitations of the backward count method, we decided not to use biomarkers (such as basal body temperature measures or cervical mucus observation) to avoid the potential influence of using these measures on the outcome variables.

Measures

Sexual desire. The Flemish version of the 14-item Sexual Desire Inventory (SDI) (Spector et al., 1996) was used to measure sexual desire, defined as "an interest in sexual activity." The scale measures the frequency and strength of thoughts in seeking out or being receptive to sexual stimuli. For the frequency items, participants chose one of eight options (0 = not at all to 7 = more than once a day). For the strength items, participants scored their sexual desire on a nine-point Likert scale (0 = no desire to 8 = strong desire). Participants were asked to answer questions about their sexual desire with reference to the previous month. The SDI yields a score for dyadic sexual desire (interest in behaving sexually with a partner) and solitary sexual desire (interest in behaving sexually by oneself). On both subscales, a higher score indicates a stronger sexual desire. The original SDI has good reliability and validity. The internal consistency of the Flemish version used in this study was good for both subscales (solitary sexual desire: Cronbach's alpha (α) = .88; dyadic sexual desire: α = .81).

Relationship and sexual satisfaction. The Dutch version of the 20-item Maudsley Marital Questionnaire (MMQ) (Arrindell et al., 1983; Arrindell & Schaap, 1985) was used to measure relationship, sexual, and general life dissatisfaction in both male and female partners. Items are scored on a Likert scale from 0 to 8. A higher score indicates stronger dissatisfaction. We adapted the original questionnaire's time format: participants were asked to take the previous month as a reference instead of the last two weeks. Internal consistency in the present sample was satisfactory to good (relationship satisfaction: α = .77; sexual satisfaction: α = .49; general life satisfaction: α = .54).

Affect. The Positive and Negative Affect Schedule (PANAS) measures two dimensions of affect in 20 items and can be used to measure affect as a state or trait (Engelen et al., 2006; Watson et al., 1988). The current study used the Dutch state version to ask participants to what extent they experienced the listed emotions during the past four days. The scale consists of five points (ranging from 1 = very little to 5 = very much). The internal consistency of the scale was good for men and women (positive affect: α = .89; negative affect: α = .86).

Premenstrual complaints. The Calendar of Premenstrual Experiences (COPE) (Mortola et al., 1990) is a prospective inventory used to assess the severity of premenstrual complaints and bleeding (spotting, bleeding and severe bleeding) throughout the entire cycle. Female partners completed the calendar throughout their contraceptive or menstrual cycle. It further contains the ten most common physical and 12 most common affective symptoms of premenstrual syndrome. A cut-off score of 42 during the total luteal phase is used to discriminate women with and without premenstrual syndrome (Mortola et al., 1990).

Sexual activity. For the assessment of sexual frequency, two questions were asked. First, a filter question was asked about sexual activity during the current assessment time ("have you and your partner been sexually active during the previous assessment time?"). Second, the number of sexual events was assessed ("On how many occasions have you and your partner been sexually active together during the previous assessment time?"). In the survey, both questions were accompanied by the study's definition of sexual activity: "Sexual activity is understood as each behavior aimed at eliciting or expressing sexual desire and/or sexual arousal, such as for example, stroking each other's body, french kissing, caressing each other's genitalia, giving or receiving oral or anal stimulation, vaginal intercourse etc. So when sexual activity is addressed, this is not limited to sexual intercourse (penetration)."

Analytical approach

For the variables measured at baseline only (relationship duration, etc.), the four contraception groups were compared using classical ANOVA F-tests (SPSS, version 20). If a significant difference was found, post-hoc contrasts were used to locate the source of

the difference. For the variables that were measured for both partners separately (e.g., age) this analysis was split up by gender.

For the variables that were measured repeatedly, analyses were always performed separately for the COC and the NHC group, and for the male and female participants. All analyses pertaining to repeated measures were performed in SAS, version 9.3. Linear mixed effect models (with several factors) were fitted to predict sexual desire and sexual frequency. For the NHC group only a main effect of assessment time was tested. Linear mixed effect models were either modelled by random intercept (to account for dependencies between subjects), or by a marginal model with an unstructured variance-covariance matrix for the error terms. This procedure allowed us to use all available data points and not only those of women who completed the study protocol.

All analyses in the COC groups were first tested for a possible interaction effect between assessment time and COC groups. If a significant main effect of assessment time was found, post-hoc least square contrasts (comparing all assessment times or cycle phases) were used to locate the source of the difference.

In the analyses reported below, a number of statistical tests were performed, increasing the chance that there would be at least one false positive result. For each separate test, however, this probability was not influenced by the multiple comparisons (Rothman, 1990). Therefore, the nominal p-values have not been corrected for multiplicity, but only results reaching a 0.010 significance level are reported. In the text a "significant" result indicates a $p < .010$ and a "trend", a result where $.010 < p < .050$.

RESULTS

Descriptive characteristics at baseline

Table 2 shows the baseline (T1 in Table 1) characteristics of all participating couples, broken down by contraceptive method and sex. Participants in the NHC group showed few differences when compared to the other contraceptive groups. First, both NHC women and men were older than the participants in the COC groups (women: $F(3,79) = 19.72$, $p < .001$; men: $F(3,79) = 18.71$, $p < .001$) and consequently, had a longer average relationship duration at the time of the study (F (3,79) = 9.51, $p < .001$).

Table 2. Baseline characteristics of the participating couples, by contraceptive method and gender

	NHC° (*n* = 26)		20EE° (*n* = 30)		35EE/CPA° (*n* = 12)		30EE/DRSP° (*n* = 21)	
	Women	Men	Women	Men	Women	Men	Women	Men
Variable	*M (SD)*	*M (SD)*	*M (SD)*	*M (SD)*	*M (SD)*	*M (SD)*	*M (SD)*	*M (SD)*
Age***	31.38 (7.55)	32.46 (7.75)	23.07 (4.50)	24.39 (4.72)	21.18 (1.60)	22 (1.79)	21.4 (2.48)	22.3 (2.60)
Relationship duration***	8.65 (6.83)		3.34 (2.05)		3.26 (1.56)		3.7 (1.99)	
Contraceptive duration (months)	62.67 (49.14)		57.61 (49.80)		34.55 (25.93)		40.8 (20.03)	
COPE	29.83 (29.74)		27.5 (27.05)		28.44 (15.16)		35 (31.05)	
SDI								
Dyadic sexual desire	34.96 (6.05)	38.83 (8.10)	33.43 (7.92)	40.86 (6.14)	39.91 (8.22)	39.73 (6.92)	32.45 (9.58)	39.7 (10.98)
Solitary sexual desire	9.29 (4.59)	11.92 (5.69)	7 (5.91)	10.96 (5.09)	9.73 (4.86)	9.73 (5.61)	8.8 (5.40)	10.9 (5.82)
MMQ								
Relationship dissatisfaction	9.5 (8.01)	6.08 (6.61)	6.82 (5.73)	6.61 (6.25)	7.55 (5.85)	9.82 (6.42)	8.05 (7.47)	7.35 (4.98)
Sexual dissatisfaction*	4.54 (4.58)	4.17 (3.91)	6.75 (4.98)	3.18 (3.3)	3 (3)	4.73 (4.13)	7.2 (4.99)	4.5 (4.74)
General life dissatisfaction*	8.79 (5.05)	5 (2.89)	5.25 (3.23)	5.71 (3.29)	6.09 (3.11)	6.55 (5.07)	6.35 (3.10)	6.5 (4.88)
PANAS								
Positive affect	31.92 (8.96)	34.71 (5.30)	34.11 (5.84)	33.39 (7.45)	29.27 (6.48)	33.45 (6.83)	29.95 (7.17)	33.85 (6.83)
Negative affect	16.46 (7.38)	14.75 (5.32)	13.75 (2.63)	12.54 (3.04)	16.27 (4.98)	13.18 (4.19)	15.40 (6.21)	13.85 (4.38)

Note. NHC: group using nonhormonal contraception; 20EE: group using oral contraception with 20 mcg ethinylestradioland 75 mcg gestoden/desogestrel; 35EE/CPA: group using oral contraception with 35 mcg ethinylestradiol and 2 mg cyproterone acetate; 30EE/DRSP: group using oral contraception with 30 mcg ethinylestradiol and 3 mg drosprirenone;
COPE: Calendar of Premenstrual Experiences; SDI: Sexual Desire Inventory; MMQ: Maudsley Marital Questionnaire; PANAS: Positive Affect and Negative Affect Scale
*$p < .05$. ** $p < .01$. *** $p < .001$. *p*-values indicate baseline differences between hormonal contraceptive groups

Second, the NHC-women were more dissatisfied with their life in general in comparison to the women in the other contraceptive groups (MMQ general life dissatisfaction: F (1,79) = 9.42, p = .003). Third, women in the 35EE/CPA-group reported lower sexual dissatisfaction compared to women in the 20EE- and 30EE/DRSP-groups (MMQ sexual dissatisfaction: (F (1,79) = 6.48, p = .013). No baseline differences between NHC-and COC groups were found for the duration of contraception method use, sexual desire, premenstrual complaints, relationship satisfaction and affect. Regarding all further analyses on T2 – T8, data of ten sessions were missing (on a total of 89 couples X 8 assessment times X 2 partners = 1428 or less than 1%).

Hypothesis 1: sexual desire levels will remain stable throughout the contraceptive cycle

Table 3 shows linear mixed effect models for solitary and dyadic sexual desire throughout the contraceptive and menstrual cycle in male and female partners; specifically, the main effects of using a certain COC (group effect), of the phase of the contraceptive or menstrual cycle (effect of assessment time), and, of the interaction of both. The main effect of a COC group indicates a different distribution of the variable between different COC groups; the main effect of assessment time indicates a different distribution between the seven assessment times within the contraceptive or menstrual cycle. An interaction effect between both indicates the effect of assessment time differs between COC groups.

In the models for the COC groups, the main effects of COC group and the interaction effects for both solitary and sexual desire were not significant (Table 3). Solitary and dyadic sexual desire also showed no significant changes across the menstrual cycle in both the male and female partners. After visual inspection of the trends in Figure 1, between-phase comparisons for a possible trough on pill day 2 (T3) or peak at pill day 14 (T6) were tested but were not significant (p = .222, and p = .217 respectively). It appears that solitary and dyadic sexual desire remained stable during the contraceptive cycle in both partners, confirming our hypothesis.

In the models for the NHC group, no main effects of assessment time were seen. Again, after visual inspection of Figure 2, between phase-comparisons tested the hypothesis of whether sexual desire would increase around the time of ovulation and

decrease during menses, both in comparison to all other phases. In the NHC-women, these between-phase comparisons showed trends towards significance for both solitary and dyadic sexual desire (solitary: $p = .007$ and $p < .001$, dyadic: $p = .009$ and $p = .018$). Solitary and dyadic sexual desire showed no cycle effects across the menstrual cycle in the female participants, despite trends in the between-phase comparisons.

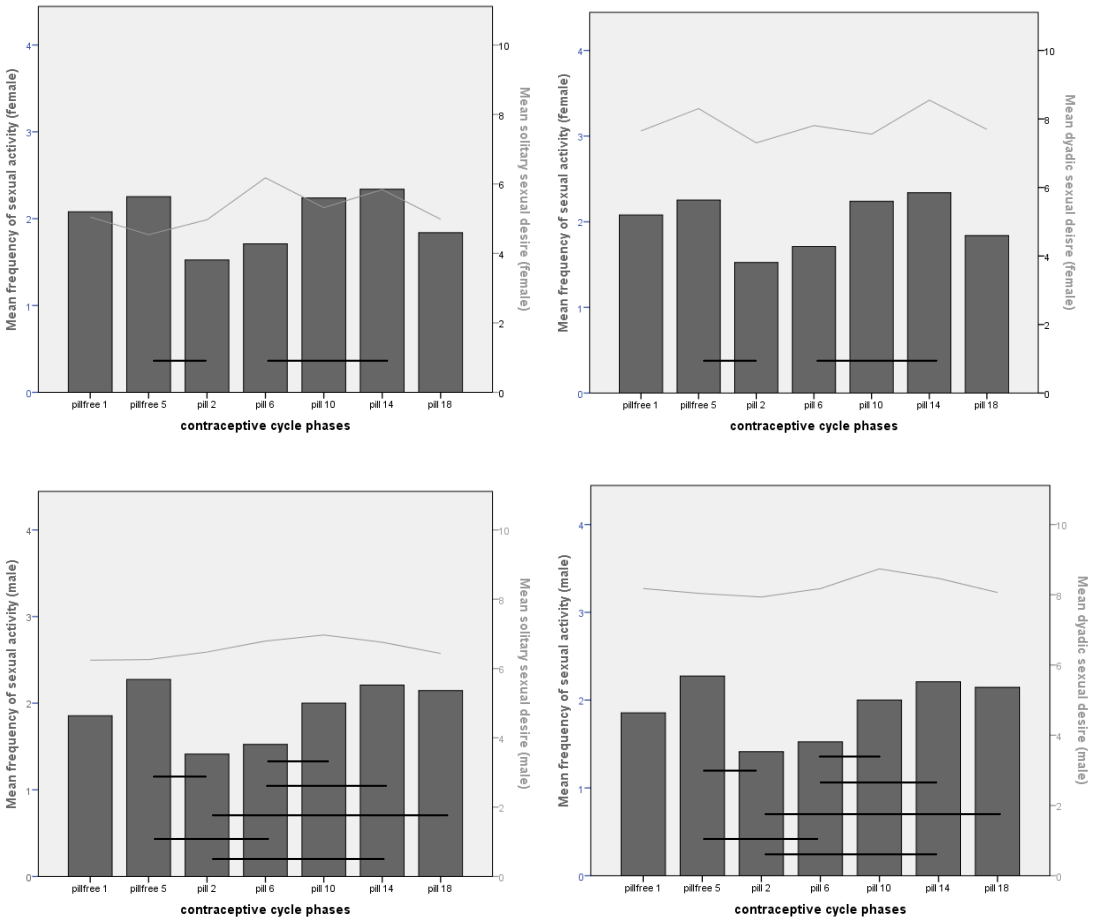

Figure 1. Patterns of sexual desire and sexual activity across the cycle in COC groups.

Lines indicate significant differences between phases (all significance level of $p < .010$).

Table 3. Linear mixed effect models on sexual desire and activity

Solitary sexual desire							
Female COC groups				Male COC groups			
Predictors	*df1*	*df2*	*F*	*Predictors*	*df1*	*df2*	*F*
Group	2	55	0.32	Group	2	55	0.84
Assessment time	6	55	0.79	Assessment time	6	55	0.53
Group X T	12	55	1.97	Group X T	12	55	1.70
Positive affect***	1	55	12.28	Positive affect	1	55	4.71
Negative affect	1	55	0.57	Negative affect	1	55	0.67
Bleeding days	1	55	2.77	Bleeding days	1	55	1.64
Weekend days	1	55	1.42	Weekend days	1	55	0.95
Solitary (baseline)***	1	55	22.99	Solitary (baseline)	1	55	4.61
Female NHC group				Male NHC group			
Predictors	*df1*	*df2*	*F*	*Predictors*	*df1*	*df2*	*F*
Assessment time	6	22	2.84	Assessment time	6	22	0.71
Positive affect**	1	22	8.94	Positive affect	1	22	0.07
Negative affect	1	22	0.87	Negative affect	1	22	1.54
Bleeding days**	1	22	11.00	Bleeding days	1	22	0.15
Weekend days**	1	22	12.06	Weekend days	1	22	1.20
Solitary (baseline)	1	22	0.04	Solitary (baseline)	1	22	4.40
Dyadic sexual desire							
Female COC groups				Male COC groups			
Predictors	*df1*	*df2*	*F*	*Predictors*	*df1*	*df2*	*F*
Group	2	55	0.39	Group	2	55	0.48
Assessment time	6	55	3.29	Assessment time	6	55	1.43
Group X T	12	55	1.68	Group X T	12	55	1.31
Positive affect***	1	55	40.52	Positive affect***	1	55	23.12
Negative affect	1	55	0.00	Negative affect	1	55	0.16
Bleeding days	1	55	1.11	Bleeding days**	1	55	11.41
Weekend days	1	55	0.64	Weekend days	1	55	0.61
Dyadic (baseline)	1	55	5.70	Dyadic (baseline)	1	55	2.63
Female NHC group				Male NHC group			
Predictors	*df1*	*df2*	*F*	*Predictors*	*df1*	*df2*	*F*
Assessment time	6	22	1.92	Assessment time	6	22	3.27
Positive affect	1	22	6.68	Positive affect**	1	22	8.28
Negative affect	1	22	2.63	Negative affect	1	22	0.21
Bleeding days	1	22	3.04	Bleeding days	1	22	0.44
Weekend days	1	22	0.11	Weekend days	1	22	3.63
Dyadic (baseline)	1	22	2.82	Dyadic (baseline)	1	22	0.13

Frequency of sexual activity							
Female COC groups				Male COC groups			
Predictors	*df1*	*df2*	*F*	*Predictors*	*df1*	*df2*	*F*
Group	2	55	2.18	Group	2	56	1.14
Assessment time	6	55	2.99	Assessment time**	6	56	3.56
Group X T	12	55	1.08	Group X T	12	56	1.86
Positive affect**	1	55	8.41	Positive affect	1	56	3.85
Negative affect	1	55	1.16	Negative affect***	1	56	14.53
Bleeding days	1	55	0.05	Bleeding days	1	56	0.89
Weekend days	1	55	0.02	Weekend days	1	56	1.65
Female NHC group				Male NHC group			
Predictors	*df1*	*df2*	*F*	*Predictors*	*df1*	*df2*	*F*
Assessment time	6	22	3,34	Assessment time	6	22	0.92
Positive affect***	1	22	15.19	Positive affect	1	22	3.11
Negative affect	1	22	6.03	Negative affect**	1	22	8.61
Bleeding days**	1	22	8.96	Bleeding days	1	22	0.80
Weekend days	1	22	1.21	Weekend days	1	22	2.89

Note. T: assessment time. ** $p < .010$. *** $p < .001$.

Hypothesis 2: negative affect will not predict sexual desire during the contraceptive cycle

In the models depicted in Table 3, positive and negative affect were included as potential predictors of sexual desire. In the COC groups, positive affect appeared to be a significant predictor for both solitary and dyadic sexual desire: stronger positive affect predicted stronger sexual desire in the female partner. For the male partners, positive affect was only predictive of dyadic and not solitary sexual desire. Regarding negative affect, our hypothesis was supported: in both partners negative affect did not predict their solitary or dyadic sexual desire.

In the NHC group, positive affect had a significant predictive value but only for solitary sexual desire in the female partners and only for dyadic sexual desire in the male partners. The hypothesis that negative affect would not predict solitary or dyadic sexual desire in both partners was thus also confirmed in our control group.

Apart from the models in Table 3, potential cycle effects of negative affect were also assessed separately. In both COC and NHC women, a cycle effect was present. COC women reported a peak of negative affect at the end of the pill-free week (T1), while NHC women showed an increased negative affect during the premenstrual phase (T1) [F (6,421) = 4.71, $p < .001$ and F (6,175) = 3.82, $p < .001$ respectively].

Hypothesis 3: bleeding avoidance and weekend preference will not predict sexual desire during the contraceptive cycle

In the COC groups, there was no predictive value of bleeding or weekend days on the solitary or dyadic sexual desire of the female partners. Male partners, however, reported higher levels of dyadic sexual desire during assessment times with fewer bleeding days (Table 3). Therefore, the hypothesis was only supported for the female partners.

In the NHC group, the female partners indicated a stronger solitary sexual desire during assessment times with fewer bleeding days, confirming the earlier trough in the menstrual phase (see hypothesis 1). Further, they experienced higher dyadic sexual desire during assessment times with more weekend days (Table 3). For the male

partners, however, there was no predictive value of bleeding days or weekend days on solitary or dyadic sexual desire. The hypothesis that nonhormonal factors such as bleeding and weekend do not affect sexual desire was thus only supported for the male partners in the NHC group.

Hypothesis 4: weekend preference and bleeding avoidance will result in "heaping" of activity during the contraceptive cycle

Similar to models for sexual desire, Table 3 shows linear mixed effects models for the frequency of sexual activity during the contraceptive and menstrual cycle. In the COC groups, no interaction effect of COC group and assessment time was found. The main effects of COC groups were not significant. According to the male partners' reports, the frequency of sexual activity was not constant during the contraceptive cycle. Regarding the between-phase comparisons, the male partners reported a decrease in sexual frequency during pill day 2 (T3), compared to the other phases (Figure 1). While the effect of assessment time only showed a non-significant trend (p = .013), a similar – although less clear- trend could be observed in the COC women. Since the nonhormonal predictors of bleeding and weekend days were not significant in either female or male partners (Table 3), and the sexual frequency showed more of a menstrual decline than a pre- or post- menses "heaping", the hypothesis was not supported.

In the NHC group, a trend towards an effect of assessment time was seen only in the female partners (p = .017). When looking at between-phase comparisons, women reported a lower sexual frequency during the menstrual phase (see Figure 2). In this group, this was confirmed by the predictive value of bleeding days as reported by the women: more bleeding days predicted a lower sexual frequency. This effect was, however, not confirmed by the male partners, who did not report such an effect. Sexual activity decreased during the menstrual phase, but the hypothesis of "heaping" of sexuality postmenses was not supported.

Hypothesis 5: negative affect will not predict sexual frequency during the contraceptive cycle

In the models depicted in Table 3, positive and negative affect were included as potential predictors of sexual frequency. In the COC groups, positive affect was a significant predictor of the sexual frequency as reported by the female partners; this was, however, not the case from the perspective of the male partners. Negative affect showed an opposite relationship: this was only a significant predictor for the male partners. The hypothesis that negative affect does not predict sexual frequency during the contraceptive cycle was hence only supported from the female perspective.

In the NHC groups, the findings were similar: for female partners, positive affect predicted the frequency of sexual activity, while for male partners, negative affect predicted the frequency of sexual activity.

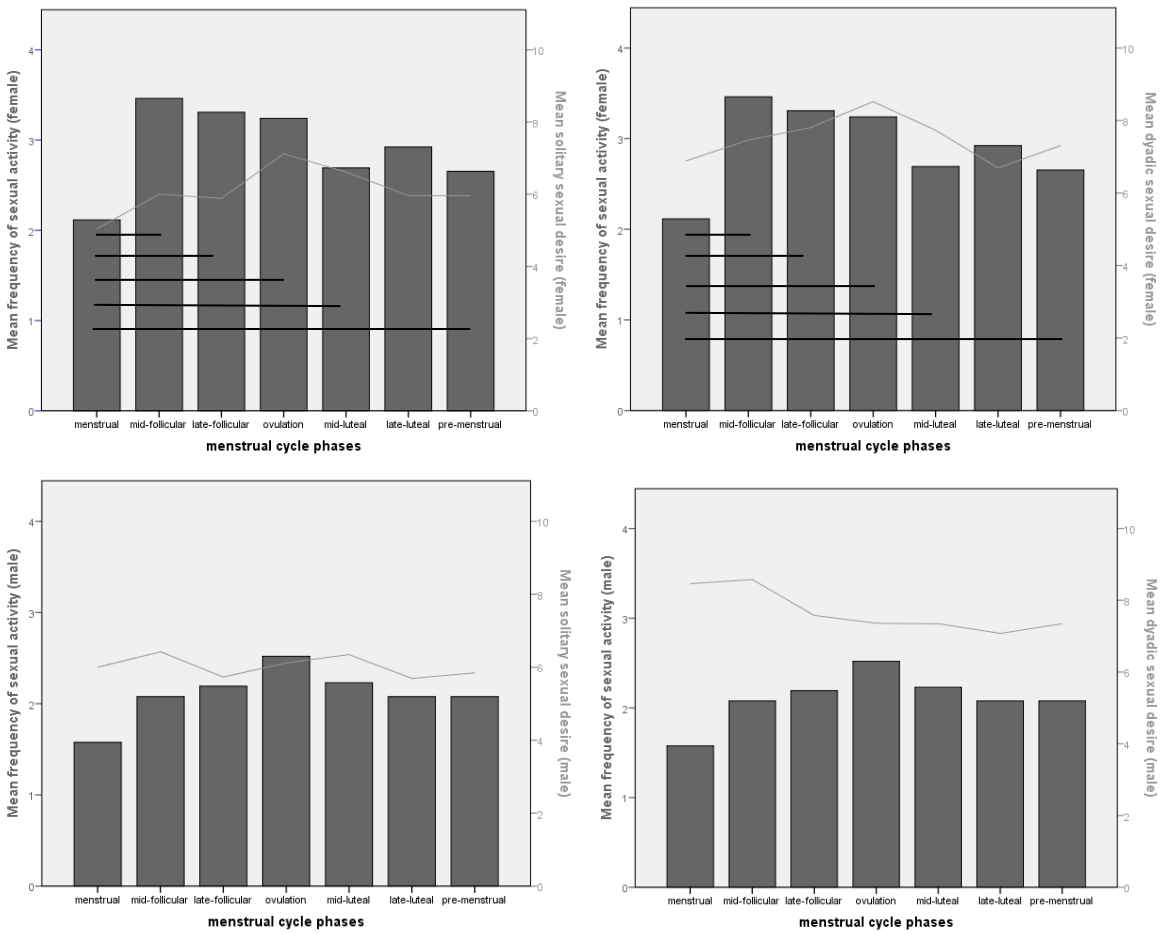

Figure 2. Patterns of sexual desire and sexual activity across the cycle in NHC-groups.

Lines indicate significant differences between phases, arrows indicate significant rises in sexual desire (all significance level of $p < .010$).

DISCUSSION

Summary and interpretation of the findings

The current study set out to investigate potentially different patterns of sexual desire and sexual behaviour in COC users, and compared the patterns of sexual desire and activity with those of a control group of NHC users. As a first step, we looked at the distribution of levels of sexual desire in both partners of COC using couples during the contraceptive cycle. Modelling solitary and dyadic sexual desire, the factors of positive and negative affect were included to test hypotheses on their predictive value on sexual desire. In a second step, a similar model applied to the frequency of sexual activity was tested during the contraceptive cycle. Within this model, the psychosocial factors of bleeding avoidance and weekend preference were added as potential predictors of behaviour.

Patterns of sexual desire across the menstrual cycle. Both male and female partners concordantly experienced no significant peaks or troughs in their solitary or dyadic sexual desire levels across the cycle. This pattern was similar in all three groups of COC users, irrespective of the estrogen-progestin composition or dosage of the hormonal contraception used. This stable pattern confirms earlier studies in monophasic COC users (Alexander et al., 1990; Warner & Bancroft, 1988). Our study has added to this previous research by confirming the concordant perception of this pattern by both the male and the female partner.

In our control group of NHC users, a similar picture appeared. Both solitary and dyadic sexual desire showed no peaks during the ovulatory phase, not in the female or male partners. Despite the use of effective nonhormonal contraception, these women experienced a higher level of desire for solitary sexual activity as well as a higher level of desire for partnered sexual activity at mid-cycle. This observation contradicts several previous studies reporting a mid-cycle peak in sexual desire in freely cycling women (Bullivant et al., 2004; Roney & Simmons, 2013). Contrary to our results in the COC groups, the NHC men were not concordant in sexual desire levels with their female partners. It appears that in users of nonhormonal contraception, hormonal factors might

indeed influence the sexual desire levels of women, despite the absence of a desire to conceive.

Frequency of sexual activity across the menstrual cycle. The current study assessed potential cycle effects on the frequency of sexual activity that was defined as a broad spectrum of activities "aimed at eliciting or expressing sexual desire and/or sexual arousal, not limited to sexual intercourse (penetration)." It was shown that COC users experienced a decreased frequency of sexual activities around restarting a new pill cycle (i.e., pill day 2 and the preceding three days). Based on studies in freely cycling women where quite a universal decrease in sexual activity during the menstrual phase was observed (e.g., Brewis & Meyer, 2005), one could also predict that the withdrawal bleeding in COC women will affect sexual frequency. However, the current study could not establish a relationship between the number of bleeding days and this decreased sexual activity (in either men or women). Since no increase in sexual frequency after the withdrawal bleeding was seen, COC users did not report a tendency towards catching up after a more abstinent time, not supporting a hypothesis on "heaping" sexual activity. The other psychosocial factor included in these analyses, weekend preference, also did not show a relation with sexual frequency. This is in contrast to a recent study, which identified this as an important predictor (Roney & Simmons, 2013). But since the majority of the COC sample in our study consisted of students (some of which were possibly separated from their partners at the weekend and did not have the stress of a working week), this might have been due to the composition of the present sample.

Concluding that bleeding avoidance had predictive value for sexual frequency remains difficult considering the lack of a significant association. Due to the study design, the daily bleeding reports were transformed into a new variable (number of bleeding days per assessment time) that fitted into the seven assessment times across the cycle. Possibly this has obscured this relationship.

Connecting the trough in sexual frequency around starting a new pill cycle to the stable sexual desire levels, differential desire and activity patterns in COC users are confirmed. While a clear connection with bleeding avoidance remains to be repeated in future studies, the current observations make this a plausible potential predictor.

Affect and sexual desire and activity changes. The current study added the potential confound of affect in the analyses for both sexual desire and sexual activity, to test the hypothesis that negative effect would not covary with sexual desire, especially

in the female partners. Confirming previous studies in pill users (Graham & Sherwin, 1993), it was found that negative affect indeed did not impact the level of sexual desire across the contraceptive cycle. We did find, however, a predictive effect of positive affect on both the solitary and dyadic sexual desire of the female partners, but only on the dyadic desire of the male partners. Furthermore, positive affect correlated with frequency of sexual activity from the female perspective, while negative affect appeared to be an important factor from the male perspective.

Strengths and limitations

The current prospective study assessed sexual desire and activity during the contraceptive and menstrual cycles. Moreover, to get a clearer picture of relevant heterosexual couple processes in both COC- and NHC-users, the perception of the male partner was included in all measures, expanding on the intra-individual measures and assessing concordance in the perception between partners. Due to the broad focus on both sexual desire and a variety of sexual behaviours in one study, it was further possible to identify the discordance between sexual desire and more partnered sexual behaviour, affirming previous literature (e.g., Bullivant et al., 2004).

However, the findings are also limited by a number of factors. First, pill users were all current users and not pill starters. As pill starters have a high discontinuation rate (up to 47%) (Hatcher & Nelson, 2004; Sanders, Graham, Bass, & Bancroft, 2001), a certain selection bias might have altered the results. Second, the current design analysed data in a between-subject design, which is again a potential source for a selection bias. Third, the psychosocial factors of bleeding avoidance and weekend preference were reduced to seven assessment times, potentially reducing the chances of finding relationships with other variables. Fourth, only one contraceptive or menstrual cycle was studied, not allowing for between-cycle variations. Roney and Simmons (2013), however, only found 2.7% of the variation in sexual desire was due to between-cycle differences. Fifth, the samples of the three COC subgroups were rather small and may have had limited power. Sixth, the NHC sample was significantly older than the COC sample. While this difference could have obscured the relationship between weekend preference and frequency of sexual activity (as noted above), this age difference might also have biased other results. Finally, due to the financial constraints of a daily collection of (hormonal) biomarkers

and potential effects on the study outcome variables, the menstrual phases were determined by use of the backward count method, which might have affected the results.

Conclusion

The current study adds to the knowledge of sexual desire patterns and a menstrual decrease in sexual frequency in freely cycling women, and provides information on COC users. It was shown that differential patterns for sexual desire and sexual activity are also present in the COC group, and moreover, are quite concordant between male and female partners. Use of COCs appears to cause a “flattening” of sexual desire across the contraceptive cycle, and a pattern of decreased sexual activity at the end of the pill-free week.

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CHAPTER 5

HYPOACTIVE SEXUAL DESIRE IN TRANS WOMEN: PREVALENCE AND ASSOCIATION WITH TESTOSTERONE LEVELS [1]

ABSTRACT

An unknown proportion of trans women (post-operative male-to-female individuals on oestrogen replacement) experiences hypoactive sexual desire disorder (HSDD). It was suggested that absence of ovarian androgen production, together with oestrogen treatment-related increase in SHBG levels, could be leading to HSDD, due to low levels of biologically available testosterone (T). This study documents the HSDD-prevalence and the possible association to androgen levels in a cross-sectional design, including trans women (n = 62) and a control group of freely cycling women (n = 30). Questionnaires measuring sexual desire, relationship and sexual satisfaction were completed. Serum levels of total T, LH and SHBG were measured in blood samples obtained at random in transsexual women and in the early follicular phase in control women. The trans group had lower levels of total and calculated free T (both $p < .001$) than the control group. HSDD was reported in 34% of the trans and 23% of the control women (p = .30). Both groups reported similar levels of sexual desire (p = .97). For trans women, no significant correlation was found between sexual desire and total (p = .64) or free T (p = .82). In freely cycling women, these correlations were significant (p = .006, resp. p = .003). HSDD is reported in one third of trans women. This prevalence is not substantially different from controls, despite markedly lower (free) T levels, which argues against a major role of T in this specific group.

[1] Based on Elaut, E., De Cuypere, G., De Sutter, P., Gijs, L., Van Trotsenburg, M., Heylens, G., Kaufman, J.M., Rubens, R., & T'Sjoen, G. (2008). Hypoactive sexual desire in transsexual women: prevalence an association with testosterone levels. *European Journal of Endocrinology, 158,* 393-399.

INTRODUCTION

Our knowledge on the role of androgens in female sexuality is limited (Scepkowski, Georgescu, & Pfaus, 2006; Wierman et al., 2006): many unanswered questions remain concerning the normative data on (free) testosterone across the lifespan. Some studies have observed an association between measures of female sexual desire and serum concentrations of total and free testosterone (T) (Santoro et al., 2005; Turna et al., 2005) while others could not confirm this (Davis, Davison, Donath, & Bell, 2005). Although a biopsychosocial approach to female sexuality remains in order, there seems to be a consensus upon a role of T in motivational aspects of sexuality such as sexual desire (Sherwin, 1985; Sherwin, Gelfand, & Brender, 1985). Clinicians still wonder under which cut-off levels of total or free T complaints of low sexual desire most often occur and a well defined clinical syndrome is still missing (Wierman et al., 2006).

Aware of this debate on the relationship between sexual desire and testosterone, specialists working in centres for treatment of gender dysphoria are confronted with trans women[2] (i.e., post-operative male-to-female individuals on lifelong oestrogen replacement) complaining of low sexual desire. Assuming gender-confirming surgery is performed skilfully without damage to the neurovascular bundle innervating the neo-clitoris, these complaints might be related to serum androgen levels below the normal female range. Considering a possible role of T in female sexual desire among the general population (Santoro et al., 2005; Turna et al., 2005), the lack of ovarian androgen production and the effect of continuous oestrogen treatment on the production of SHBG in trans women might lead to hypoactive sexual desire disorder (HSDD) due to low levels of free T. Although an earlier study from our group showed decreased levels of free T in a majority of transsexual women (De Cuypere et al., 2005), the association between sexual desire and T in this group remains to be examined. Considering the observation of sexual desire complaints in trans women, and the – much debated (Bancroft, Loftus, & Long, 2003; Rosen & Laumann, 2003) - high prevalence of a lack of sexual interest

[2] With the goal of a consequent use of terminology in the current dissertation, some vocabulary has been altered compared to the original publication. The term “transsexual women” was replaced by “trans women” in this chapter. Similarly “ovulating women” was replaced by “freely cycling women”, and “sex reassignment surgery” by “gender-confirming surgery.”

among women in the general population (25.6% in Northern European women (Laumann et al., 2005), it would be relevant to assess this prevalence in transsexual women.

The objective of this study was to assess the prevalence of HSDD and the association between serum androgens and sexual desire in trans women. Considering the ongoing debate on both topics in women in general, a control group of freely cycling women was included. The hypothesis was that the trans women would have lower serum androgens in comparison to the control group – due to the continuous oestrogen replacement and the lack of an ovarian androgen source. Considering a possible association between androgens and sexual desire, a higher prevalence of HSDD was expected to be seen in the trans women.

METHOD

Definitions

Since the DSM-IV definition of HSDD has provoked serious criticism (Basson, 2002), this study set out to work in accordance with the Sexual Function Health Council's consensus definition (Basson et al., 2000), dated 1998. This interdisciplinary team defined HSDD as 'the persistent or recurrent deficiency (or absence) of sexual fantasies, thoughts, desire for sexual activity (alone or with a partner) *and* inability to respond to sexual cues that would be expected to trigger responsive sexual desire. These symptoms need to be causing personal distress."

In order to make a correct estimate of the prevalence of HSDD according to the above definition, a distinction was made in the questionnaires between "spontaneous sexual desire" and "responsive sexual desire". This was explained as follows: "Some women experience *spontaneous sexual desire* (meaning having sexual thoughts, dreams, fantasies or initiating sexual activity). Other women mainly experience sexual desire when approached or touched by their partner or when perceiving sexual stimuli from a book or television, called *responsive sexual desire*. Another group of women experience both at different times." Two questions were asked about the frequency of spontaneous and responsive sexual desire (never/rarely; from time to time; often/usually). A third

question ("Is your sexual life hampered by problems of sexual desire felt by either yourself or by your partner?") reflected the presence of personal distress caused by potential problems concerning sexual desire. Participants could indicate a problem with too much/little sexual desire in themselves/their partner. We defined the diagnosis of HSDD (nominal variable) as follows: when a participant indicated that she never/rarely experienced either spontaneous or responsive sexual desire, and that her sexual life was hampered by a lack of sexual desire within herself ánd that this lack caused her distress.

Study population

Between January and October 2005, 62 trans and 30 ovulating women were recruited. Transsexual women on continuous oestrogen replacement were mainly reached through their follow-up visits to the Centre for Sexology and Gender Problems (University Hospital Ghent, Belgium) (37%) and the Centre for Gender Dysphoria (VU University Medical Centre Amsterdam, the Netherlands) (45.2%). Since both the Flemish and the Dutch centre work according to similar diagnostic criteria in treating gender dysphoric patients, the comparability of all recruited patients was guaranteed. Eleven trans women (17.7%) responded to banners on transgender community websites and participated through a local laboratory in the Netherlands. The majority of trans women used transdermal estradiol (mainly in gel form resulting in a 3.0 mg daily dose of estradiol) or oral estradiolvalerate (1 to 4 mg) (40.3% and 33.9%). The remaining participants used oral conjugated oestrogens (11.3%) or ethinylestradiol (9.7%).

The control group of freely cycling women was recruited through posters in the Ghent University Hospital and consisted mainly of staff and students. Eligible participants were healthy women between 18 and 45 years of age. Exclusion criteria were use of steroidal contraception (combination pill, mini-pill, vaginal ring, contraceptive patch or progestin IUD), medication possibly influencing androgen levels or sexual desire (like antidepressants or glucocorticoids) and other confounders for SHBG such as alcoholism, cirrhosis, Cushing syndrome, and hyper- and hypothyroidism (Wu, Ames, Evans, France, & Reid, 2001). We chose not to include cisgender (or not-trans) women who have been oophorectomized and treated with oestrogens in our control group as this is the first study to address sexual desire in relation to androgens in gender dysphoric individuals and we aimed to describe the difference in androgen status

between groups caused by the presence/absence of ovaries. Table 1 shows characteristics of both groups. Because of the age criterion in the ovulating women, both groups differed significantly in age ($p < .001$).

Study procedures

A website was designed where participants read about the background and objectives of the study to guarantee an informed consent. They completed questionnaires on sexual desire and relationship/sexual satisfaction online and subsequently contacted the research team for the withdrawal of a morning blood sample. A minority of the Dutch trans women received a package which would allow their general practitioner or a local clinical laboratory to draw a morning blood sample. This package contained both all necessary medical material as well as instructions for the participant and their general practitioner or local laboratory to perform the blood draw correctly and without any costs. After the blood collection, serum and red blood cells were separated locally. A courier company immediately transported the serum to the Ghent University Hospital (Belgium) where it was stored at - 80° Celcius until analysis. Most trans women however were recruited at their follow-up visits to one of the two participating centres and had a venous blood sample collected between 8 and 12 am at their centre. They subsequently filled out the questionnaires online. All trans women had their blood sample drawn at random, regardless of the timing of oestrogen intake. All Flemish freely cycling women had their blood drawn between 8 and 12 am in the early follicular phase (third or fourth day after the start of menstruation).

This study complied with the recommendations of the Declaration of Helsinki and was approved by the Ethical Committee of the Ghent University Hospital.

Measures

Sexual desire. The Dutch version of the 14-item Sexual Desire Inventory (Spector, Carey, & Steinberg, 1996) was used to measure sexual desire, defined as “an interest in sexual activity”, as a cognitive variable. The scale measures the frequency and strength of thoughts in regards to seeking out or being receptive to sexual stimuli. For the frequency-items participants chose one of seven options. For the strength-items,

participants scored their sexual desire on a 9-point Likert scale ranging from 0 (no desire) to 8 (strong desire). Participants were asked to take the previous month as a referent. Adding items resulted in a score for *dyadic sexual desire* (interest in behaving sexually with a partner) and *solitary sexual desire* (interest in behaving sexually by oneself). The Sexual Desire Inventory has a good reliability and validity (Spector, Carey, & Steinberg, 1996). Internal consistency was high, in the group of trans (Cronbach's α = .93) and freely cycling women (Cronbach's α = .92).

Sexual and relationship satisfaction. The Dutch version of the 20-item Maudsley Marital Questionnaire (Arrindell, Boelens, & Wambert, 1983) was used to measure relationship, sexual and general life satisfaction. Only participants with a steady partner filled it out. Every item is scored on a Likert scale from 0 to 8. Participants were asked to take the previous two weeks as a referent. On all subscales, a higher score indicates more problems. The Maudsley Marital Questionnaire has a good reliability and validity (Arrindell, Boelens, & Lambert, 1983). Internal consistency was high, as well in the group of trans (Cronbach's α = .84) and freely cycling women (Cronbach's α = .87).

Diagnosis of HSDD. At the time this study was conducted, no validated questionnaires were available to establish an HSDD-diagnosis. Working with the consensus definition by Basson and others (2000), a very strict adaptation was made as described above.

Hormone assays. Serum T was assayed in 2 ml serum samples with an in house RIA in duplicate after ether extraction followed by paper chromatography (Vermeulen & Verdonck, 1976; Vermeulen & Verdonck, 1978): intra- and inter-assay coefficient of variation for this assay was 5.6% (at a concentration of 35 ng/dl, i.e. 1.21 nmol/L) and 8.5% (at a concentration of 25 ng/dl, i.e. 0.87 nmol/L), respectively; lower limit of quantification is 2 ng/dl (0.07 nmol/L). Commercial kits for RIA were used to determine the serum concentrations of sex hormone binding globulin (SHBG; Orion Diagnostica, Espoo, Finland) and dehydroepiandrosterone sulphate (DHEA-S; DSL Inc., Webster, Texas); intra-assay coefficients of variation were between 2.5% and 8.3% and between 3.1% and 5.6% for SHBG and DHEA-S, respectively. For all measurements, all samples from transsexual women and controls were assayed in a same assay run. Serum FT was calculated from the total serum hormone concentration, serum SHBG and serum albumin, using a validated equation derived from the mass action law (Vermeulen, Verdonck, & Kaufman, 1999).#

Table 1. Characteristics of participants

Characteristic	Transsexual women (n = 62)	Ovulating women (n = 30)	p[a]
Age (in years)			
M ± *SD*	43.0 ± 10.0	31.0 ± 7.1	<.001
Range	22 - 65	19 - 45	
Body Mass Index (kg/m²)			
M ± *SD*	24.1 ± 4.7	22.8 ± 4.3	.120
Range	15.2 - 38.6	18.4 - 38.4	
Sex Reassignment Surgery (in years)			
Time since surgery	5.2 ± 5.8		
Duration of oestrogen replacement	7.4 ± 5.8		

Note. Significance levels are according to non-parametric Mann-Whitney U-tests.

Statistical analysis

Since the distribution of the dependent variables (sexual desire, sexual/relationship satisfaction) did not follow a normal distribution, nonparametric Mann Whitney U-tests were used to test between-group differences of these ordinal variables. A χ^2 - test was used to compare the nominal variable (diagnosis of HSDD) between both groups. Partial correlations tested the association between levels of T and sexual desire.

RESULTS

Sexual desire

All participants completed the Sexual Desire Inventory reflecting solitary and dyadic sexual desire. As shown in Table 2, there were no significant differences between ovulating and transsexual women, either in solitary sexual desire (p = 0.97), or in dyadic sexual desire (p = 0.26).

Table 2. Psychosexual outcomes

Variable	Trans women	Freely cycling women	p [a]
Sexual Desire Inventory	(n = 62)	(n = 30)	
Solitary sexual desire	9.2 ± 6.2	9.2 ± 6.2	0.97
Dyadic sexual desire	29.2 ± 14.8	32.7 ± 14.0	0.26
Maudsley Marital Questionnaire	(n = 27)	(n = 21)	
Relationship satisfaction	11.3 ± 11.8	10.5 ± 8.3	0.82
Sexual satisfaction	18.0 ± 9.4	6.2 ± 8.8	0.002
General life satisfaction	8.7 ± 6.3	7.3 ± 2.7	0.55

Note. Data are presented as $M \pm SD$.
[a] Significance levels are according to non-parametric Mann-Whitney U-tests.

Relationship/sexual satisfaction

One sample t-tests showed that the control group did not differ significantly from the normal female population (Arrindell, Boelens, & Lambert, 1983) (relationship satisfaction: $t(20) = -0.18$, $p = .86$; sexual satisfaction: $t(20) = 0.50$, $p = .62$; general life satisfaction: $t(20) = 0.11$, $p = .91$), confirming its representativeness. Trans women reported significantly less sexual satisfaction ($p = .002$) than freely cycling women. Regarding relationship and general life satisfaction ($p = .82$ and $p = .55$), trans and control women did not differ significantly.

Prevalence of HSDD

HSDD was diagnosed in 33.9% of trans and in 23.3% of control women. Although the percentage is higher in the trans women, there was no difference in the prevalence of HSDD ($\chi^2(1) = 1.06$, $p = .30$) between both groups. Our hypothesis concerning the frequency of HSDD was thus not confirmed. Furthermore, these percentages did not differ significantly from the general female population (25.6%) (Laumann et al., 2005) (95% confidence interval, 22.1% to 45.7%).

Hormonal data

In Table 3, serum concentrations of SHBG, DHEA-S, free T and total T are presented. In both groups, all concentrations were as physiologically expected. Our hypothesis concerning the serum concentrations of androgens was thus confirmed. The levels of total T and calculated free T were significantly lower in trans women when compared to those of the control women (both $p < .001$). More specifically, 66.1% of trans women had levels of total T below the P25 in ovulating women (P25 = 23.88 ng/dl) (0.8 nmol/L). For calculated free T, 59.7% of trans women had levels below the P25 in control women (P25 = 0.28 ng/dl) (0.01 nmol/L). Two ANCOVA's showed that these lower levels were a main effect of *group* and not of the higher *age* of the trans group [$F(1) = 12.573$, $p = .001$ for total T and $F(1) = 9.235$, $p = .003$ for free T]. Serum levels of SHBG ($p = 1.00$) and DHEA-S ($p = .57$) did not differ between both groups.

Table 3. Serum concentrations in trans and freely cycling women

	Trans women (n = 62)	Freely cycling women[a] (n = 30)	Normal female range[b]	p[c]
Total T (ng/dl)				
M ± *SD*	20.0 ± 9.6	33.9 ± 17.9		<0.001
Range	2.4 - 53.0	16.6 - 109.1	10.0 - 80.0	
Free T (ng/dl)				
M ± *SD*	0.26 ± 0.16	0.47 ± 0.31		<0.001
Range	0.03 - 0.99	0.19 - 1.61	0.20 - 0.50	
SHBG (nmol/l)				
M ± *SD*	63.1 ± 38.1	55.7 ± 19.9		1.00
Range	20.7 - 197.6	17.7 - 98.1	15.5 - 114.0	
DHEA-S (µg/dl)				
M ± *SD*	219.5 ± 115.9	228.8 ± 88.5		0.57
Range	5.5 - 536.5	94.9 - 409.0	98.8 - 340.0	

Note. [a] Early follicular values.
[b] Reference ranges according to local laboratory.
[c] Significance values are for comparison between the transsexual and ovulating women according to non-parametric Mann-Whitney U-tests.

Trans women using oral preparations of oestrogen replacement had significantly higher levels of SHBG than those using transdermal preparations (73.3 ± 45.1 nmol/L versus 47.5 ± 23.7 nmol/L; p = .02). Levels of total T and calculated free T did not differ between groups according to the mode of administration (data not shown). Differences in serum concentrations (and psychosexual measures) between different types of oral substitution (ethinylestradiol, conjugated oestrogens and estradiolvalerate) could not be tested due to low numbers in some groups.

Association between sexual desire and hormone levels

With the age of the transs women being higher than those of the control women, and the known age-related decline in levels of DHEA-S (Laughlin, Barret-Conner, Kritz-Silverstein, & von Muhlen, 2000; Randolph et al., 2003), the correlations between androgen levels and measures of sexual desire (Table 4) have been corrected for age by using partial correlations. In trans women, no significant relation was found between androgen levels and measures of sexual desire. However, in the control women a significant positive correlation was found between solitary sexual desire and levels of total T (r = .50, p = .006) and free T (r = .53, p = .003). In both groups no significant differences in serum concentrations of DHEA-S, total T or free T were found between participants with and without HSDD (data not shown). In the transsexual women there was no relation between having an HSDD-diagnosis and having a FT level below the P25 in ovulating women ($\chi^2(1) = 0.25$, p = .61).

Table 4. Partial correlations between sexual desire measures and hormone concentrations

Hormone	Trans women (*n* = 62)		Freely cycling women (*n* = 30)	
	Solitary sexual desire	Dyadic sexual desire	Solitary sexual desire	Dyadic sexual desire
	r (p)	*r (p)*	*r (p)*	*r (p)*
DHEA-S	0.07 (0.59)	0.13 (0.34)	0.20 (0.29)	0.35 (0.06)
Total T	-0.06 (0.64)	-0.03 (0.83)	0.50 (0.006)[a]	0.29 (0.13)
Free T	0.03 (0.82)	0.10 (0.42)	0.53 (0.003)[a]	0.33 (0.08)

Note. All correlations are corrected for age.
[a] Values lower than the 5 percent level of significance

DISCUSSION

This study is to our knowledge the first to address sexual desire and serum androgens in a relatively large group of trans women. Using a strict measure of HSDD, one out of three transsexual women suffers from a lack of sexual desire after sex-reassignment surgery. Since research concerning HSDD-prevalence in this group has not been yet reported, comparisons with other samples are not possible. HSDD does not appear to be substantially more prevalent in this group than in the general female population.

Trans women experience sexual desire of similar frequency and intensity as ovulating women. Nevertheless, there seems to be a general "sexual discontent" in transsexual women such as can be gathered from the lower sexual satisfaction this group experiences in its sexual partnerships. Since sexual satisfaction was not the focus of this study, we were not able to explore the reasons behind this.

The serum concentrations of DHEA-S are comparable in trans and freely cycling women, indicating a similar level of adrenal androgen production. Serum concentrations of total T measured by RIA following extraction and chromatographic separation and calculated free T are, as expected, markedly lower in the trans women. In 59.7% of the trans women concentrations remain below the P25 of FT found in freely cycling women. In an earlier study, 32.1% of trans women had serum levels of FT within the expected female range (direct RIA-method used) (De Cuypere et al., 2005). According to the same criterion, this is 35.5% in the current study.

In the trans women, we could not establish an association between sexual desire and androgens. In the freely cycling women, a positive association was observed: higher serum concentrations of total T and free T accompany a higher frequency and intensity of solitary sexual desire. This result is in line with observational research in pre-menopausal women where an association exists between free T and sexual desire (Turna et al., 2005). The absence of this association in trans women could have several reasons. First, the majority has very low levels of total and free T. This complicates finding a relation with sexual desire. Second, the profound decrease in T levels trans women experienced during confirming treatment (both hormonal and surgical) could play a role. It is possible that such a decrease demands a certain "sexual reconditioning"

from the individual and the partnership. Research on surgical menopausal women has described - if to a lesser extent - somewhat similar events: removal of the ovaries causes a decrease in T levels and sexual desire (Dennerstein, Koochaki, Barton, & Graziottin, 2006; Mazer, Leiblum, & Rosen, 2007; McHorney et al., 2004; Nathorst-Böös, von Schoutz, & Carlström, 1993). This psychological process of adjusting to a lower serum level could be of influence on the association between T and sexual desire. Third, not only androgens play a role in sexual motivation. It is very well possible that the relief of finally being in the desired body and being socially accepted as a woman causes a healthy sexual appetite despite very low T levels. Fourth, the functionality and esthetics of the new genitals could have their influence on sexual satisfaction and possibly on sexual desire.

As to the limitations of this study, we have no information on the used method of non-hormonal contraception in the ovulating group, making it impossible to investigate this potential influence on sexual desire. Also, the subtle nuances of transsexual women's sexual desire might not have been adequately measured as the questionnaires were designed for women in general, even though they did allow detecting differences in sexual satisfaction. Furthermore, despite the fact that we were able to study a substantial number of trans women, and that the findings for our control group are in good agreement with those for the general population, the power of the comparison between trans and control women was limited. Nevertheless, the observations in this study converge to indicate that low T does not play a prominent role in low sexual desire in transsexual women: i.e. a markedly high prevalence of low total or free T in the trans women is accompanied by an at most modest increase of the prevalence of HSDD, whereas within this group, there is no relationship between androgen levels and indices of sexual desire. Measurement of low T in women is technically difficult and has been an impediment in defining a clinical syndrome of androgen deficiency in women (Wierman et al., 2006). In the present study we addressed this technical problem by extracting T from an adequately large, 2 ml serum sample and by using a well validated method involving a chromatographic separation step.

In conclusion, HSDD is reported in one third of trans women. This prevalence is not substantially different from controls and reports from the general population. The levels of total and free T in trans women were found to be at or below the lower end of the spectrum for total and free T seen in the control group. No apparent association exists

between these levels and the complaints of low sexual desire patients experience, which argues against a major role of total or free T in this specific group. These observations should therefore be broadened by studies in the psychological and social field to help explain possible mediating factors.

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CHAPTER 6

CONTRIBUTION OF ANDROGEN RECEPTOR SENSITIVITY TO THE RELATION BETWEEN TESTOSTERONE AND SEXUAL DESIRE: AN EXPLORATION IN TRANS WOMEN.[1]

ABSTRACT

Low sexual desire is present in one third of trans women (post-operative male-to-female transsexual persons on estrogen replacement). Studies report lower endogenous testosterone (T) levels in this group compared to community dwelling women. No relationship between T and sexual desire has been found in trans women. Considering its role in androgen sensitivity, cytosine-adenine-guanine (CAG) trinucleotide repeat sequence in the *androgen receptor* might modify the relationship between T levels and sexual desire in trans women. This study aims to assess the potential contribution of the number of CAG repeats in the association between testosterone and sexual desire in 34 trans women that participated in a cross-sectional study. Sexual desire and hormonal levels were assessed. The CAG repeat length ranged from 14 to 28 with a median of 21. CAG polymorphism was correlated with free T (r = .39; p = .023) but not with total T (r = .19; p = .28). The observed interaction between total T and CAG was significant only for solitary sexual desire (p = .002). The interaction of CAG repeats and free T on sexual desire failed to reach significance. We could not establish that CAG repeat length is a consistent modulating factor in the relationship between total or free T and sexual desire in male-to-female transsexuals.

[1] Based on Elaut, E., Bogaert, V., De Cuypere, G., Weyers, S., Gijs, L., Kaufman, J.-M., & T'Sjoen, G. (2010). Contribution of androgen receptor sensitivity to the relation between testosterone and sexual desire: an exploration in male-to-female transsexuals. *Journal of Endocrinological Investigations, 33, 37-41.*

INTRODUCTION

The relationship between androgen levels and motivational aspects of female sexuality is since long a subject of debate (Wierman et al., 2006, 2007; Traish, Guay, & Spark, 2007). Davis and colleagues (2005) found no association between measures of female sexual desire and total or free testosterone (T), while other studies did establish a significant correlation (Santoro et al., 2005; Turna et al., 2005). Also, previous results from our study group confirmed the association of sexual desire with free T in a sample of freely cycling women (Elaut et al., 2008). This relationship was however not found in a group of trans women[2] (after gender-confirming surgery and on continuous estrogen treatment). Trans women lack a gonadal androgen source and hence have androgen levels that are significantly lower than those of community dwelling women (De Cuypere et al., 2005). Despite the fact that one in three trans women experiences complaints of low sexual desire, our previous study showed no association between androgen levels and sexual desire (Elaut et al., 2008).

Androgen sensitivity can alter the extent to which one can react to circulating serum androgen levels (Albertelli, Scheller, Brogley, & Robins, 2006; Crabbe et al., 2007). This androgen sensitivity is partly mediated by genetic variation in the *androgen receptor (AR)*, located on the X chromosome at Xq11-12 (Brown et al., 1989). The aminoterminal transactivating domain of the *AR* is encoded by exon 1 and contains a highly polymorphic cytosine-adenine-guanine (CAG) trinucleotide repeat sequence which results in a variable number of glutamines in a functionally important polyglutamine tract in the *AR* protein (Brown et al., 1989). The number of CAG repeats varies from 8 to 31 in non-transsexual males (Edwaqrds, Hammond, Lin, Caskey, & Chakraborty, 1992), and a shorter repeat length within the normal range is associated with a higher *AR* transactivation and androgen sensitivity. The CAG polymorphism seems to affect the hypothalamic-pituitary feedback regulation with longer CAG repeats being associated with diminished androgen feedback/sensitivity and relative elevation of circulating T

[2] With the goal of a consequent use of terminology in the current dissertation, some vocabulary has been altered compared to the original publication. The term “transsexual women” was replaced by “trans women” in this chapter. Similarly “ovulating women” was replaced by “freely cycling women”, and “sex reassignment surgery” by “gender-confirming surgery.”

levels (explaining 6 to 8.5 % in total and 10 to 14 % in free T variability) (Crabbe et al., 2007). There are a few studies describing the CAG repeat length in trans women in the context of assessing its role in the etiology of transsexualism. Henningsson and colleagues (2005) stated that while CAG did not differ between trans women and non-trans males, the *AR* gene, the estrogen receptor (subtype β) and the aromatase gene may partially contribute to the risk of developing gender dysphoria if present in certain combinations. A recent Australian study identified a significant longer mean CAG repeat lengths in comparison to non-trans male controls, possibly resulting in less effective testosterone signalling (Hare et al., 2009). However, in humans no studies on the role of CAG repeat lengths in sexual desire in humans have been conducted, neither in the general population, nor the gender dysphoric population.

Taken into account that the *AR* gene CAG repeat polymorphism is a determinant of androgen sensitivity, the aim of this study was to test the hypothesis that this polymorphism might be a modulating factor in the relationship between androgen levels and sexual desire in trans women. Most trans women obviously have received neonatal androgen imprinting and also experienced a male pubertal development. The possibility that this imprinting may have a persisting effect on sexual desire, both solitary and dyadic, cannot be dismissed.

METHOD

Study population and procedures

A website was posted on the internet where participants could read the background and objectives of the study to guarantee informed consent. Between January and October 2005, 34 Caucasian trans women were recruited.

Twenty-three (67.6%) trans women on continuous estrogen replacement were contacted through their follow-up visits to the Centre for Sexology and Gender Problems (Ghent University Hospital). They had a venous blood sample collected between 8 and 12 am at the hospital and subsequently filled out the questionnaire online at home. Eleven trans women (32.4%) responded to banners on transgender community websites and participated through a local laboratory in the Netherlands (see Elaut et al., 2008).

They received a package allowing their general practitioner or a local laboratory to draw a morning blood sample correctly and without any personal cost. Following blood collection serum and red blood cells were separated locally. A courier company transported the serum immediately to the University Hospital of Ghent (Belgium) where it was stored at -80° Celsius until analysis.

The majority of trans women used transdermal estradiol (mainly in gel form resulting in a 3.0 mg daily dose of estradiol) (52.9%) or oral estradiolvalerate (1 to 4 mg) (35.3%). The remaining participants used oral conjugated estrogens (*n* = 1 or 2.9%), ethinylestradiol 0.02 mg (*n* = 1 or 2.9%) or ethinylestradiol 0.035 mg with cyproteronacetate 2 mg (*n* = 2 or 5.8%). This study complied with the recommendations of the Declaration of Helsinki and was approved by the Ethical Committee of the Ghent University Hospital.

Main outcome measures

Sexual desire. A validated Dutch version of the 14-item Sexual Desire Inventory was used to measure sexual desire as a cognitive variable and defined as 'an interest in sexual activity' (Spector, Carey, & Steinberg, 1996). The scale measures the frequency and strength of thoughts in regards to seeking out or being receptive to sexual stimuli. For the frequency-items participants chose one of seven options. For the strength-items, participants scored their sexual desire on a 9-point Likert scale ranging from 0 (no desire) to 8 (strong desire). Participants were asked to take the previous month as a referent. Adding up the items of the questionnaire resulted in a score for *dyadic sexual desire* (interest in behaving sexually with a partner) and *solitary sexual desire* (interest in behaving sexually by oneself). The original Sexual Desire Inventory has a good reliability and validity (Spector, Carey, & Steinberg, 1996). The internal consistency of the Dutch version used in this study was high (Cronbach's α = .93).

Hormone assays. Serum T was assayed in duplicate in 2 ml serum samples with an in house radioimmunoassay (RIA) after either extraction followed by paper chromatography (Vermeulen & Verdonck, 1976, 1978): the intra- and inter-assay coefficient of variation for this assay was 5.6% (at a concentration of 1.21 nmol/L) and 8.5% (at a concentration of 0.87 nmol/L), respectively; the lower limit of quantification was 0.07 nmol/L. Commercial kits for RIA were used to determine the serum

concentrations of sex hormone binding globulin (SHBG; Orion Diagnostica, Espoo, Finland) and dehydroepiandrosterone sulphate (DHEA-S; DSL Inc., Webster, Texas); intra-assay coefficients of variation were between 2.5% and 8.3% and between 3.1% and 5.6% for SHBG and DHEA-S, respectively. For all measurements, all samples were assayed in a same assay run. Serum free T was calculated from the total serum hormone concentration, serum SHBG and serum albumin, using a validated equation derived from the mass action law (Vermeulen & Verdonck, 1978; Vermeulen, Verdonck, & Kaufman, 1999).

Determination of *AR* CAG repeat length. Genomic DNA was extracted from EDTA-treated blood using a commercial kit (Purgene Kit; Gentra Systems, Minneapolis, MN). The *AR* exon 1 region encoding the CAG repeat was amplified using PCR with forward primer 5'-GAATCTGTTCCAGAGCGTGC3', fluorescently labeled with FAM and reverse primer 5'-TTCCTCATCCAGGACCAGGTA-3'. Each PCR was initiated with a 5-min denaturation step at 95° C and terminated with a 20-min extension step at 72° C, in-between reaction profiles were as follows: denaturation at 95° C for 60 s, annealing at 62° C for 60 s, and extension at 72° C for 90 s, for 35 cycles. The PCR products were mixed with a Genescan 400HD ROX size standard and deionised formamide and electrophoresed on a 96-capillary 3730 *xl* Genetic analyzer (ABI Prism®, Perkin-Elmer Applied Biosystems, CA, USA).

Statistical analysis

Considering the broad age range in the study group and the known-age related decline in levels of androgens (Laughlin, Barret-Conner, Kritz-Silverstein, & von Mühlen, 2000; Randolph et al., 2003), age was included as a first covariate in all correlation and regression analyses. Since adiposity is also a negative determinant of androgen levels (Vermeulen, Goemaere, & Kaufman, 1999), BMI was included as a second covariate in the correlation analyses (Pearson partial correlations) as well as in the further regression analyses. The necessary transformations (LN or SQRT) were performed on all independent variables in order to enhance normality. The contribution of CAG repeat length to the variability in hormonal levels and sexual desire was assessed by a univariate regression analysis with correction for age and BMI, allowing a comparison of

both factors between CAG quartiles. Since the correlation between androgen levels and CAG repeat length was not linear, the choice was made to use an ANCOVA. To investigate the interaction between CAG and hormone levels on sexual desire, a one-way ANCOVA with correction for age and BMI as cofactors was performed. DHEA-S, total T and free T were divided in median groups and tertiles, while CAG was categorised in quartiles. All statistical analyses were performed using SPSS 15.0 software. $P < .05$ was considered significant in all analyses.

Results

Participant characteristics, CAG repeat length, and correlations with androgen levels

Characteristics for the study population are summarized in Table 1. The mean time since surgery was 48 months. Serum androgen levels of two participants still using anti-androgens were not located at the lower end of the androgen concentration range, and there was no influence on previous correlation analyses (Elaut et al., 2008); therefore it was decided not to remove them from further data analysis. The CAG repeat length ranged from 14 to 28 with a median of 21. No correlation existed between the CAG polymorphism and total T (r = .191; p = .280) or DHEA-S (r = .106; p = .549). The number of CAG repeats was positively correlated with free T (r = .389; p = .023).

Table 1. Participant characteristics (n = 34)

	M ± SD	Range
Age (years)	43.0 ± 10.3	22 – 62
Time since surgery (months)	48.7 ± 66.6	4 – 291
BMI (kg/m²)	24.3 ± 5.2	15.2 - 38.6
Sexual Desire Inventory		
solitary	8.4 ± 6.0	0 – 19
dyadic	27.5 ± 13.6	0 – 52
CAG repeat length (median)	21	14 – 28

Interaction between androgen levels, CAG repeat length and sexual desire

ANCOVA's showed no association existed between the serum androgen levels (in median groups) and measures of sexual desire (solitary sexual desire: total T: p = .461; free T: p = .282; and DHEA-S: p = .473 – dyadic sexual desire: total T: p = .646; free T: p = .882; and DHEA-S: p = .258). Also, no main effect of CAG repeat length on sexual desire could be found, not in a crude analysis (data not shown), nor after adjustment for age and BMI (solitary sexual desire: p = .342 and dyadic solitary desire: p = .637). In further analysis we wished to determine whether the association between serum androgen levels and sexual desire differed across categories of CAG repeats, and this after a correction for age and BMI. Therefore, univariate analysis disclosing two independent predictors assessed the interaction between the CAG repeat and total or free T or DHEA-S, respectively with sexual desire being the dependent variable.

Interactions with total or free T

The observed interaction between total T (median groups) and CAG repeats (quartiles) was significant for solitary sexual desire (p = .002) but not for dyadic sexual desire (p = .070). This indicates that the effect of total T on solitary sexual desire varies between different CAG repeats. To analyse which groups differed in solitary sexual desire it is advisable to digress to single-factor analysis with the combination of the different levels of factor total T and factor CAG. The overall F-test for this single-factor analysis (ANCOVA) was significant (p = .008). More specifically, within the group of trans women with total T levels beneath the median value, a lower solitary sexual desire is associated with a number of CAG repeats of 20 or 21 in comparison to trans women with a higher solitary sexual desire and a number of CAG repeats at the lower (≤ 19) (p = .021) or higher end [(22; p = .022) (> 22; p = .011)] of the range (Figure 1). Univariate analysis assessing the interaction between free T (median groups) and CAG repeat length for solitary or dyadic sexual desire were not significant (p = .169 and p =.459, respectively).

Table 2. Serum hormonal levels by quartiles of CAG (*n* = 34)

	CAG ≤ 19	CAG = 20 or 21	CAG = 22	CAG > 22	normal female range[a]
TT (pmol/L)	762.1 ± 290.6	797.2 ± 442.4	772.3 ± 521.0	814.4 ± 246.0	346.7 – 2773.6
FT (pmol/L)	8.4 ± 3.6	10.7 ± 5.3	15.6 ± 13.0	11.7 ± 5.0	6.9 – 17.3
LH (U/L)	36.4 ± 22.0	20.7 ± 18.4	30.9 ± 20.4	22.0 ± 14.3	2 – 13
SHBG (nmol/L)	70.1 ± 26.0	53.0 ± 31.1	33.9 ± 23.3	50.5 ± 23.5	21 – 139
DHEA-S (µg/L)	2192.7 ± 1038.1	2346.2 ± 1571.4	2120.8 ± 1359.6	2128.4 ± 677.0	609 – 3370

Note. TT: total T, FT: free T.

[a] Reference ranges for women according to local laboratory.

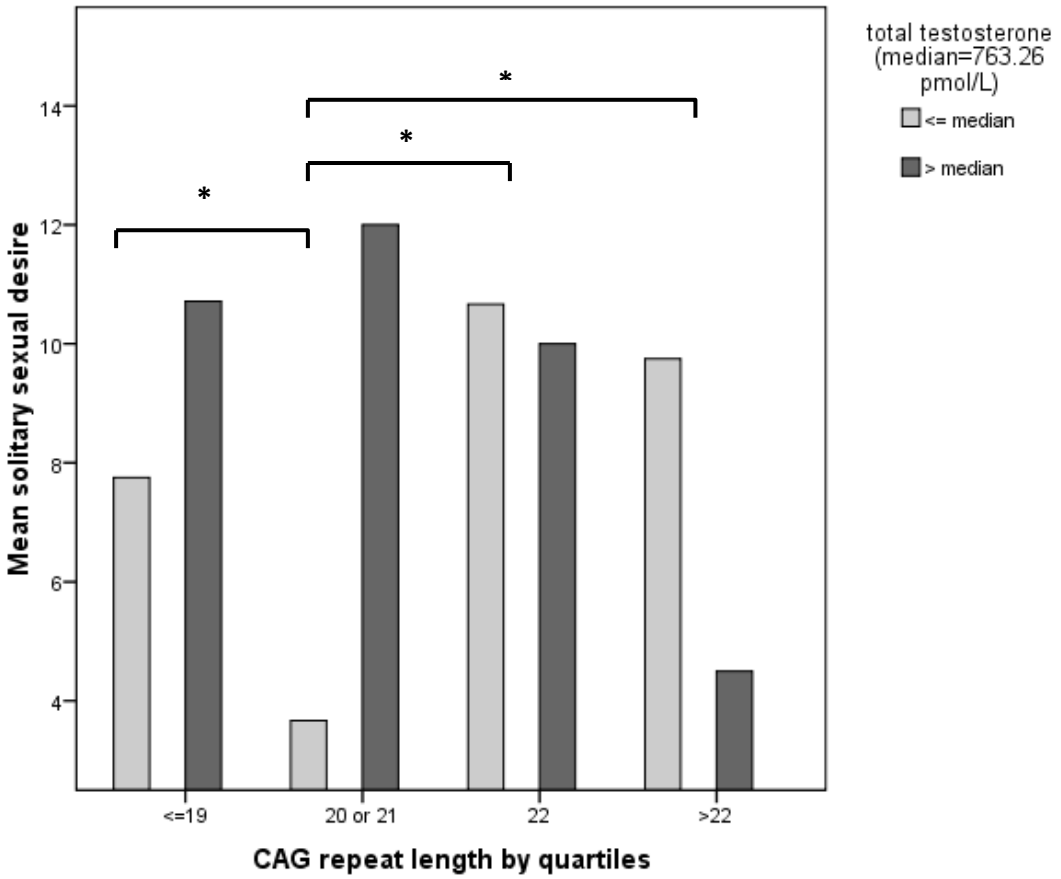

Figure 1. Interaction between AR CAG repeat length and total T on solitary sexual desire.

* difference between groups, significance level $p < .05$

Interaction with DHEA-S

The ANCOVA's for interaction between DHEA-S (median groups) and CAG repeat length on solitary and dyadic sexual desire were not significant (p = .156 respectively p = .149). The ANCOVA's for interaction between DHEA-S (tertiles) and CAG repeat length on solitary and dyadic sexual desire were significant (p = .040 respectively p = .027). However, we were not able to further distinguish the groups that were significantly different (as above) since the number of individuals in each group was too small.

DISCUSSION

The aim of this study was to test the hypothesis that the CAG repeat length might be a modulating factor in the relationship between androgen levels and sexual desire in trans women. The *AR* CAG repeat length was associated with free but not total T, in accordance with a recent study in healthy men (Crabbe et al., 2007). However, the mechanism is likely to be different in trans women with a continuous estrogen replacement and a lack of gonadal androgen source and thus absence of classical feedback regulation of androgen secretion.

An interaction was observed between the *AR* CAG repeat length polymorphism and total T on solitary sexual desire: this would mean that trans women with low total T suffer from low sexual desire when their CAG amounts to 20 or 21 in comparison to those with a CAG at the lower or higher end of the spectrum. However, no similar observation could be repeated for the interaction between the polymorphism and free T. Also, the interaction between CAG repeat length and total T was found to affect only solitary and not dyadic sexual desire. One could argue that the construct of solitary sexual desire (the interest to behave sexually by oneself) might be closer related to 'sexual arousability', originally defined by Whalen as "the rate at which an individual approaches maximal sexual arousal" (1966), in comparison to dyadic sexual desire (the interest to behave sexually with a partner). While the latter construct implicates the involvement of a partner in the desired sexual activity, it measures a different but related dimension of sexual desire. Nevertheless, the transactivation activity of the *AR* is inversely related to CAG number i.e., low CAG number means higher activity. Interestingly, the current results point to a higher solitary sexual desire in participants

with less active or more active receptors in comparison to those who have a median number of CAG repeats. This finding would suggest that both long and short CAG repeats are behaving in the same way, which is in contrast with the accumulated knowledge in the CAG literature. Although it's statistical significance, the interaction between the polymorphism and total T on solitary sexual desire lacks any biological explanation.

In cisgender (or non-trans) women a relationship between androgens and sexual desire has been observed despite a cycling estrogen milieu (Turna et al., 2005; Santoro et al., 2005). However, we can wonder whether the pharmacological influences or the genetic polymorphism has the larger impact on the hormone levels in this population. While the authors established a similar effect from an oral or transdermal administration of estrogen replacement on androgen levels existed in this specific patient group in a previous article (Elaut et al., 2008), the continuous treatment may have a more pronounced effect on hormone levels and may therefore overrule all possibilities of finding a subtle genetic component in the androgen-sexual desire relationship.

An interaction was also observed between the CAG repeat length polymorphism and DHEA-S on solitary and dyadic sexual desire. The small sample size did not allow a further exploration of the differing groups. As to the limitations of the study, the most important weakness concerns the modest number of 34 trans women who could be included. This did not only result in a low power but also prevented us from further exploring the interaction between CAG repeat length and DHEA-S. Given this small number of participants, the data should be interpreted with the utmost caution. However, the current results are to be considered a first exploration of the effects of the *AR* on sexual desire in male-to-female transsexuals. Also, only androgen levels and androgen sensitivity were measured as determinants of sexual desire. Psychological, relationship and lifestyle factors, know to influence sexual desire in men (Corona et al., 2005), were not included in the analysis. Further, the measurement of T in the lower female range remains technically difficult. Since the levels of free T are of an even lower order, these low free T levels and the uniform low T levels among trans women possibly complicate replicating the results of the interaction between total T, CAG and sexual desire for free T.

In conclusion, CAG repeat length is not a consistent modulating factor in the relationship between total, free T or DHEA-S and sexual desire in our cohort of trans

women. The current model of a linear effect of androgens on sexual desire in men and women should certainly be broadened by a more interactional approach with attention for genetic androgen sensitivity but also for partner- and relationship variables.

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CHAPTER 7

SEXUAL DESIRE IN TRANS PERSONS AND THE RELATION WITH GENDER-CONFIRMING TREATMENT[1]

ABSTRACT

Sex steroids and genital surgery are known to affect sexual desire, while studies into the sexual desire of gender dysphoric individuals and the relation with Gender Confirming Treatment (GCT) are rare. This chapter summarises two studies. *Study one* is a cross-sectional follow-up study in 45 trans men after GCT, who filled out a standardised questionnaire on sexual desire, and, in retrospect, reported on sexual desire before treatment, hormonal data were assessed. It was found that 73.9% of trans men reported an increased sexual desire following hormone substitution and genital surgery. No direct associations between sexual desire and testosterone were found. However, trans men with elevated LH-levels, indicative of suboptimal hormone therapy, reported significant lower solitary sexual desire levels, compared to those with low levels (p = .007). *Study two* assessed 214 trans women and 138 trans men in a cross-sectional follow-up design, after at least three months of hormone therapy. Questionnaires asked for frequency of sexual desire, complaints of low sexual desire, and treatment satisfaction. In retrospect, 69.7% of trans women reported a decreased sexual desire, while 71.0% of trans men reported an increase. The prevalence of HSDD (personal and/or relationship distress due to low sexual desire) in trans women and men was 22% and 5%, respectively.

[1] Based on (1) Elaut, E., Katrien, W., Van Caenegem, E., Van de Peer, F., Dedecker, D., Van Houdenhove, E., & T'Sjoen, G. (2011). Sexual desire in female-to-male transsexual persons: exploration of the role of testosterone administration. *European Journal of Endocrinology, 165,* 331-337*,* and (2) Wierckx, K., Elaut, E., Van hoorde, B., Heylens, G., De Cuypere, G., Monstrey, S., Weyers, S., Hoebeke, P., & T'Sjoen, G. (2014). Sexual desire in trans persons: association with sex reassignment treatment*. Journal of Sexual Medicine, 11,* 107-118.

INTRODUCTION

It is well known that sex steroids play a role in motivational aspects of sexual functioning, such as sexual desire, particularly in cisgender (or non trans) men (Bancroft, 2005). Studies have observed an improved sexual desire with testosterone (T) administration in hypogonadal young and aging men (Carani et al., 1990; Yassin, & Saad, 2007; Wang et al., 2004), but not in men with T levels within the normal range (Buena et al., 1993). In contrast, our knowledge on the role of androgens in female sexual desire is very scarce with contradictory evidence (Bancroft, 2005). Epidemiological studies have shown no correlation between serum T levels and sexual desire in cisgender women (Riley, & Riley, 2000; Turna et al., 2005), whereas others could not confirm this (Davis, Davison, Donath, & Bell, 2005; Santoro et al., 2005).

Effects of estrogens on the sexual desire in both cisgender men and women are poorly understood (Bancroft, 2005). Considering the aromatisation of T into estradiol in many tissues, it may well be possible that T effects on sexual desire are mediated by estradiol. The few studies that have examined the relation between circulating estradiol levels and sexual desire in cisgender men show no clear association (Basar et al., 2005; Grades et al., 2008). In cisgender women, some (Avis, Stellato, Crawford, Johannes, & Longcope, 2000), but not all (Cawood, & Bancroft, 1996; Dennerstein, Burrows, Wood, & Hyman, 1980) studies reported on a relation between estrodial levels and sexual desire.

In view of these (known) effects of sex steroids in cisgender men and women, the potential effects of cross-sex hormonal substitution on the sexual desire of gender dysphoric individuals undergoing Gender-Confirming Treatment (GCT)[2] can only be hypothesised. In trans women, a decline in serum T levels or action together with increased sex hormone binding globulin and high estradiol levels could be lowering sexual desire. In contrast, sexual desire in trans men might be facilitated with increasing serum T levels. These theoretical effects may however be influenced by brain masculinisation of feminisation, prior to hormone substitution. Aside from hormone

[2] With the goal of a consequent use of terminology in the current dissertation, some vocabulary has been altered compared to the original publications. The terms “transsexual women” and “transsexual men” were replaced by “trans women” and “trans men” in this chapter. Similarly “sex reassignment surgery” was replaced by “gender-confirming surgery.”

substitution effects, the experience of breast removal or augmentation and genital surgery clearly affects the sexual life of trans persons (Klein, 2009). Surgical interventions in trans women consist of orchiectomy, penectomy, vaginoplasty and clitoroplasty, while trans men undergo mastectomy, hysterectomy, and ovariectomy. Due to the availability of and extensive experience at our centre with phalloplasty, most trans men immediately proceed to this creation of a full-sized phallus (Monstrey et al., 2009).

Considering the extensive potential effects of GCT, the current chapter presents two studies exploring the sexual desire of trans persons, and its relation to GCT. Study one aims at providing a validated measure of solitary and dyadic sexual desire in a group of trans men after completing GCT. In addition, a marked association between sexual desire and serum androgen levels is hypothesised in this group. Study two set out to quantify, in retrospect, the perceived changes in sexual desire in relation to the GCT in a large cohort of both trans women and men, almost all treated by the same interdisciplinary team. Furthermore, a measure of complaints of low sexual desire was constructed to quantify a group experiencing distress.

STUDY 1

Method

Participants. All Flemish trans men who received GCT between 1987 and 2009 at the Ghent University Hospital were invited to participate in the study by letter (n = 79). Of that group, 47 agreed to participate, leading in a response rate of 64%. Three additional participants offered to participate after being informed by others, resulting in a total sample of 50. Exclusion criteria were treatments or disorders affecting sex hormone status, body composition, and bone metabolism (untreated hypo- or hyper-thyroidism, Cushing's syndrome, alcohol abuse, mucoviscidosis, current (< 2 years) or prolonged use of corticosteroids, estrogens, anti-androgens or fluorides. Since the first year after finalising GCT (often called 'the honeymoon period') does present a realistic image for long-term functioning, participants who underwent genital surgery during the

last year were excluded from the study (*n* = 1). Three participants refused to fill out the Sexual Desire Inventory, resulting in a final study sample of 45.

In the Ghent University Hospital, gender dysphoric individuals are treated with an interdisciplinary approach, consisting of hormone substitution and genital surgery for most. All participants had been hormonally substituted for at least two years before proceeding with genital surgery. The follow-up period consisted on average of 8 years (Range: 2-22 years). While hormone substitution is currently not standardised, almost all participants were treated by the same endocrinologist. Hormone substitution consisted of: intramuscular T (T) treatment (parental T esters 250 mg/2 to 3 weeks; *n* = 32), T undecanoate 1000 mg/12 weeks (*n* = 7), or transdermal T gel (50 mg daily; *n* = 5).

Due to the extensive experience with phalloplasty in our centre (Monstrey, Hoebeke, Dont, Selvaggi, Hamdi, Van Landuyt, & Blondeel, 2005; Monstrey, Hoebeke, Selvaggi, Ceulemans, Van Landuyt, Blondeel, Hamdi, Roche, Weyers, & De Cuypere, 2009), 38 trans men in our study sample had proceeded immediately to phalloplasty. The majority of participants who initially had chosen a metaidoioplasty (*n* = 9), proceeded towards phalloplasty afterwards (*n* = 8). Two trans men did not (yet) undergo genital surgery.

We chose not to include a control group consisting of men and women from the general population, as hormonal status, psychosocial factors and sexual functioning are very specific in the current study sample.

Table 1. Participant characteristics

	M ± *SD*	Range
Age (years)	37 (8.17)	22 - 54
Age at time of SRS (years)	30 (7.68)	16 - 44
Height (cm)	165.11 (6.73)	147.4 - 183.9
Weight (kg)	69.17 (12.04)	45.0 - 98.5
BMI (kg/m²)	25.33 (3.88)	18.3 - 34.0
Active smoking (%)	37	28
Stopped smoking (%)	34.8	
Use of testosterone therapy (%)	100	
Duration of Ttherapy (years)	9.42 (5.82)	3.0 - 27.0

Procedure. All participants who agreed to participate received paper-and-pencil questionnaires via regular mail. For further evaluation, a one day hospital visit was planned. This included a fasting morning blood sample, dermatologic, urological, speech, bone, and body composition evaluation, which will be reported in other publications (e.g., Cosyns et al., 2014; Wierckx et al., 2011). This study complied with the recommendations of the Declaration of Helsinki and was approved by the Ethics Committee of the Ghent University Hospital. Informed consent was provided by all participants.

Measures

Sexual desire. Sexual desire was measured using the Dutch version of the Sexual Desire Inventory (Spector, Carey, & Steinberg, 1996). This self-report questionnaire contains 14 items. Subscales measure the intensity and frequency of the desire to behave sexually with a partner (dyadic sexual desire) or by oneself (solitary sexual desire). For the frequency-items, participants chose one out of seven options. For the strength items, participants scored their sexual desire on a 9-point Likert scale ranging from 0 (no desire) to 8 (strong desire). The participants were asked to take the previous month as a reference. Adding items resulted in a score for dyadic and solitary sexual desire. Higher scores indicate a higher level of sexual desire with a maximum score of 62 for the dyadic subscale and 23 for the solitary subscale. The Sexual Desire Inventory has a good reliability and validity (Spector, Carey, & Steinberg, 1996). Internal consistency in the present study population was high (Cronbach's α = .89). All but four participants filled out the SDI. In two questionnaires one items was missing; we inserted the personal mean of the other items of this subscale.

Other items concerning sexual desire and sexual functioning in the past month were added: frequency of experiencing sexual desire, frequency of experiencing sexual desire towards their partner, frequency of sexual activities, frequency of masturbation (5 point Likert-scale from not at all to daily), current sexual desire compared to after sex reassignment (5 point Likert-scale from much higher to much lower), frequency of experiencing excessive sexual desire (5 point Likert-scale from almost never to almost always), time one can live without any sexual activities (9 point Likert-scale from always

to less than a day), sexual satisfaction with the current partner (5-point Likert scale from very unsatisfied to very satisfied, or not applicable).

Biochemical determinations. Venous blood samples were obtained between 0800 and 1200 h after overnight fasting, due to practical reasons regardless of the timing of T administration. All blood samples were stored at -80 °C until batch analysis. Commercial kits for Radio-Immuno Assay (RIA) were used to determine the serum concentrations of total T and sex hormone binding globuline (SHBG) (Orion Diagnostica, Espoo, Finland); Luteinizing hormone (LH) (electrochemiluminiscence immunoassay (ECLIA); Modular, Roche Diagnostics, Mannheim, Germany. Intra- and interassay coefficients of variations were less than 10 en 15% for all measurements respectively. For all measurements, samples from female-to-male transsexual persons were assayed in a same assay run. Serum free T was calculated from the total serum hormone concentration, serum SHBG and serum albumin, using a validated equation derived from the mass action law (Vermeulen, Verdonck, & Kaufman, 1999). We defined supra- and subphysiological levels of T and LH as hormone levels exceeding the upper or lower limit of the reference ranges according to values of our local laboratory.

Analyses

The normal distribution of all variables was tested by the Kolmogorov-Smirnov one-sample test. Normally distributed variables were described in terms of mean and standard deviation and skewed variables in terms of median, first and third quartiles. Kruskall Wallis tests were used to determine differences in the hormone levels according to type of T treatment and to determine differences in sexual desire between female-to-male transsexual persons, male-to-female transsexual persons and community dwelling men. ANOVA was used to explore associations between hormonal levels (T, free T and LH) and measures of sexual desire. Post hoc analyses were performed by LSD tests. Mann Whitney U tests were used to test differences in sexual desire between participants with T levels above the P75 and below P25, participants with supra or sub physiological levels of T and the rest of the group.

Results

Sexual desire and related aspects of sexual functioning. Most participants mentioned an increased sexual desire post-treatment: 38.6% (*n* = 17) described the sexual desire level during follow-up as much higher, 34.1% (*n* = 15) indicated it to be higher, while 25.0% (*n* = 11) reported no change. One participant reported a decreased post-treatment desire. One participant refused to answer this question.

Most participants masturbated after GCT: 60% masturbated daily or weekly, a quarter masturbated once or twice a month, while a minority masturbated less than once a month (4.4%) or not at all (11.1%). Masturbation frequency significantly correlated with both solitary and dyadic sexual desire (r = .80, p < .001 and r = .47, p = .001, respectively).

Up to one third of the trans men (32.1%) in a partnership reported to have sexual intercourse several times a week, half mentioned to have sexual intercourse several times a month (48.1%), and 22% were not sexually active with their partner during the past month. Frequency of sexual intercourse was not correlated with either solitary or dyadic sexual desire (r = .20, p = .307 and r = .20, p = .315, respectively).

Relation between sexual desire and hormone levels. Inherently to including participants with different hormone regiments, the duration since last T administration and the date of visit was different between types of hormone substitution (p < .001). As a consequence, all ANOVA's were corrected for this parameter. No differences in total T, LH, hematocrit levels were detected between treatment types (data not shown). Testosterone treatment aims at serum concentrations in the normal physiological range for men. At the time of measurement, 9% had levels below the reference values of our laboratory (< 321 ng/dl), whereas 26.7% exceeded the upper limit of 1005 ng/dl.

No associations were found between levels of free T and solitary or dyadic sexual desire (ANOVA with correction for type of T treatment and time since last T administration, data not shown). Also, no significant associations were observed between total T and solitary or dyadic sexual desire (data not shown). Solitary or dyadic sexual desire did not differ between participants with total or free T levels beneath P25 and above P75 (Mann-Whitney *U* test: total T: p = .30 and p = 0.60; free T: p = .24 and p = .40). Finally, no differences were shown in participants with supra- or subphysiological T levels in comparison with T levels within the normal range (data not shown).

Supraphysiological LH levels are assumed to reflect inadequate hormone substitution while suppressed levels point towards an excess in cross-sex hormone treatment. Therefore, the associations between LH and sexual desire were explored by ANOVA's. These showed an independent association of LH with solitary and dyadic sexual desire, after adjustment for age and weight (p = .001 and p = .024 respectively). As shown in Figure 1, post hoc analysis pointed towards stronger solitary sexual desire in trans men with low LH levels (< P25), compared to those with higher LH levels (P25-P50, P50 - P75 and > P75). Similar post hoc analysis for dyadic sexual desire demonstrated no clear trend (data not shown). Furthermore, LH levels were associated with the frequency of experiencing excessive sexual desire (ANOVA; p = .007): post hoc analysis demonstrated that participants with low LH (< P25) reported excessive sexual desire more frequently than participants with LH levels between P25 and 50 (LSD; p = .001) or LH levels above P75 (LSD; p = .001).

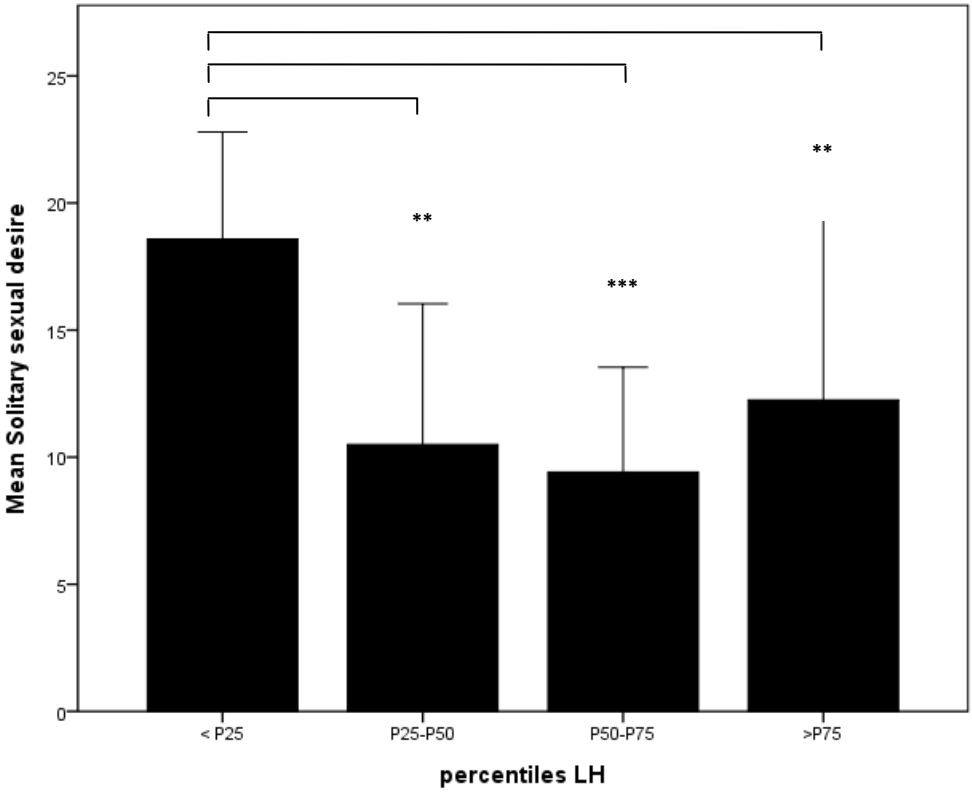

Figure 1. Solitary sexual desire scores by different LH percentiles. Data is presented as M ± SD; ANOVA post hoc test (LSD). * p < .05. ** p < .01. *** p < .001.

STUDY 2

Method

Participants. All Flemish trans men and women who had been indicated to receive GCT at the Ghent University Hospital between 1986 and June 2012 and who underwent at least three months of hormone substitution were invited to participate. Three hundred fifty-two participants (138 trans men and 214 trans women) agreed to participate, leading to a response rate of 54%. Ten persons were deceased at the time of the follow-up (Figure 2).

Trans women were on hormone substitution for a median duration of 7 years (Range: 3 months – 35 years). Ten trans women were no longer on estrogen therapy due to previous thromboembolic events (*n* = 5), dissatisfaction (*n* = 2), or another cause (*n* = 3). Hormone substitution mostly consisted of transdermal estradiol (17-β estradiol gel 1.5 mg/24h, *n* = 76, 35.5%), estradiol patch 50 µg/24h (*n* = 29, 13.6%); or daily intake of oral estrogens (estradiol valerate 2mg [*n* = 91, 42.5%], estriol 2 mg [*n* = 1, 0.4%], ethinyl estradiol 50 µg [*n* = 2, 0.9%], and oral contraceptive ethinyl estradiol 30-50 µg [*n* = 5, 2.3%]. One hundred thirty-nine (64.5%) underwent genital surgery (orchiectomy, penectomy, and vaginoplasty), 60 (28%) were planning this surgery in the future, while four (1.8%) were still in doubt. Eleven (5%) did not wish genital surgery or could not undergo this due to medical reasons. Half of trans women (53.5%) had breast augmentation, 17.8% had vocal cord surgery or cricoids reduction, while 21.5% had facial feminising surgery.

Trans men were on hormone substitution for a median duration of 6 years (Range: 3 months – 49 years). Hormone substitution consisted of intramuscular T treatment with either a mixture of T esters (T undecanoate 100 mg, T isocaproate 60 mg, T fenylpropionate 60 mg, T propionate 30mg/mL) every 2 to 3 weeks (*n* = 64, 46.4%); T undecanoate 1000 mg per 12 weeks (*n* = 62, 44.9%); transdermal T 50 mg daily (*n* = 9, 6.5%); or oral T undecanoate (*n* = 2, 1.4%). Eighty-six percent underwent hysterectomy and ovariectomy, 76 (59.4%) had undergone phalloplasty. Nine chose metaidoioplasty, of which eight proceeded with phalloplasty. Sixty-three percent of those who underwent phalloplasty had an erection prosthesis implanted.

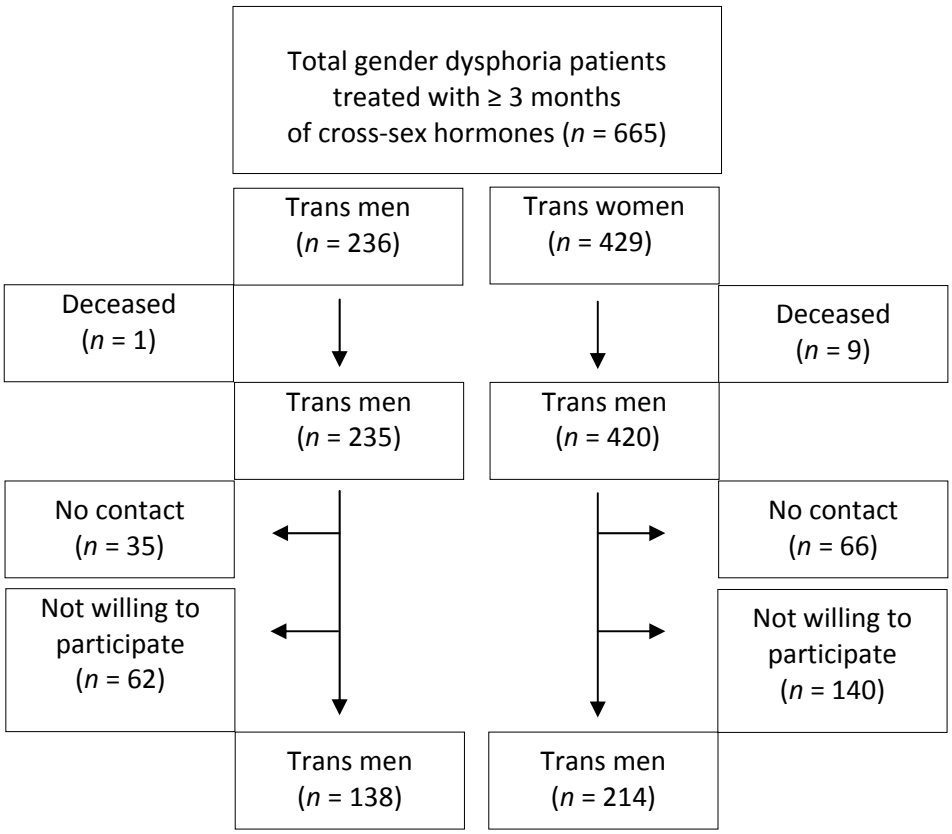

Figure 2. Participant enrollment

Procedure. All participants who agreed to participate received a paper-and-pencil questionnaire or filled out the survey online. This follow-up study was part of a more broad interdisciplinary study on physical health, incidence of possible treatment-related adverse events, socio-demographic status, health related quality of life, and treatment-related symptoms such as changes in sexual desire, surgical results, and satisfaction with hormonal and surgical treatment, which will be reported on in other publications (Wierckx et al., submitted; Wierckx et al., 2013). This study complied with the recommendations of the Declaration of Helsinki and was approved by the Ethics Committee of the Ghent University Hospital. Informed consent was provided by all participants.

Table 2. General characteristics of the study population

	Trans women (*n* = 214)	Trans men (*n* = 138)
Age at time of study (years) ***	45 [32.8 - 52]	37.5 ± 11.0
Nationality (%)		
Belgian	86.0	87.0
Other	14.0	12.5
Civil status (%) ***		
Married/living together	36.0	44.5
Not married or living together	36.4	47.4
Divorced	25.2	8.0
Widow	2.3	0
Children (%) ***	41.1	23.9
Birth before HRT (%)	81.8	36
Work status (%) ***		
Unemployed	14.2	9.4
Employed	55.9	64.5
Retired	9.5	1.5
Student	5.2	13.0
Unable to work	13.7	9.4
Household	1.4	2.2
Monthly income (%)		
≤999 euro	10.3	14.2
1.000-1.999 euro	42.2	35.8
2.000-2.999 euro	27.5	24.6
3.000-5.999 euro	16.7	23.9
≥ 6.000 euro	3.4	1.5
GCT (%) ***	64.8	85.5
Time since SRS (years)	6.0 [2 - 11]	7.0 [4 - 13]
Duration of hormonal therapy (years) *	6.0 [3 - 11]	7.0 [4 - 13]
Active smoking (%)	29.9	29.4
BMI	24.4 [21.7 - 27.9]	24.3 [22 - 27.5]

Note. Data are presented as % or median (first to third quartiles). Categorical variables using Chi square test; Continuous variables using linear regression analysis. NS: not significant; GCT: gender confirming treatment (defined as orchiectomy/penectomy/ vaginoplasty in trans women and hysterectomy/ovariectomy in trans men)

* $p < .05$. ** $p < .01$. *** $p < .001$.

Measures

Sociodemographic characteristics and treatment status. Civil status, current working situation, current job and household income were addressed. All participants were asked whether they had children (yes/no) and if so, to describe the method of conception for each child. Participants also reported on the following items: marital status, duration of relationship and current sexual orientation (5 point scale from only attracted to men to only attracted to women or other).

Current and past hormonal treatments were addressed through a self-developed questionnaire. Patients were questioned about the medical procedures they underwent during transition. Satisfaction with different surgical procedures was evaluated by the participants on a 5-point Likert scale from very unsatisfied to very satisfied. Moreover, trans men were asked whether they had experienced surgical complications of metoidioplasty, phalloplasty or implantation of erection prosthesis. Trans women were asked whether they had experienced surgical complications of the vaginoplasty procedure.

Low sexual desire and change in sexual desire levels. Several aspects of sexual desire were measured. First, we evaluated Hypoactive Sexual Desire Disorder (HSDD), as defined by Elaut and colleagues (2008), who used the Sexual Function Health Council's consensus definition (Basson et al., 2000). HSDD was defined as "the persistent or recurrent deficiency (or absence) of sexual fantasies, thoughts, desire for sexual activity, alone or with a partner, and the inability to respond to sexual cues that would be expected to trigger responsive sexual desire. These symptoms must be causing personal distress."

Sexual desire in trans women was therefore assessed by the evaluation of spontaneous and responsive sexual desire in the past month using a five-point scale from never to almost always. In addition, respondents were asked about the presence of distress caused by low sexual desire (yes or no) and to describe whether this caused distress for themselves, their partner, and/or their relationship. Respondents met the distress level when they experienced personal or relational distress.

HSDD in trans women was scored when a participant indicated that (i) she never/rarely experienced either spontaneous (ii) or responsive sexual desire, and when this was (iii) causing her personal or relational distress. HSDD in trans men was defined

according to Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR, APA 2000). HSDD was scored when a participant indicated that (i) he never/rarely experienced sexual desire in the past month, and when this was (ii) causing him personal or relational distress.

Further, participants were asked to compare their levels of sexual desire before and after GCT (five-point scale from much higher to much lower), frequency of experiencing too low sexual desire in the past month (five-point scale from never to almost always), experience of symptoms of high sexual desire, and experience of symptoms of low sexual desire (four-point scale from no to severe).

Physical and mental functioning. QOL was measured using the Dutch version of the Short Form-36 Health Survey (SF-12). This questionnaire includes 12 questions with fixed response choices, organized in two scaled scores, based on the weighted sums of the questions in their section. These scores were converted into a summary score for each section: physical functioning and mental functioning, with higher scores indicating higher levels of functioning or wellbeing (Ware, 1944, 2002). Internal consistency with the SF-12 was high (total group: Cronbach's α = 0.8).

Analyses

The normal distribution of all variables was tested by the Kolmogorov-Smirnov one-sample test. Normally distributed variables were described in terms of mean and standard deviation (SD) and skewed variables in terms of median, first and third quartiles. Comparisons of continuous variables between trans women and men were made by linear regression analyses with group as independent variable. Dichotomous and categorical variables were analyzed using respectively logistic regression and Chi Square test. Data were analyzed using PASW-software, v.19 (SPSS Inc., Chicago, IL). Statistical significance was set at $p < 0.05$ and all tests were two tailed. Given the well-known association between age and sexual desire, linear and logistic regression analyses were adjusted for age.

Results

Sexual desire and HSDD in trans women. Most trans women (83.4%) never or rarely experienced spontaneous sexual desire, 75.8% never or rarely experienced responsive sexual desire, while 73% never or rarely experienced either spontaneous or responsive sexual desire. Of those, about a third indicated to be distressed by this, personally or within the relationship, resulting in an HSDD-prevalence of 22.1%. This means that three quarters of trans women did *not* experience this lack or absence of sexual desire as distressing (Figure 3).

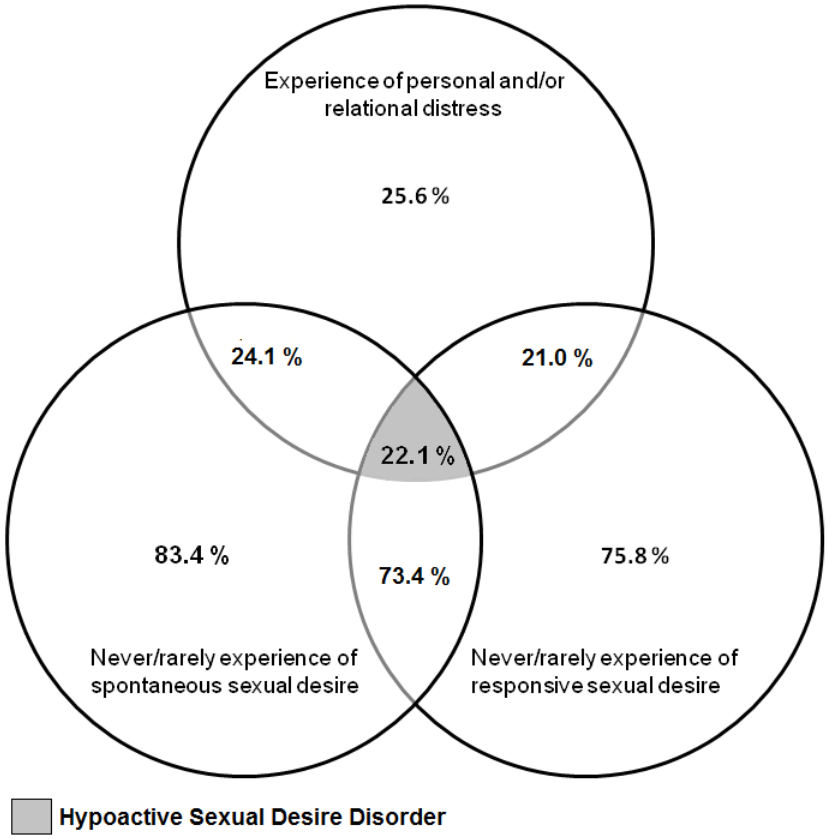

Figure 3. Prevalence of HSDD in trans women

A quarter of trans women (24.2%) often or always experienced too low sexual desire, while 67.7% rarely or never experienced this. In retrospect, most trans women (69.7%) described their sexual desire at follow-up as (much) lower compared to before GCT-treatment, 17.4% reported no change, while 13% reported an increase (Figure 4).

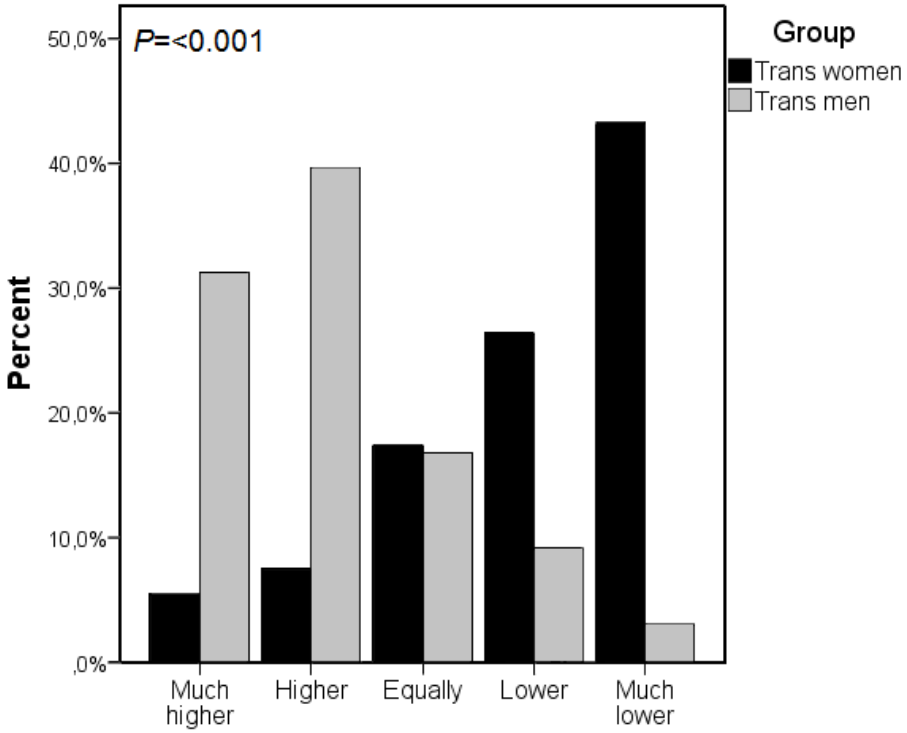

Figure 4. Current sexual desire in trans men and women compared to sexual desire before GCT

GCT and other factors associated to sexual desire in trans women. Neither the type of hormonal substitution, duration of hormonal therapy, or satisfaction with hormonal therapy were associated with the frequency of spontaneous or responsive sexual desire (data not shown). Participants who already underwent a vaginoplasty reported more spontaneous sexual desire compared to those who were still scheduled for surgery. Satisfaction with genital surgery and complications during vaginoplasty were not associated with sexual desire measures (data not shown). While neither involvement in a romantic relationship or relationship duration were related to the frequency of sexual desire, participants involved in a relationship more often reported HSDD (p < .001). Trans women sexually (mostly) attracted to men mentioned higher levels of spontaneous and responsive sexual desire compared to trans women (mostly) attracted to women (post hoc ANOVA; p = .008 and p = .009 respectively). Further, age was negatively associated with the frequency of both spontaneous and responsive sexual desire (p = .008 and p < .001, respectively). Having children, physical well-being, and

mental well-being were not associated with frequency of sexual desire or the prevalence of HSDD (data not shown).

Sexual desire and HSDD in trans men. Thirty percent of trans men never or rarely experienced sexual desire and on in six indicated to be distressed by this lack, personally or within the relationship, leading to an HSDD-prevalence of 5% in the current sample. Of the trans men experiencing sexual desire often or always (30.6%), a majority reported no associated distress (76.9%), 12.8% reported personal or relationship distress, while 10.3% expressed exclusive distress for their partners. Of the total sample, 3.6% often or always reported sexual desire and reported this to cause personal or relationship distress.

In retrospect, the majority of trans men (71.0%) reported an increase of sexual desire after GCT, whereas 12.3% reported a decrease and 17% reported no change (Figure 4).

GCT and other factors associated to sexual desire in trans men. A shorter T treatment duration was associated with more symptoms of high sexual desire (p = .005), but no association was seen with type of T treatment or satisfaction with it (data not shown). Genital surgery was not at all associated with sexual desire scores: whether or not trans men underwent phalloplasty and/or erection prosthesis implant, time since genital surgery, satisfaction or complication with the surgery were all not associated with sexual desire (data not shown). HSDD was more prevalent in trans men who were less satisfied with phalloplasty (Fisher's exact test; p = .02). Further, a shorter relationship duration was associated with higher frequency of sexual desire (p = .03), but no associations were found with sexual orientation, age, having children, physical and mental well-being (data not shown). However, unemployed trans men had a lower sexual desire (p = .015).

Comparison between trans women and men. More symptoms of high sexual desire were observed in trans men, while trans women reported more symptoms of low sexual desire. HSDD was also more prevalent in trans women compared to trans men (p < .001). Satisfaction with genital surgery was similar in both groups (data not shown).

DISCUSSION

The current chapter presented two studies exploring the sexual desire of trans persons, and its relation to GCT. *Study one* aimed at providing a validated measure of solitary and dyadic sexual desire in a group of trans men after completing GCT. In addition, an association between sexual desire and serum androgen levels was hypothesised but not confirmed. *Study two* set out to quantify, in retrospect, the perceived changes in sexual desire in relation to the GCT in a large cohort of both trans women and men. Also, HSDD prevalence in both trans women and men was established. The findings of both studies will be discussed together in more detail below.

Prevalence of sexual desire changes in trans women and men

A first aim of the current studies, was to quantify sexual desire and sexual desire changes in both trans women and man, in the context of a GCT. In retrospect, seven in ten trans women experienced a decreasing sexual desire after GCT, and as many trans men experienced an increase. While many factors that could not be investigated in the current studies (such as decreased gender dysphoria and more satisfactory sexual relationships since GCT), could have explained the results in the trans men, they could not account for the change in the trans women – as previous research showed a somewhat smaller but significant decreased gender dysphoria in trans women (compared to trans men) after GCT (Smith, Van Goozen, Kuiper, & Cohen-Kettenis, 2005). It appears that these perceptions of an inverse effect on sexual desire in both groups seem to relate to the received treatment. One other study has looked at sexual desire in relation to GCT in trans men, and found an increase of sexual desire in a smaller part of their sample (Costantino et al., 2013). Of course, many biological, psychological as well as socio-cultural factors have been proposed to explain gender differences in sexual desire (Baumeister, Cathanese, & Vohs, 2001; Marks & Fraley, 2006).

Considering the remarks that clinicians receive of trans women on a reduced sexual desire after GCT, a quantification of the associated distress in a large cohort was timely. The current studies have shown how a fifth of trans women and a small minority of trans men suffered from personal and relationship distress due to low sexual desire. This

HSDD-prevalence in the trans women is lower compared to a previous multicenter study, but that study might have lacked power due to a small sample size (Elaut et al., 2008). Trans women in the present studies had a higher prevalence of HSDD compared to male and female population studies using a similar definition, taking distress levels into account, as they found that between 0.5 and 6% of men and 3 to 14.2% of women reported HSDD (Christensen et al., 2011; Hendrickx & Enzlin, 2013; Kedde, 2012; Shifren, Monz, Russo, Sergreti, & Johannes, 2008). In trans men, a similar prevalence of HSDD was found (5.0%) compared to the general male population (range: 0.5-6%) (Hendrickx & Enzlin, 2013; Kedde, 2012).

Trans women had a higher prevalence of HSDD and described more often a decrease in sexual desire after GCT compared to trans men. Sexual desire is a multifaceted process, resulting from the triggering of the sexual response system with a specific arousability based on (amongst others) genetics, the presence of sex steroids and neurotransmitters as well as by lifelong psychosocial learning experiences. Those sexual stimuli can be both internal (such as sexual thoughts) or external cues (sensory stimuli experienced as erotic) (Laan & Both, 2008). Since trans women have mostly grown up with a highly testosterone dependent sexual response system and have often had sexual experiences in the male gender role, it requires a certain 'reconditioning' of the sexual response system within a less androgenic hormonal milieu. The fact that two in three trans women in our group did *not* experience this lack or absence of sexual desire as distressing, points to the presence of factors that might be compensating for the loss of the 'androgen-driven sexuality'. This might consist of factors the current study could not assess, such as an increasingly positive self-image due to the transition and a boosted self-esteem from being recognized as female.

Correlates of sexual desire in trans women and men

A second aim to the present studies, was to determine suitable correlates for the observed sexual desire changes. First regarding hormonal correlates, we found that no relation between sexual desire and serum total or free T levels. A previous study from our group has also reported on a lack of association between there parameters in trans women (Elaut et al., 2008). The present study did however find an inverse association between solitary sexual desire (related to the concept of arousability) and LH levels.

Inadequate T therapy, as indicated by high LH levels, was associated with lower levels of solitary sexual desire: trans men with LH levels below P25 (indicating excess T treatment) reported higher solitary sexual desire than those with LH levels within the normal range.

The reason for not establishing a direct relation with T and sexual desire could be multiple. First, the differences in sample size between the types of T therapy in our participants could have hampered finding a relation, especially considering the relatively small sample size of study one. Second, the response to T supplementation may differ individually (Bhasin et al., 2001; Van Kesteren, Lips, Gooren, Asscheman, & Megens, 1998), further complicating finding an association. Third, several studies have indicated that T levels above a certain threshold value of T do not have a significant impact on sexual functioning (Bagatell, Heiman, Rivier, & Bremner, 1994; Gooren, 1987; Kelleher, Conway, & Handelsman, 2004). Fourth, serum androgen levels are only one aspect in the androgen cascade. Other factors, such as genetic variation of the transcriptional activity induced by the androgen receptor may modify T action (Crabbe et al., 2007; Zitzmann, Gromoll, & Nieschlag, 2005).

With regard to other correlates of sexual desire, it was found that trans women attracted to women experienced lower levels of sexual desire. These findings support previous results from Weyers and colleagues (2009). Interestingly, no differences in distress levels were observed between trans women attracted to men or attracted to women suggesting that trans women attracted to women may be less interested in sexual activity or are less open to sexually adequate stimuli compared to those attracted to men. Indeed, it has already been observed (Weyers et al., 2009) that trans women attracted to women attributed the lowest importance to sex in comparison with the others. These results may also corroborate with observations in lesbian women, as the latter had lower levels of sexual desire compared to heterosexual women (Applebaum, 1983). Similar to studies in the general population, it was found that participants involved in a partner relationship had higher distress levels (Rosen et al., 2009) resulting in a higher prevalence of HSDD.

Concerning the associations between cross-sex hormone therapy and sexual desire, it was observed that trans women who had undergone vaginoplasty experienced higher levels of sexual desire compared to those who were scheduled to undergo this surgery. It is likely that the relief of gender dysphoria due to a body image more congruent with

the gender identity has positive effects on sexual functioning or the other way around that the presence of male genitalia has negative effects on sexual functioning. As a result, trans women may experience more satisfying sexual relationships after genital surgery. In contrast, no associations were found between type of surgery and sexual desire scores in trans men, but satisfaction with phalloplasty was negatively associated with prevalence of HSDD. Interestingly, no associations were observed between surgical satisfaction and sexual desire scores in trans women.

These different associations between trans women and trans men are not well-understood. One explanation could be that trans men attribute a higher degree of importance to functionality of their newly-formed genitalia compared to trans women. Many underlying factors may contribute to these findings such as differences between functional and esthetical surgical satisfaction, body image, self-esteem etc. This is a point for further exploration and study.

Limitations of the studies

Certain limitations of these studies should be noted. First, the power of especially study one was limited, despite the fact that we were able to study a substantial number of trans men. Second, the cross- sectional design implies that no causal relations could be drawn. Also, observations on retrospective data should be interpreted with caution. Prospective studies are definitely needed to confirm the present results. Third, study one could only establish a difference in sexual desire between participants with LH below P25 and the others. We found no difference between participants with LH levels above P75 and LH levels between P25-50 and P50-75. However, the high variance in sexual desire scores in the group with LH levels above P75 as well as the limited power of this study should be considered. Forth, selection bias of our study is another possible limitation. As in all follow-up studies, participants who agreed to these studies may have a more favorable outcome than those who refused to participate. Nevertheless, the response rates were relatively high with 54% in study one, which required a full day hospital visit, and 64% in study two. Fifth, the aim of study two was to investigate associations between GST and sexual desire. However, we are aware that the subjective experience of sexual desire for an individual results from a complex interaction between the individuals' sexual response system and adequate sexual stimuli and consequently

can be affected by many biological, psychological, social, sexual and relational factors (Hayes et al., 2008), which were not all addressed in the current studies. Also, gender differences in intrinsic and extrinsic factors affecting sexual desire have led to another conceptualization of sexual desire in men and women (Basson, 2000). Given these gender differences in sexual desire, distinct definitions of HSDD in men and women have been proposed (Brotto, 2010). We defined HSDD in trans women and trans men according to the definition of the desired gender, due to changes in both hormonal environment and/or genital anatomy and function in combination with transitioning to the desired gender role. However, this approach has certain limitations considering the presence of male or female genetics, gender differences in imprinting of brain systems, and lifelong psychosocial learning experiences in the natal gender role. Finally, sexual functioning after GCT is partly dependent on the quality of and satisfaction with surgery which hampers generalization of our results to all centres.

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CHAPTER 8

GENERAL DISCUSSION

The goal of this doctoral dissertation was to add on the knowledge on the concept of sexual desire, by conducting a series of studies in two different populations. Both the population of contraception-users, and the population of trans persons (who underwent gender-confirming treatment), provide a useful opportunity to test hypotheses on biopsychosocial correlating factors of sexual desire. More specifically, we were interested in sexual desire changes, induced by switching contraceptive preparations and looking at cycle-related patterns in the first group, and, in sexual desire changes induced by having undergone gender-confirming treatment in the second group. Further, information was gathered on the biopsychosocial correlating factors varying with these changes in sexual desire. In this final chapter, we will briefly recapitulate the aims of the current doctoral dissertation and present an integrative overview of the most important findings. We will discuss the implications with regard to theory, research, policy and clinical practice. Finally, we will describe both the limitations and the strengths of the present series of studies and formulate a number of suggestions for future research in this area.

RECAPITULATION OF THE RESEARCH GOALS

The first objective of the current dissertation was to look into the sexual desire of contraception-users. While previous research has focused on potential sexual side effects by cross-sectional comparison of users of different preparations, we have added on this by using the woman as her own control, in a prospective, within-subject design. More specifically, we aimed at observing potential sexual desire changes through switching between three different contraceptive preparations. Also, in that study a number of biopsychosocial correlating factors (such as mood, self-esteem, contraceptive product and androgen sensitivity) were assessed to monitor their relation with female sexual desire (Chapter 3). We have further attempted to determine potential cycle-related variations in sexual desire in a controlled diary study of both hormonal and non hormonal contraception-users, but also examined the role of mood, weekend preference and bleeding days during the contraceptive and menstrual cycle (Chapter 4). Compared to the body of knowledge in freely cycling women, knowledge on cycle-related patterns and its correlates are almost not existent in contraception-users.

The second goal was to make a start with acquiring knowledge on the sexual desire of previously gender dysphoric individuals who have undergone gender-confirming treatment (GCT). Since earlier researchers and clinicians were concerned with the transition to be viewed as merely sexually driven, almost no information on sexuality in general is available in this population. In an attempt to quantify the clinically presented picture of trans women (transition from male to female) complaining of low sexual desire, a first cross-sectional study looked into the prevalence of trans women reporting personal or relationship distress caused by decreased sexual desire after GCT (Chapter 5). Further, in this controlled study we attempted a first exploration of the association of these desire complaints in trans women with levels of sex steroids and androgen sensitivity (Chapter 5 and 6). In two final studies, a large cohort of both trans women and men was retrospectively assessed on the perception of GCT-related change in sexual desire. The relationship with several biopsychosocial correlates (such as hormone levels, treatment status, relationship duration, sexual orientation) was examined in this population as well (Chapter 7).

INTEGRATION OF THE MAIN FINDINGS: OVERVIEW

In the next few paragraphs, we will integrate the results presented in this dissertation. First, the findings on sexual desire in contraception-users and the role of biopsychosocial correlating factors will be summarised and then discussed within a more broad perspective. Second, we will present the results regarding sexual desire in previously gender dysphoric individuals and its relation to GCT. Table 1 shows an overview of the most important associations.

Table 1. Overview of the main findings on sexual desire changes and biopsychosocial correlates of sexual desire

	Chapter 2	**Chapter 3**	**Chapter 4**	**Chapter 5**	**Chapter 6**	**Chapter 7**
Main result(s)	Contraceptive prevalence 84%	SD change with product switch	Stable SD in contraceptive cycle, mid-cycle SD peak in menstrual cycle	HSDD in 1/3 trans women		HSDD in 1/4 trans women
Biological correlates		Free T ~ CAG X product Female SD ~ CAG: SS>SL<LL product: VR > COC & POP		Female SD (trans) ~ ≠ total or free T Female SD (control) ~ ↑ free and total T	CAG ~ ↑ free T ≠ total T SD ≠ CAG X free T	Male SD ~ ≠ total or free T ↓ LH ↓ duration T treatment
Psychological correlates		Female solitary SD ~ ≠ mood Female dyadic SD ~ ↑ SD woman (baseline) ↑ SD woman's partner ↑ mood ≠ self-esteem ≠ sexual satisfaction	Female SD (COC) ~ ↑ positive affect ≠ negative affect ≠ # bleeding days ≠ # weekend days Female SD (NHC) ~ ↑ positive affect ≠ negative affect ↓ # bleeding days ↑ # weekend days	SD trans = control		SD men > women HSDD women > men SD (men) ~ ≠ genital surgery SD (women) ~ ↑ genital surgery
Social/dyadic correlates	General population = Turkish minority in risk unplanned pregnancy In both samples: ↓ education ~ ↓ ECP-knowledge	Female SD ~ ≠ relationship satisfaction		Relationship and general life satisfaction: trans = control Sexual satisfaction: trans < control		SD (men) ~ ↓ employment ↓ relationship duration ≠ sexual orientation SD (women) ~ ≠ relationship status or duration sexual orientation (↓ lesbian women)

Note. ECP: emergency contraceptive pill, CAG: androgen sensitivity, SS, LL and SL: homozygous short and long alleles, and heterozygous alleles on CAG repeat, SD: sexual desire, CAG, GCT: gender-confirming treatment, HSDD: hypoactive sexual desire, T: testosterone, ↑, ↓ and ≠ ~ :positive, negative and no correlation, VR: vaginal ring, COC: combined oral contraception, POP: progestin-only pill, NHC: non-hormonal contraception, #: number of, X: interaction

SEXUAL DESIRE AND ITS CORRELATES IN CONTRACEPTION-USERS

Overview of the main findings on sexual desire and its correlates in contraception-users

As a first exploration of the field of contraception in Flanders, *Chapter 2* has shown that 84% of sexually active women of childbearing age are using contraception. This prevalence is similar in a group of women of Turkish descent.

A primary theme in the current dissertation is the iatrogenic effect of hormone preparations on human sexual desire. Within the population of heterosexual, contraception-using couples, we have found that female sexual desire can be influenced by switching between different contraceptive preparations in a modest but significant way (*Chapter 3*). This study further assessed the role of several biopsychosocial correlates of female sexual desire during this cross-over design. First, analyses of the biological correlates have demonstrated that not only the contraceptive product itself impacts the woman's sex steroid levels (mainly free T, as published by previous researchers, e.g. Boyd et al., 2001; Thorneycroft et al., 1999), but contraception-induced decreasing free T levels are modulated by genetically determined androgen sensitivity (as measured by the *AR* gene CAG repeat length). It was shown that solitary and dyadic sexual desire in the female participants was associated with both the contraceptive product and androgen sensitivity independently. While the vaginal ring appeared to co-vary more often with an increased sexual desire, women with both highly sensitive and rather un-sensitive androgen receptors showed a stronger sexual desire. Second, these mixed models on female sexual desire displayed psychological and relational correlates to be of an even stronger predictive value for female sexual desire. Depressive symptoms had no role in the experience of solitary sexual desire, while they did show importance in the woman's desire to behave sexually with her male partner. Especially this dyadic sexual desire in the female participants was strongly affected by the sexual desire of her partner. Finally, the woman's sexual and relationship satisfaction and her self-esteem were not associated with her sexual desire (*Chapter 3*).

While the results of *Chapter 3* looked at women switching between several contraceptives, *Chapter 4* took a closer look at similar correlates within the

contraceptive cycle of heterosexual, current COC-using couples. To facilitate a comparison of potential cycle-related sexual desire effects and its correlates, a control group of heterosexual, current NHC-using couples (freely cycling women) was included in the same study protocol. The main finding was that both male and female partners concordantly experienced no peaks or troughs in their solitary or dyadic sexual desire levels across the contraceptive cycle. In contrast, both solitary and dyadic sexual desire was shown to peak during the ovulation phase, but only in the female participants of the control group.

Chapter 4 also took into account –a more limited range- of correlates of sexual desire. It was shown that positive affect correlated with both solitary and dyadic female sexual desire, and with sexual frequency, in the perspective of the female partners of the COC-groups. The male partners only reported a relation of positive affect on their dyadic sexual desire. Further, the study looked into the relationship between sexual desire and sexual frequency and the correlates of bleeding and weekend days. While both correlates were related with neither sexual desire nor sexual frequency, a decreased frequency of sexual activity was found during the days women started a new pill cycle. NHC-women also reported a decreased sexual frequency during menstruation: sexual activity was less frequent on bleeding days. Finally, COC-women experienced an increased negative affect during their last pill days of the cycle, after which increased self-affirmation and self-enhancement motives for sexual activity were reported the following pill free days (Chapter 4).

A summarizing view on sexual desire and its correlates in contraception-users

Sexual desire changes. Chapter 3 and 4 have shown that while female sexual desire might be altered when switching between different contraceptive preparations, sexual desire is very stable across the contraceptive cycle (in COC-users compared to the menstrual cycle of freely cycling women), but not in the menstrual cycle. Despite an absent wish to conceive, freely cycling women reported a mid-cycle peak (during ovulation) in sexual desire (as had been previously reported, e.g. Bullivant et al., 2004). Chapter 3 presented the first study with a within-subject, cross-over design, making a comparison with previous, mainly cross-sectional research with parallel COC-groups, difficult. The hypothesis concerning a lower sexual desire during COC-use was confirmed, and corroborates previous publications reporting that a number of COC-starters experience decreased sexual desire (Graham, et al., 1995; Graham, & Sherwin, 1993). The finding of a stable female (and male) sexual desire within the contraceptive cycle (Chapter 4) confirms earlier retrospective reports that sexual desire is 'flattened out' during COC-use (Warner & Bancroft, 1988; Walker & Bancroft, 1990).

Biological correlates. As described in the *General introduction*, the sexual system is characterised by a certain extent of sensitivity ('central arousability'), influenced by sex steroid levels, neurotransmitters, androgen sensitivity etcetera (Both, Everaerd, & Laan, 2007). Chapter 3 has shown that –in the presence of contraception-induced lower free T levels- the female sexual desire, partly resulting from the sensitivity of the sexual system, is influenced by both androgen sensitivity and the used contraceptive preparation in an independent manner. Women with short and long CAG repeats (few active and very active *AR:* SS- and LL-groups, respectively) reported to experience stronger solitary and dyadic sexual desire, which is not consistent with our hypothesis that especially the first group with few active and sensitive receptors would report a lower sexual desire due to contraception-induced free T decrease. Possibly, the sexual desire of these subgroups (SS- and LL-group) is less impacted by the use of contraception, due to a clear compensating mechanism in the androgen receptor: during the use of all three preparations, a less sensitive receptor was compensated by higher free T levels (despite the presence of a pharmacological influence). The situation might be different for the group with an intermediate androgen sensitivity (SL-group). A

greater inter-individual variability in responsiveness to T in women compared to men (as suggested by the desensitisation hypothesis, see Bancroft, 2002, 2005, 2009) might account for this observation, but future studies are warranted to better clarify the relation between CAG repeats and sexual desire in both women and men.

Further, a direct relation with free T levels and female sexual desire was not confirmed (Chapter 3). This is in accordance with the current body of literature finding little evidence for this relationship in contraception-users (e.g., Graham, Bancroft, Doll, Greco, & Tanner, 2007). It is possible that these free T-levels in the lower range render finding a relation too difficult, or that the pharmacological intervention changes the 'conditions' in which the sexual system has been functioning previously (before HC- use), resulting in different relationships with biological correlates of the system. Earlier, Bancroft and colleagues (1980) have demonstrated that the relation between total T and the frequency of sexual thoughts can be obscured in an OC-using group with sexual difficulties. However, our study had corrected the model for dyadic sexual desire for female sexual functioning.

Finally, the contraceptive preparation in itself was found to have a modest but significant impact on female sexual desire (Chapter 3): vaginal ring use appears to be more beneficial for solitary and dyadic sexual desire in women, compared to a classic COC- and POP-product. This is in line with an earlier Italian study (Sabatini & Cagiano, 2006). Considering no interaction was seen between CAG repeat and contraceptive product on female sexual desire, this effect did not depend on the woman's androgen sensitivity.

Psycho-social correlates. Chapter 3 and 4 have also looked into psychological correlates (such as mood, self-esteem, bleeding days, weekend preference, and sexual motives) and social (relationship and sexual satisfaction, partner's sexual desire) of female sexual desire.

First, Chapter 3 and 4 both included the factor *mood* into the mixed models for sexual desire, as studies have shown that mood and sexual desire can co-vary, although not necessarily in a linear manner (see Lykins, Janssen, & Graham, 2006). Chapter 3 supports the hypothesis that contraception-users with less depressive symptoms experienced a stronger sexual desire towards their partners throughout the consecutive contraceptive cycles in the study. However, there was no relation between depressive symptoms and solitary sexual desire. Chapter 4 provided a different angle from a within-

cycle design, showing that only a stronger positive affect co-varied with higher female (solitary and dyadic) sexual desire. No association between negative effect and sexual desire could be found. The hypothesis proposing a differentiated pattern of negative affect and sexual desire was hence endorsed: negative affect increased during the last pill days in the presence of a stable sexual desire across the contraceptive cycle (Chapter 4). This result confirms similar findings of earlier studies (Graham & Sherwin, 1993; Graham et al., 1995).

Chapter 3 could not confirm the relation between sexual desire and *self-esteem*, *relationship and sexual satisfaction*. To the knowledge of the authors, earlier research has not included these correlates into their design. No relation was seen between sexual desire and relationship duration, which contradicts earlier findings of Klusmann (2002) who reported a negative association between relationship duration and sexual desire (only in women) in a student sample. It is possible that the present sample size and the range of participant's ages were too small to detect an effect of this correlate.

Two important findings in Chapter 3 are the relation of female sexual desire with (a) its baseline level and (b) the level of her partner's desire, which were the most important psychological correlates in the dyadic desire model. We thus conclude that female sexual desire appears to be, apart from the presented pharmacological and genetic influences, both a stable, intra-individual and a highly relational process. These observations can be seen in the context of the incentive motivation model of sexual desire: while genetic and pharmacological influences impact the 'central arousability' of a woman's sexual system, the findings on these psychological correlates underscore the importance of the individual and relationship stimuli and learning history in the generation of sexual desire.

Chapter 4 additionally reported on the correlates of bleeding days and weekend preference. While the factors of bleeding and weekend preference did not relate to the sexual desire of COC-users, both factors were important for the female sexual desire in the NHC-group. Freely cycling women reported a decreased solitary sexual desire on their bleeding days, and a stronger sexual desire for their partner during weekend days. This last difference might however also be due to the socio-demographic differences between both samples, as the COC-sample mostly consisted of students while the NHC-sample was significantly older.

Since sexual activity was measured in the study as well, the relation with sexual frequency was also calculated. Such relations could reflect attitudes on having sex during menstruation, the availability of the partner and increased free time, respectively. Results of an earlier publication on weekend preference in sexual activity (Roney & Simmons, 2013) were corroborated: participants were sexually active more frequently during weekend days, but this finding was only present in the freely cycling women and not the COC-users. Neither weekend preference nor the factor bleeding days showed an association with sexual frequency in COC-users. However, a decrease in the frequency of sexual activities was observed around restarting a new pill cycle (i.e. pill day two and the preceding three days), a time which can be assumed to coincide with the withdrawal bleeding of the female partner. Based on studies in freely cycling women, where quite a universal decrease in sexual activity during the menstrual phase was demonstrated (Brewis & Meyer, 2005), one could assume that also the withdrawal bleeding in COC-women would impact sexual frequency. This association between sexual frequency and bleeding in the COC-users might have been obscured by the artificial division of the contraceptive cycle in eight assessment times, each spanning four cycle days.

SEXUAL DESIRE AND ITS CORRELATES WITH GCT

Overview of the main findings on sexual desire and its relation with GCT

A second aim in the current dissertation was to start a more thorough exploration of sexual desire in trans persons who underwent GCT. *Chapter 5* started with documenting the prevalence of trans women reporting personal and relationship distress caused by decreased sexual desire (Hypoactive Sexual Desire Disorder, HSDD) in a cross-sectional study, and in a control group of freely cycling women. While the trans women and the control women reported a similar level of sexual desire, one in three (34%) trans women and one in four control (23%) women were diagnosed with HSDD, a clinically relevant but not statistically significant difference. *Chapter 5* further looked into the relationship between female sexual desire and hormone levels. In trans women, no correlation was found between sexual desire and total or free T levels. Also, no relation was found between having HSDD and having a free T level below P25 of the control women. In

contrast, the control group of freely cycling women did show a positive correlation between solitary sexual desire and levels of total and free T. *Chapter 6* further investigated this lack of relation between sexual desire and T in trans women, by assessing the potential mediation of androgen sensitivity (measured by the *AR* CAG repeat length) in this group. It was found that CAG repeat length correlated positively with free T levels in trans women, but had no direct relationship with sexual desire. Solitary sexual desire was however related to an interaction between CAG repeat length and total T levels. Similar analyses with free T levels showed no results. Continuing on the results above*, Chapter 7* summarised findings on sexual desire and GCT in two cross-sectional studies. Study one first aimed at providing a validated measure of solitary and dyadic sexual desire in a group of trans men. No direct associations with total or free T levels were found, while an indirect relation with LH levels (indicative of [in] sufficient hormone substitution) was demonstrated. Study two set out to quantify, in retrospect, the perceived changes in sexual desire in relation to GCT. Seven in ten trans men reported an increased sexual desire (71%), while seven in ten trans women felt that the GCT had decreased their sexual desire. Study two further added that HSDD was present in 5% of trans men and 22% of trans women. Finally, with regards to correlates of sexual desire, treatment duration and partnership duration were important for trans men, while in trans women only having had genital surgery was related to sexual desire.

A summarizing view on sexual desire and its relation with GCT

Prevalence of sexual desire changes in trans men and women. A first aim of Chapter 5 to 7 was to quantify sexual desire (with a validated questionnaire) and, in retrospect, to quantify sexual desire changes in relation to the GCT, in both trans women and men. The first explorations in Chapter 5 were expanded on in the studies discussed in Chapter 7. In retrospect, seven in ten trans women experienced a decreased sexual desire since GCT, and as many trans men reported an increase. While many factors that could not be investigated in the present studies (e.g., decreased gender dysphoria, more satisfactory sexual relationships since GCT), could have explained the results in the trans men, they could not completely account for the change in trans women. While previous research showed a somewhat smaller but significant reduction of gender dysphoria after GCT in trans women (Smith, Van Goozen, Kuiper, & Cohen-Kettenis, 2005), it appears

that these perceptions of an inverse effect of GCT on sexual desire in both groups seem to relate to the received treatment. These results mostly corroborate the findings of Costantino and colleagues (2013), who found an increase in sexual desire in a smaller portion of their sample. Further, we must remark that 17% of both trans men and women felt that the GCT had not changed their experience of sexual desire, and 12% of trans men reported a decreased desire and 13% of trans women an increased. It is clear that many biological, psychological, relationship as well as socio-cultural factors will moderate this GCT-induced effect.

Chapter 5 and 7 further assessed the prevalence of HSDD in both trans men and women, defined as a suffering from personal and relationship distress due to low sexual desire. Using a rather strict definition, 5% of trans men were diagnosed with HSDD. Chapter 5 found a prevalence of 33% while chapter 7 found 22% in trans women. This difference might be due to the smaller sample size of Chapter 5. Also, the data gathered in Chapter 7 were part of an inter-disciplinary study, were selection bias on this sexual aspect of functioning might be reduced. When we compare these number to population studies who take into account a distress factor for sexual complaints, we see that especially trans women report a higher HSDD-prevalence, compared to the general population: studies in men pointed towards 0.5 and 6% of HSDD in men (Hendrickx, & Enzlin, 2013; Kedde, 2012), and towards 3 to 14% in women (Christensen et al., 2011; Hendrickx, & Enzlin, 2013; Kedde, 2012; Shifren, Monz, Russo, Sergreti, & Johannes, 2008). In this context, we must point out that while seven in ten trans women never or rarely experienced either ‘spontaneous’ or ‘responsive’ sexual desire, only a third showed distress. Two in three trans women did *not* experience this lack or absence of sexual desire as distressing.

Trans women had a higher prevalence of HSDD and more often described a decrease in sexual desire after GCT compared to trans men. As described in the *General introduction*, sexual desire is a multifaceted process, resulting from the triggering of the sexual response system with a specific arousability based on (amongst others) genetics, the presence of sex steroids and neurotransmitters as well as by lifelong psychosocial learning experiences. Those sexual stimuli can be both internal (such as sexual thoughts) or external cues (sensory stimuli experienced as erotic) (Laan & Both, 2008). Since trans women have mostly grown up with a highly testosterone dependent sexual response system and have often had sexual experiences in the male gender role, it requires a

certain 'reconditioning' of the sexual response system within a less androgenic hormonal milieu. The fact that two in three trans women in our group did *not* experience this lack or absence of sexual desire as distressing, points to the presence of factors that might be compensating for the loss of the 'androgen-driven sexuality'. This might consist of factors the current study could not assess, such as an increasingly positive self-image and a boosted self-esteem from being recognized in the desired, female gender role.

Correlates of sexual desire in trans men and women. A second objective of Chapters 5 to 7 was to determine suitable correlates for the observed sexual desire changes. Chapters 5 and 7 first assessed relations with hormonal correlates, and could both not find an association with total or free T and sexual desire in trans men or women. Only one other study has reported on this relationship, and could also not establish an association between a range of hormonal and sexual parameters (Costantino et al., 2013).

Chapter 6 further looked into this lack of relation between sexual desire and T in the group of trans women of Chapter 5, by assessing the potential mediation of androgen sensitivity (also measured by the *AR* CAG repeat length) in this group. CAG repeat length had no direct relationship with sexual desire, but solitary sexual desire was associated with an interaction between CAG repeat length and total T levels. Within the group of trans women with lower total T levels (beneath the median), trans women with a CAG repeat at the lower (< median) or the higher (≥ median) end of the range, reported a stronger solitary sexual desire compared to trans women with a median CAG repeat length. Considering this contradictory quadratic relation between CAG and solitary sexual desire, and the lack of a significant result for similar analyses with free T levels, it was concluded that CAG repeat length is not a consistent modulating factor in the relationship between total and free T and sexual desire in trans women.

Chapter 7 however demonstrated an inverse association between solitary sexual desire (related to the concept of arousability) and LH levels in trans men. Inadequate T therapy, as indicated by high LH levels, was associated with lower levels of solitary sexual desire: trans men with LH levels below P25 (indicating excess T treatment) reported higher solitary sexual desire than those with LH levels within the normal range.

With regard to psycho-social correlates of sexual desire, Chapter 7 found that trans women attracted to women experienced lower levels of sexual desire. These findings support previous results from Weyers and colleagues (2009). Interestingly, no

differences in distress levels were observed between trans women attracted to men or attracted to women, suggesting that trans women attracted to women may be less interested in sexual activity or are less open to sexually adequate stimuli compared to those attracted to men. Indeed, it has already been observed (Weyers et al., 2009) that trans women attracted to women attributed the lowest importance to sex in comparison with the others. These results may also corroborate with observations in lesbian women, as the latter had lower levels of sexual desire compared to heterosexual women (Applebaum, 1983). Similar to studies in the general population, Chapter 7 found that trans women involved in a partner relationship had higher distress levels (Rosen et al., 2009) resulting in a higher prevalence of HSDD. Prevalence of HSDD in trans men was too low to test the association with a partner relation in that group.

Concerning the associations between cross-sex hormone therapy and sexual desire, it was observed that trans women who had undergone vaginoplasty experienced higher levels of sexual desire compared to those who were scheduled to undergo this surgery. It is likely that the relief of gender dysphoria due to a body image more congruent with the gender identity has positive effects on sexual functioning, or the other way around, that the presence of male genitalia has negative effects on sexual functioning. As a result, trans women may experience more satisfying sexual relationships after genital surgery. In contrast, no associations were found between type of surgery and sexual desire scores in trans men, but satisfaction with phalloplasty was negatively associated with prevalence of HSDD. Interestingly, no associations were observed between surgical satisfaction and sexual desire scores in trans women.

These different associations between trans women and trans men are not well-understood. One explanation could be that trans men attribute a higher degree of importance to functionality of their newly-formed genitalia compared to trans women. Many underlying factors may contribute to these findings such as differences between functional and esthetical surgical satisfaction, body image, self-esteem etc. This is a point for further exploration and study.

METHODOLOGICAL AND CLINICAL IMPLICATIONS

In the following paragraphs, we will present the methodological and clinical implications of the current dissertation. First, we outline several methodological strengths and weaknesses of the presented studies in both study populations.

Methodological implications of the studies in contraception-users

Study design. In both study populations of this dissertation, unique samples have been presented. First, both samples of contraception-users (Chapter 3 and 4) have started out from a couple's perspective. No earlier study in the field of contraception and sexual desire has included the factor of the partner's sexual desire (Chapter 3), or has assessed both partners' reports on sexual desire across the contraceptive cycle (Chapter 4). Moreover, to the knowledge of the authors, Chapter 3 is the first study conducted with a cross-over, within-subject design, allowing us to compare a woman's sexual response between consecutive contraceptive preparations. Previous studies have mainly compared parallel groups of contraception-starters and hence, might be biased by psychosocial or relational factors coinciding with starting contraception. We believe the current cross-over approach to be a more clinically relevant perspective, presenting health care workers with findings similar to their daily practice. Also, the design of the study of within-cycle patterns of sexual desire in Chapter 4 was unique: previous studies have looked at cycle-related changes in sexual desire in OC-users from either a retrospective approach (Warner & Bancroft, 1988) or in a very limited heterogeneous sample (Bancroft, Davidson, Warner, & Tyrer, 1980).

However, a number of limitations in the used methodology in contraception-users need to be addressed. First, the prospective cross-over study (Chapter 3) had a rather limited sample size, which was partly compensated by the within-subject design. Second, no wash-out period with only condom-use between consecutive contraceptive preparations or before starting study-participation was used. Since female participants were of childbearing age, such a wash-out was anticipated to be a large obstacle in recruitment. Third, the entire sample of Chapter 3 and the COC-using sample in Chapter 4 showed an underrepresentation of older couples with longer relationship duration.

This could hamper the generalisation of our findings to the general population. Fourth, considering the previously reported high rates of OC-discontinuation (e.g. Sanders, Graham, Bass, & Bancroft, 2001), it is possible that the study sample of Chapter 3 was biased. The cross-over design included participants using both hormonal and non-hormonal baseline contraception: the second group might have consisted of unsatisfied OC-users, or those women might have selected themselves out completely. When asked for specific reasons for participation at study inclusion, most participants indicated that they saw the study as an opportunity to try out several means of less familiar (progestin-only pill) or new preparations (vaginal ring). Finally, also as a consequence of a heterogeneous group regarding baseline contraception and the lack of a validated measure for HC-side effects, Chapter 3 could not conclude on the role of androgen sensitivity in HC-induced side effects.

Biopsychosocial approach. A notable strength of the current dissertation is the use of a range of biopsychosocial correlates in studying the concept of sexual desire. This approach provides a unique opportunity to study the relative importance of several correlates and their interrelations. The results of a cross-over design in contraception-users (Chapter 3) shows that in the field of sexuality and contraception, the answer is never only genetics, hormones or mood, relationship or personality, but specifically assessing on and testing of the interactions between all of these is a worthy approach.

Methodological implications of the studies in trans persons after GCT

Sample size. Previous studies on trans persons have rarely included large samples. For the studies on sexual desire and its relation to GCT, we were able to collect data in a substantial sample of trans persons. Keeping in mind the relative rarity of gender dysphoria (De Cuypere et al., 2007), the availability of an interdisciplinary gender team residing in one university hospital, offering gender dysphoric individuals in Belgium a standardised treatment protocol, has enabled us to collect data in an unusually large cohort of trans individuals.

However, also the studies in trans persons after GCT show several limitations. First and foremost, it is clear that a retrospective, cross-sectional design can only present correlational findings and offers no causal relationship between sexual desire changes

and GCT. The presented results absolutely need confirmation within prospective, repeated measures designs across the GCT to tackle the risk of participants presenting socially desirable responses or memory effects. Second, while having the majority of trans participants treated in one inter-disciplinary team, this might have hampered the generalisation of the presented results to the larger population of trans individuals. Similarly, the differences in sample size between the types of T therapy in our participants could have hampered finding a relation between hormone levels and sexual desire, especially considering the relatively small sample size of study one.

Clinical implications of findings in contraception-users

As explained by the present dissertation, switching hormonal contraception can impact the sexual desire of women, which is again related to several biopsychosocial correlates. Although studies in this field have long neglected the impact of contraception on female sexual desire, it appears that health care workers (e.g., especially general practitioners, medical specialists and sexologists) should be informed on the role of contraception in female sexuality. When providing women and their partners with contraceptive counselling, general practitioners and medical specialists should keep in mind that finding a suitable and satisfying contraceptive method might be more than a trial-and-error process of 'matching the right woman with the right product'. This dissertation confirms that certain contraceptive methods are more often associated with a higher or lower sexual desire, even after correction for several factors. Further, all health care personal providing treatment potentially affecting sexuality should be aware that female sexual desire is both a genetic, individual and relationship process. Finally, clinicians providing counselling and psychotherapy in the domain of human sexology should always take into account all relevant biopsychosocial factors when assessing complaints of low sexual desire, e.g. complaints of pill-induced decreases of sexual desire.

Clinical implications of findings in trans persons

If the presented results on the relation between sexual desire and GCT are confirmed in prospective study designs, these prove to be highly relevant for the transgender population at large. While the topic of sexuality was long avoided out of fear of reducing gender-confirming treatment to this one aspect, it appears the majority of trans persons perceive it to be impacting their sexual desire, and possibly their sexual life more broadly. Health care workers counselling applicants for gender-confirming treatment should be knowledgeable on the potential impact of gender-confirming treatment (positive and negative) and discuss these with applicants to achieve realistic expectations of treatment.

FUTURE RESEARCH

In this section, we strive to formulate a few suggestions for future research that might contribute to a better and more complete understanding of the concept of sexual desire and its correlates.

Measuring sexual desire

Contrary to most studies in contraception-users, and to all previous studies in trans persons, the presented studies have used a validated measure to assess the frequency and intensity of both solitary and sexual desire. While financial and practical considerations can sometime lead researcher to use a single-item measure for sexual desire, the presented series of studies are suggestive of a thorough assessment of this aspect of female sexual functioning to be able to use the measure in mixed models for repeated analyses. Considering the recent findings on the co-occurence of sexual desire and arousal, future research in both contraception-users and trans persons might benefit from designs looking at both differentiation between and co-variation between both aspects of sexual functioning.

Longitudinal research on biopsychosocial factors

A second research suggestion pertains to setting up prospective, biopsychosocial designs in first-users of hormonal contraception, controlling for the baseline values of all affected biopsychosocial factors. In those women, contraceptive effects are not yet influenced by previous contraception experiences and expectations. Both previous research and the current dissertation have unfortunately not been able to find sufficient funding to set up highly time-consuming and costly, complex studies that would provide us with a more complete understanding of biopsychosocial processes in contraception-starters. For instance, this would better inform us on the question whether, in women with a cycling estrogen milieu, the pharmacological of a contraceptive preparation or the genetically determined androgen sensitivity has the larger impact. Considering its established role in contraception-users in the present dissertation, future research on HC-starters could include this measure as this might provide clinical implications, e.g. women with very low numbers of CAG repeats (and hence potentially sensitive to contraception-induced changing sex steroid levels) could be monitored or prescribed preparations with a lower impact on those levels.

Also in trans persons, longitudinal research would offer a better understanding of the occurring sexual desire changes, and would allow researchers to distinguish the relative importance of biological (androgen sensitivity, previous and current sex steroid levels), psychological (resolution of gender dysphoria, improved self-esteem, more positive body-image, and quality of life), and social-relational (more qualitative partnerships, more satisfying sexual life, experience of minority stress) factors on this aspect of sexual functioning.

GENERAL CONCLUSION

Sexual desire changes are an inevitable and normal part of any personal and partnership context, and might be influenced by many of life's inter- and intra-personal factors. In this doctoral dissertation, we have presented a series of studies documenting sexual desire changes, and its bio-psycho-correlates, in contraception-users and trans persons having undergone gender-confirming treatment. As was expected, sexual desire of contraception-users can be influenced by switching preparations. Moreover,

biological (androgen sensitivity and contraceptive preparation), psychological (mood) and socio-relational factors (partner's sexual desire) all play a significant role in these sexual desire changes. From a closer perspective however, sexual desire changes are less related to the time of the contraceptive cycle, and more to a woman's positive affect. Following expectations on very limited previous evidence, sexual desire changes across gender-confirming treatment were found to be perceived by seven in ten trans persons, while a minority of especially trans women experiences distress of decreased sexual desire. Given that sexual desire changes have now been documented more clearly in both study populations, we hope that the present findings will generate both more fundamental as clinically-driven research in this field.

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SEKSUEEL VERLANGEN

Definitie

Het huidige doctoraatsonderzoek omschrijft seksueel verlangen zoals het wordt gehanteerd in het gebruikte meetinstrument, de "Sexual Desire Inventory" (Spector, Carey, & Steinberg, 1996). Deze auteurs definiëren seksueel verlangen als "de interesse in seksuele activiteit." Verder stellen ze dat "het primair een cognitieve variabele betreft, die gemeten kan worden door de sterkte en frequentie van gedachten aan toenadering tot of ontvankelijk zijn voor seksuele stimuli."

Een theoretisch model van seksueel verlangen

Vertrekkend vanuit dit vooraf gedefinieerd concept van seksueel verlangen, plaatsen we seksueel verlangen binnen een recent theoretisch kader van het "incentive motivatie" model. Dit model stelt dat seksueel verlangen het resultaat is van een complex en gelaagd proces, dat bestaat uit verschillende stappen: (1) de aanwezigheid van een seksuele stimulus die het seksueel systeem activeert, (2) wat een beoordeling – vanuit het werkgeheugen- in gang zet die de seksuele stimulus verwerkt, leidend tot (3) de activatie van het bewuste geheugen waarbij de betekenis van de stimulus gelinkt wordt in het expliciet geheugen, en (4) leidt tot een activerende emotionele arousal in het pre-attentieve impliciete geheugen. Uiteindelijk is de activatie van het seksuele responssysteem geassocieerd met verschillende evaluatieprocessen, die ervoor zorgen dat de responsgeneratie al dan niet plaats vindt (Gijs, Laan, & Both, 2009).

HEEFT HORMONALE CONTRACEPTIE EEN EFFECT OP VROUWELIJK SEKSUEEL VERLANGEN?

Vijfig jaar "de pil": inleiding en prevalentie van gebruik

Na de doorbraak van Gregory Pincus en zijn collega's (Pincus et al., 1959) die leidde tot de ontwikkeling van de pil, keurde de Amerikaanse Food and Drug Administration

(FDA) op 9 mei 1960 het gebruik ervan door gehuwde vrouwen goed. Later kregen ook ongehuwde koppels toegang tot dit “recht op niet-procreatieve seks” (Tone, 2001; Watkins, 1998). Tijdens de eerste decennia van zijn bestaan, deed de pil veel stof opwaaien in zowel populaire als wetenschappelijke publicaties. Vandaag is de pil de meest populaire contraceptieve methode in West-Europa (Skouby, 2004).

Overzicht van eerdere studies naar hormonale contraceptie en vrouwelijk seksueel verlangen

Initieel waren er maar weinig zorgen over negatieve effecten op het vrouwelijk seksueel functioneren, wel integendeel. Door het scheiden van de seksuele en contraceptieve act (Zell & Crisp, 1964), verwachtten de meesten een verbeterd welzijn en seksueel verlangen onder vrouwen, die niet langer zwangerschap zouden vrezen (Glick, 1967).

Hoewel er omvangrijke literatuur bestaat over de mogelijke nevenwerkingen van orale contraceptie (OC), is het verbazend hoe weinig we begrijpen van de seksuele effecten op vrouwen. In de late jaren 80 kreeg het veld een boost door steun uit de hoek van de Wereldgezondheidsorganisatie (WHO), die eerst een literatuurstudie over de effecten van OC op welzijn en seksualiteit beval (Bancroft & Sartorius, 1990), gevolgd door een reeks studies (o.a., Bancroft, Sherwin, Alexander, Davidson, & Walker, 1991a, , Graham & Sherwin, 1993; Graham, Ramos, Bancroft, Maglaya, & Farley, 1995; Sanders, Graham, Bass, & Bancroft, 2001). Deze studies wezen naar drie belangrijke resultaten over het seksuele leven van OC gebruiksters: (1) seksuele en emotionele neveneffecten zijn de belangrijkste redenen om te stoppen met gebruik, (2) een negatief effect op seksualiteit bestaat in een minderheid van de gebruiksters, en (3) een verschillend cyclisch patroon van seksueel verlangen bestaat tussen gebruikers van OC en niet-hormonale contraceptie.

Seksuele en emotionele effecten zijn de belangrijkste redenen om te stoppen met gebruik. Verschillende studies tonen aan dat stoppen van OC gebruik frequent is (tot 47%, Sanders, Graham, Bass, & Bancroft, 2001). Hoewel deze studie toont dat 8% van de vrouwen seksuele nevenwerkingen rapporteert als reden, toonde een logistische regressie dat de beste voorspeller van stoppen heel andere redenen kent, namelijk

verlaagde frequentie van seksuele gedachten, seksuele opwindbaarheid en emotionele nevenwerkingen.

Negatieve effecten op vrouwelijke seksualiteit bestaan. Sinds de jaren 80 zijn slechts twee placebo-gecontrolleerde studies uitgevoerd. Graham en Sherwin (1993) stellen dat een significante daling in seksueel verlangen optreedt bij OC gebruik. Een latere publicatie onderzocht 150 vrouwen (uit twee centra: Edinburgh en Manilla) wiens partner of zijzelf gesteriliseerd waren. Zij bevestigden deze daling in meer dan de helft van de vrouwen na de start van OC (Graham, Ramos, Bancroft, Maglaya, & Farley, 1995).

Recentere studies onderzochten andere vormen van hormonale contraceptie (HC), zoals de Nuvaring® en preparaten met het nieuwe progestageen drospirenone. Studies naar de Nuvaring® melden een toename in seksueel verlangen (Guida et al., 2005; Sabatini & Ciagano, 2006). Resultaten over preparaten met drospirenone (b.v. Yasmine®) zijn tegenstrijdig (Caruso et al., 2005; Oranratanaphan & Taneepanichskul, 2006).

Een verschillend patroon van seksueel verlangen binnen de cyclus. Onderzoek in vrij ovulerende vrouwen is niet steeds consistent, maar wijst naar een midcyclische piek in seksueel verlangen (Bullivant et al., 2004; Roney & Simmons, 2013). Slechts twee studies keken naar potentiële cyclische patronen van seksueel verlangen in OC gebruiksters (Walker & Bancroft, 1990; Warner & Bancroft, 1988): seksueel verlangen zou afgevlakt worden in een contraceptieve cyclus en minder pieken en dalen kennen dan een menstruele cyclus.

BIOPSYCHOSOCIALE FACTOREN IN DE RELATIE TUSSEN HC EN SEKSUEEL VERLANGEN

Biologische correlaten

Geslachtshormonen en vrouwelijke seksualiteit. Geslachtshormonen beïnvloeden de “centrale opwindbaarheid” van het seksuele systeem (Pfaff, 1980, 1990). Hoewel studies in menopauzale vrouwen aantonen dat oestrogenen van belang zijn voor normale vaginale lubricatie (Nathorst-Böös, Wilkund, Mattson, Sandin, & von Schoultz, 1993; Sherwin, 1991), is de rol in het vrouwelijk seksueel verlangen minder duidelijk (Avis, Stellato, Crawford, Johannes, & Longcope, 2000). Studies naar de toediening van

androgenen in menopauzale vrouwen toonden wel een relatie met testosteron (T) (Sherwin & Gelfand, 1985a, 1985b). Deze studies leidden tot de idee dat T de "cognitief-motivationele" aspecten van vrouwelijke seksualiteit zou beïnvloeden. Populatiestudies kunnen daarentegen geen verband aantonen tussen seksueel verlangen en T waarden bij vrouwen (Davis, Davison, Donath, & Bell, 2005; Guthrie, Dennerstein, Taffe, Lehert, & Burger, 2004).

Daling in vrij testosteron door HC. Bij het gebruik van HC daalt de hoeveelheid vrij, of biologisch beschikbaar T in het bloed (b.v., Thorneycroft et al., 1999). Het mechanisme achter deze HC-geïnduceerde daling van vrij T en de relatie met seksueel verlangen heeft complexe studieresultaten opgeleverd. Tot nu toe hebben drie studies een verband tussen T en vrouwelijk seksueel verlangen in OC gebruiksters gepubliceerd (Alexander & Sherwin, 1993; Bancroft, Davidson, Warner &Tyrer, 1980; Bancroft, Sherwin, Alexander, Davidson, & Walker, 1991b).

Het meten van androgeengevoeligheid: de CAG repeat length. Het is mogelijk dat voorafbestaande hormonale verschillen tussen vrouwen (b.v. zoals gesuggereerd door de desensitisatiehypothese: zie Bancroft, 2002, 2005) hun verschillende reactie op HC gebruik kunnen verklaren. Naast het bekijken van hormoonwaarden kan het dus tevens van belang zijn om androgeengevoeligheid te bekijken in de context van HC effecten op vrouwelijk seksueel verlangen. Androgeengevoeligheid wordt gemedieerd door de variatie in het androgeen receptor (*AR*) gen op het X-chromosoom. Deze cytosine-adenine-guanine (CAG) trinucleotide sequens reguleert de activatie van geslachtshormoon-gevoelige cellen door androgenen (Brown, et al., 1989; Lundin, Giwercman, Richthoff, Abrahamsson, & Giwercman, 2003). Het inhiberende effect van de CAG repeat op T waarden (meer CAG repeats geassocieerd met zwakkere *AR* activiteit en dus hogere T waarden) bij mannen, is niet bevestigd bij vrouwen. Daar zou een een stimulerend effect bestaan waarbij meer CAG repeats geassocieerd zijn met hogere *AR* activiteit en lagere T waarden (Westberg et al., 2001).

Psychosociale correlaten

Effect van HC op stemming of seksueel verlangen? Of beiden? Een terugkerend thema in de vroege literatuur is de idee dat negatieve seksuele effecten in gebruiksters secundair zijn aan negatieve effecten op stemming (Cullberg, 1972). Onderzoek wijst

echter op een niet-lineair verband tussen beide concepten (b.v., Lykins, Janssen, & Graham, 2006). Twee studies tonen inderdaad dat een verminderd seksueel verlangen in OC gebruiksters plaats kan vinden zonder een negatievere stemming (Graham & Sherwin, 1993; Graham, Ramos, Bancroft, Maglaya, & Farley, 1995).

De "relationele" aard van vrouwelijk seksueel verlangen. De link tussen relationeel welzijn en seksueel functioneren is herhaaldelijk bevestigd in onderzoek (b.v., Brezsnyak & Whisman, 2004). Inherent is de idee dat het seksuele verlangen van vrouwen vooral relationeel gedreven en afhankelijk zou zijn (Meana, 2010). Hoewel studies aantonen dat de seksuele fantasieën van vrouwen vaker romantisch zouden zijn (b.v., Zurbriggen & Yost, 2004), toont onderzoek van Meston en collega's (2007) dat mannen en vrouwen niet verschillen in hun redenen om seks te hebben: op het item "verlangen naar ervaren van emotionele intimiteit" konden zij bovendien geen genderverschillen in frequentie terugvinden.

Relationele tevredenheid. Sinds de vroege studies naar seksueel verlangen wordt verondersteld dat relationele ontevredenheid weerspiegeld wordt in het seksueel verlangen van partners (Verhulst & Heiman, 1988). De vicieuze cirkel van meer relationele ontevredenheid, die seksuele intimiteit en seksueel verlangen doet afnemen, leidt koppels vaak tot een progressief disfunctioneel patroon (LoPiccolo & Friedman, 1988). Onderzoek naar HC heeft echter nog nooit een koppelperspectief gehanteerd.

Seksueel functioneren. Uiteraard bepaalt het algemene seksuele functioneren mee het seksueel verlangen. Eén studie onderzocht het belang van seksuele problemen in het verband tussen OC gebruik en seksueel verlangen: enkel in de groep vrouwen zonder seksuele klachten kon een verband tussen T en seksueel verlangen worden geobserveerd (Bancroft, Davidson, Warner, & Tyrer, 1980).

Partner-factoren. Naast relationele en seksuele dynamiek, is tevens het belang van partner-factoren onderzocht. Een Finse populatiestudie (Witting et al., 2008) toont dat o.a. het hebben van een partner met een sterk seksueel verlangen en adequate seksuele vaardigheden bijdragen aan het vrouwelijk seksueel verlangen.

HOE BEINVLOEDT GENDER-CONFIRMERENDE BEHANDELING HET SEKSUELE VERLANGEN?

Gender disforie en de gender-confirmerende behandeling

DSM-5 (APA, 2013) definieert "gender disforie" vandaag als de lijdensdruk die ontstaat vanuit de discordantie tussen het biologische geslacht en de genderidentiteit (of het subjectieve gevoel man of vrouw te zijn). De gender-confirmerende behandeling (GCB), zoals ze momenteel wordt toegepast (voor een overzicht, zie T'Sjoen, van Trotsenburg, & Gijs, 2013), bestaat uit drie verschillende fasen: (1) diagnostische fase, (2) hormonale substitutie, en (3) chirurgische interventie. Hierbij moet worden opgemerkt dat niet alle trans vrouwen (transitie van man naar vrouw) en trans mannen (transitie van vrouw naar man) gebruik maken van alle beschikbare chirurgische mogelijkheden.

Overzicht van eerder onderzoek naar GCB, seksueel verlangen en correlaten

Eerder onderzoek heeft zich totnogtoe vooral gefocust op een beter begrip en kennis omtrent chirurgie (b.v., Monstrey et al., 2009; Lawrence, 2006), de aanwezigheid van spijt na de GCB (b.v., Olsson, & Möller, 2006), en het afnemen van de lijdensdruk of disforie (b.v., Smith, van Goozen, Kuiper, & Cohen-Kettenis, 2005). Hoewel hormonale substitutie en genitale chirurgie verondersteld kunnen worden potentieel grote seksuele effecten te hebben, is het verbazend hoe weinig aandacht zowel kliniek als onderzoek hebben besteed aan de seksualiteitsbeleving in deze populatie. Vooral studies naar seksueel verlangen zijn zeldzaam: gefragmenteerde resultaten zijn beschikbaar over toename of afname van seksueel verlangen, maar niet over correlaten. Deze situatie is waarschijnlijk het gevolg van de vroegere assumptie dat gender disforie een "hyposeksuele" toestand was (Person, & Ovesey, 1974a, 1974b; Pomeroy, 1969) en de angst van gender disfore individuen om gezien te worden als louter gedreven tot transitie door seksuele redenen. Vandaag wordt het seksueel functioneren als een belangrijke uitkomst van de GCB gezien (Klein & Gorzalka, 2009).

GCB en seksueel verlangen in trans vrouwen. Een vroege gecontrolleerde en prospectieve studie vergeleek twee groepen van trans vrouwen na twee jaar follow-up: één groep na routine procedure (en dus nog steeds op de wachtlijst voor een vaginoplastie, groep R), en een andere groep die op moment van follow-up een jaar en negen maanden geleden chirurgie had ondergaan (group A) (Mate-Kole, Freschi, & Robine, 1990). Het hoogste seksueel verlangen werd gerapporteerd in group A. Een andere studie stelt dat trans vrouwen een lager seksueel verlangen melden dan een groep cisgender (of niet trans) vrouwen zonder seksuele klachten (Weyers et al., 2009). Een recente Nederlandse studie meldt dat een kwart van de trans vrouwen een verlaagd of afwezig seksueel verlanen kent (de Graaf, Bakker, & Wijsen, 2014).

GCB en seksueel verlangen in trans mannen. Slechts twee studies keken naar de ervaring van seksueel verlangen bij trans mannen. Een Italiaanse studie stelde dat seksueel verlangen, masturbatie en seksuele fantasieën toenamen na twaalf maanden hormonale behandeling en zes maanden na chirurgie (geen falloplastie) (Costantino et al., 2013). Volgens dezelfde recente Nederlandse studie zou 12% van de trans mannen een zwak of afwezig seksueel verlangen melden (de Graaf, Bakker, & Wijsen, 2014).

Conclusie. Gezien de informatie over de relatie tussen GCB en seksueel verlangen zowel in trans vrouwen als trans mannen zo beperkt is, zal het geen verbazing wekken dat informatie over welke correlaten dit verband beïnvloeden, helemaal ontbreekt.

DOELSTELLINGEN VAN HET DOCTORAATSONDERZOEK

De eerste doelstelling van het huidige doctoraatsonderzoek was om het seksueel verlangen van contraceptie-gebruiksters nader te gaan bekijken. Terwijl eerder onderzoek zich heeft gericht op potentiële seksuele nevenwerkingen met cross-sectionele designs in gebruiksters van verschillende contraceptieve preparaten, gebruikten wij de vrouw als haar eigen controle in een prospectief, within-subject opzet. Specifieker wensten we potentiële veranderingen in seksueel verlangen te gaan observeren tijdens het veranderen tussen drie verschillende contraceptieve preparaten. In deze studie werden tevens verschillende biopsychosociale factoren gemeten om hun relatie met vrouwelijk seksueel verlangen na te gaan (Hoofdstuk 3). Verder hebben we getracht om potentiële cyclus-gerelateerde variaties in het seksueel verlangen vast te

stellen in een gecontroleerde dagboekstudie bij gebruiksters van hormonale en niet-hormonale contraceptie. Hierin onderzochten we tevens de rol van stemming, weekend voorkeur en dervingsbloeding tijdens de contraceptieve en menstruele cyclus (Hoofdstuk 4). In vergelijking met de literatuur in vrouwen met een vrije cyclus, is de kennis omtrent cyclus-gerelateerde patronen van seksueel verlangen en zijn correlaten quasi onbestaand.

De tweede doelstelling betrof het vergaren van meer kennis over het seksueel verlangen van voorheen gender disfore individuen die een GCB hebben ondergaan. In de kliniek brengen trans vrouwen klachten van een verlaagd seksueel verlangen. Met het doel deze klachten te objectiveren, keek een eerste cross-sectionele studie naar de prevalentie van persoonlijke en relationele last door verminderd seksueel verlangen bij trans vrouwen na een GCB (Hoofdstuk 5). In deze gecontrolleerde studie startten we verder met een eerste verkenning van het verband met deze klachten van verminderd verlangen in trans vrouwen met hormoonniveaus and androgeengevoeligheid (Hoofdstukken 5 en 6). In de twee laatste studies werd een grote cohorte van zowel trans vrouwen als trans mannen retrospectief bevraagd omtrent de perceptie van GCB-gerelateerde veranderingen in seksueel verlangen. Ook werd in deze groep het verband met verschillende biopsychosociale correlaten (zoals hormoonniveaus, behandelstatus, relatieduur en seksuele oriëntatie) onderzocht (Hoofdstuk 7).

EEN BEKNOPT OVERZICHT VAN DE BELANGRIJKSTE BEVINDINGEN

Seksueel verlangen bij contraceptie-gebruikende paren

Veranderingen in seksueel verlangen. Hoofdstukken 2 en 3 hebben getoond dat vrouwelijk seksueel verlangen kan veranderen door het wisselen tussen verschillende contraceptieve preparaten, én dat seksueel verlangen zeer stabiel is doorheen de contraceptieve cyclus. Hoofdstuk 3 betreft de eerste studie met een within-subject, cross-over opzet, waardoor vergelijkingen met eerder, vaak cross-sectioneel, onderzoek moeilijk is. De hypothese van een verlaagd seksueel verlangen tijdens OC gebruik is bevestigd, en ligt in de lijn van eerdere publicaties waarin OC starters een dalend seksueel verlangen rapporteren (Graham, et al., 1995; Graham, & Sherwin, 1993). De

bevinding van een stabiel (vrouwelijk en mannelijk) seksueel verlangen binnen de contraceptieve cyclus (Hoofdstuk 4) bevestigt eerdere retrospectieve resultaten dat seksueel verlangen als het ware afgevlakt wordt bij OC gebruik (Warner & Bancroft, 1988; Walker & Bancroft, 1990).

Biologische correlaten. Het seksuele systeem wordt gekenmerkt door een bepaalde gevoeligheid of "centrale opwindbaarheid", beïnvloed door o.a. neurotransmitters, geslachtshormonen en androgeengevoeligheid (Both, Everaerd, & Laan, 2007). Hoofdstuk 3 toonde dat –in de aanwezigheid van een HC-geïnduceerd lager vrij T- vrouwelijk seksueel verlangen beïnvloed wordt door zowel androgeengevoeligheid (zoals gemeten met CAG repeats) en het gebruikte contraceptieve preparaat, en dit op onafhankelijke wijze. Vrouwen met korte en lange CAG repeats (minder actieve en zeer actieve androgeen receptor: SS- en LL-groep) ervoeren een sterker solitair en dyadisch seksueel verlangen, wat niet consistent is met onze hypothese dat vooral de eerste groep een verlaagd seksueel verlangen zou melden. Mogelijk is het seksueel verlangen van deze beide groepen minder bepaald door contraceptiegebruik door een compensatiemechanisme in de androgeenreceptor: tijdens het gebruik van alle preparaten werd een minder gevoelige receptor gecompenseerd met een een hogere T waarde.

Een directe relatie tussen vrij T waarden en vrouwelijk seksueel verlangen werd niet bevestigd (Hoofdstuk 3). Dit strookt met de beperke evidentie voor deze relatie in HC-gebruiksters (b.v., Graham, Bancroft, Doll, Greco, & Tanner, 2007). Het is mogelijk dat de lage waarden het vinden van een verband bemoeilijkt, of dat de farmacologische interventie de voorwaarden van het seksueel systeem verandert.

Ook het preparaat zelf kende een effect op het vrouwelijk seksueel verlangen (Hoofdstuk 3): het gebruik van de Nuvaring® lijkt het solitair en dyadisch seksueel verlangen van vrouwen te bevorderen, in vergelijking met een klassiek OC-preparaat en een POP. Dit strookt met eerdere bevindingen uit een Italiaanse studie (Sabatini & Cagiano, 2006). Gezien er geen interactie geobserveerd werd tussen androgeengevoeligheid en contraceptief product, hangt dit effect niet af van de androgeengevoeligheid van de vrouw.

Pscyhosociale correlaten. Hoofdstukken 3 en 4 namen tevens de factor *stemming* mee in de modellen voor vrouwelijk seksueel verlangen. Hoofdstuk 3 ondersteunt de hypothese dat HC gebruiksters met minder depressieve klachten een sterker dyadisch

verlangen ervaren. Er bestond geen verband met solitair seksueel verlangen. Hoofdstuk 4 bekeek affect binnen cyclus-gerelateerde patronen en toonde dat een sterker positief affect samengaat met een sterker vrouwelijk (solitair en dyadisch) seksueel verlangen binnen één cyclus. Geen associatie met negatief affect werd gevonden. De hypothese van een verschillend effect van positief en negatief affect is dus bevestigd: negatief affect stijgt tijdens de laatste dagen van de pilcyclus in de aanwezigheid van een stabiel seksueel verlangen (Hoofdstuk 4). Dit bevestigt bevindingen uit eerdere studies (Graham & Sherwin, 1993; Graham et al., 1995).

Hoofdstuk 3 kon geen verband terugvinden tussen seksueel verlangen, zelf-waarde, en relationele en seksuele tevredenheid. De afwezigheid van een verband tussen seksueel verlangen en relatieduur spreekt de bevindingen van een eerdere, cross-sectionele studie tegen (Klusmann, 2002).

Twee belangrijke bevindingen uit Hoofdstuk 3 zijn: (1) het verband tussen vrouwelijk seksueel verlangen en het niveau bij de start van de studie, en (2) het verband met het niveau van *seksueel verlangen bij de partner*. Deze twee psychologische factoren bleken belangrijkst in het model voor dyadisch seksueel verlangen. We besluiten dan ook dat vrouwelijk seksueel verlangen, naast de farmacologische en genetische invloed, tevens een stabiel, intra-individueel en sterk relationeel proces betreft (weliswaar binnen deze beperkte studieduur). In de context van een “incentive motivatie” model betekent dit dat genetische en farmacologische invloeden de “centrale opwindbaarheid” van het seksuele systeem beïnvloeden, terwijl de psychologische factoren het belang benadrukken van individuele en contextuele stimuli, én van de leergeschiedenis in beiden, in het ontstaan van seksueel verlangen.

Hoofdstuk 4 rapporteerde bovendien over de verbanden met de *dervingsbloeding* en de *weekend voorkeur*. Terwijl beide factoren geen verband vertoonden met het seksueel verlangen van COC-gebruiksters, waren beide factoren wel van belang voor het vrouwelijk seksueel verlangen van de gebruiksters van niet-hormonale contraceptie. Vrouwen in deze groep ervaarden een lager solitair verlangen tijdens de dervingsbloeding, en een sterker dyadisch verlangen tijdens het weekend.

Tot slot werd tevens de *frequentie van seksuele activiteit* gemeten (Hoofdstuk 4). Deelnemers waren vaker seksueel actief tijdens het weekend, maar dit resultaat was enkel aanwezig in de gebruikers van niet-hormonale contraceptie en niet in COC gebruiksters. Noch weekend voorkeur noch de dervingsbloeding vertoonde een verband

met seksuele frequentie in de COC gebruiksters. Een daling in de seksuele frequentie was echter wel te observeren omtrent de start van een nieuwe pilcyclus, een moment dat vermoedelijk toch samenvalt met de dervingsbloeding. Gebaseerd op studies bij gebruiksters van niet-hormonale contraceptie, waar een universele daling in seksuele frequentie tijdens de menstruatie wordt gezien (Brewis & Meyer, 2005), kan men veronderstellen dat de dervingsbloeding ook in COC gebruiksters mogelijks een effect zou kunnen heben.

Veranderingen in seksueel verlangen door GCT

Veranderingen in seksueel verlangen bij trans vrouwen en trans mannen. Vooreerst hebben we het seksuele verlangen van beide genders voor het eerst gekwantificeerd met een gevalideerde vragenlijst (Hoofdstukken 5 - 7), waarna de GCB-gerelateerde veranderingen in dat verlangen werden bevraagd (Hoofdstuk 7). Zeven op tien trans vrouwen stelden een lager seksueel verlangen te ervaren sinds de GCB, en evenveel trans mannen ervoeren een toename. Hoewel vele factoren die het seksueel verlangen kunnen beïnvloeden niet werden gemeten in de huidige studies (b.v., afgenomen gender disforie, hogere tevredenheid over seksuele relaties sinds GCB), kunnen zij de resultaten –zeker in de trans vrouwen- niet volledig verklaren. Deze percepties van een tegengesteld effect van GCB op seksueel verlangen in beide groepen lijkt verband te houden met de ondergane behandeling. Deze resultaten bevestigen de bevindingen van Costantino en collega's (2013), die een toegenomen seksueel verlangen vonden in een kleinere groep trans mannen. Verder moeten we opmerken dat 17% van zowel trans vrouwen als mannen géén gewijzigd seksueel verlangen ervoeren sinds de GCB. Ongetwijfeld zullen biologische, psychologische, relationele en socio-culturele factoren dit effect van de GCB modereren.

Verder bevroegen we de prevalentie van HSDD in zowel trans vrouwen als trans mannen, gedefinieerd als het ervaren van persoonlijke en relationele hinder door een verlaagd seksueel verlangen. Onder deze strenge definitie werden 5% van de trans mannen en 22% van de trans vrouwen hiermee gediagnosticeerd. Vergeleken met populatiestudies die lijdensdruk bevragen in de prevalentie van seksuele klachten, zien we dat vooral de trans vrouwen een hogere HSDD-prevalentie vertonen: studies in mannen wijzen naar cijfers tussen 0.5% en 6% (Hendrickx, & Enzlin, 2013; Kedde, 2012),

tegenover 3 tot 14% onder vrouwen (Christensen et al., 2011; Hendrickx, & Enzlin, 2013; Kedde, 2012; Shifren, Monz, Russo, Sergreti, & Johannes, 2008). We moeten opmerken dat hoewel zeven op tien trans vrouwen nooit of zelden spontaan of responsief seksueel verlangen ervaren, slechts een derde lijdensdruk hiervan ondervindt. Twee op drie trans vrouwen ervaart dit verlaagd seksueel verlangen dus *niet* als hinderlijk.

Biologische correlaten. Zowel hormonale als genetische correlaten werden nagegaan, althans bij trans vrouwen (Hoofdstukken 5 – 7). Er bestond geen verband tussen totaal of vrij T en het seksuele verlangen bij trans vrouwen of trans mannen (Hoofdstuk 5 & 7). Ook de enige andere beschikbare studie hieromtrent (Costantino et al., 2013) kon geen associatie vinden met een range van hormonale parameters. Er bleek echter wel een verband tussen solitair seksueel verlangen en LH waarden van trans mannen: inadequate T therapie, geflecteerd in hoge LH waarden, was geassocieerd met lager solitair seksueel verlangen (Hoofdstuk 7).

Ook de genetische factor van androgeengevoeligheid bleek geen goede moderator in de relatie tussen totaal en vrij T en seksueel verlangen in trans vrouwen (Hoofdstuk 6).

Psychosociale correlaten. Het blijkt dat lesbische trans vrouwen een lager seksueel verlangen rapporteren dan hetero trans vrouwen (Hoofdstuk 7). Deze bevindingen bevestigen andere resultaten uit onze groep (Weyers et al., 2009). Gelijklopend met studies onder de algemene bevolking (Rosen et al., 2009) blijken trans vrouwen in een partnerrelatie een sterkere hinder te ondervinden van een verlaagd seksueel verlangen, resulterend in een hogere HSDD-prevalentie (Hoofdstuk 7). Wat betreft het verband tussen seksueel verlangen en GCB, blijkt dat trans vrouwen die reeds een vaginoplastie ondergingen, een sterker seksueel verlangen kenden dan zij die nog gepland stonden voor deze ingreep (Hoofdstuk 7). Het is waarschijnlijk dat het verlichten van de gender disforie, en het beschikken over een lichaam meer congruent met de genderidentiteit, positieve effecten sorteert op het seksueel functioneren. Geen verband tussen chirurgie en scores van seksueel verlangen werden gevonden voor de trans mannen, maar de tevredenheid over de falloplastie hing samen met de prevalentie van HSDD.

Deze verschillende verbanden bij trans vrouwen en trans mannen zijn moeilijk te verklaren. Eén mogelijkheid is dat trans mannen een sterker belang hechten aan de functionaliteit van hun nieuwe genitaliën in vergelijking met trans vrouwen. Vele

onderliggende factoren, zoals verschillen in functionele en esthetische chirurgische tevredenheid, lichaamsbeeld, zelfwaarde etc., kunnen hiertoe bijdragen.

IMPLICATIES VAN DE ONDERZOEKSRESULTATEN

Methodologische implicaties van de studies bij contraceptie-gebruiksters

Studie-opzet. Beide steekproeven van contraceptie-gebruiksters (Hoofdstukken 3 en 4) vertrokken vanuit een koppelperspectief, wat uniek is in dit onderzoeksdomein. Verder includeerden we de factor van het verlangen bij de partner (Hoofdstuk 3), alsook onderzochten we het seksueel verlangen in beide partners van het paar (Hoofdstuk 4). Hoofdstuk 3 is de eerste studie met een cross-over, within-subject opzet, wat ons toestond om de seksuele respons te vergelijken tussen opeenvolgende contraceptieve preparaten. Eerdere studies hebben vooral parallelle groepen van OC starters vergeleken, waardoor zij mogelijks een vertekening kennen in de psychosociale factoren die samengaan met het starten van OCs. Ook het opzet van de dagboekstudie naar cyclische patronen (Hoofdstuk 4) was uniek: eerdere studies keken naar seksueel verlangen bij OC gebruiksters vanuit een retrospectief opzet (Warner & Bancroft, 1988) of in een zeer beperkte heterogene steekproef (Bancroft, Davidson, Warner, & Tyrer, 1980).

De studies vertonen echter tevens een aantal beperkingen. Zo kende de cross-over studie een relatief beperkte steekproefgrootte, wat deels werd gecompenseerd door het within-subject opzet. Verder was er geen wash-out periode met enkel condoomgebruik ingebouwd tussen het opeenvolgend gebruik van de verschillende preparaten. Verder was de gehele steekproef uit Hoofdstuk 3, alsook de COC groep uit Hoofdstuk 4, een jonge groep van hoofdzakelijk studenten. De generalisatie van onze resultaten naar alle leeftijden is dan ook mogelijks beperkt. Gezien de hoge percentages van het stoppen of veranderen van HCs, moeten we er tot slot ook rekening mee houden dat ontevreden HC gebruiksters mogelijk niet opgenomen waren in Hoofdstukken 3 en 4. Wanneer gevraagd naar motivatie om aan de cross-over studie deel te nemen, stelden vrouwen vooral dat ze graag kennis wensten te maken met andere preparaten.

Biopsychosociale benadering. Een opmerkelijke sterkte van de huidige dissertatie betreft het gebruik van een range aan biopsychosociale correlerende factoren in het bestuderen van het concept seksueel verlangen. Deze benadering biedt een unieke mogelijkheid om het relatieve belang van de verschillende correlaten en hun interrelaties te bestuderen. De resultaten uit de cross-over studie (Hoofdstuk 3) toonden althans dat, in het domein van contraceptie en seksualiteit, het antwoord nooit louter genetica, hormonen, stemming, relationele context of persoonlijkheid betreft, maar dat het meten en toetsen van de interacties net een waardevolle benadering is.

Klinische implicaties van de studies bij contraceptie-gebruiksters

Zoals aangetoond door het huidige onderzoeksproject, kan het veranderen van hormonale contraceptie het seksuele verlangen bij vrouwen inderdaad beïnvloeden, hoewel dit uiteraard gerelateerd blijft aan verschillende biopsychosociale factoren. Hoewel studies in dit veld de impact van contraceptie op vrouwelijke seksualiteit lang hebben genegeerd, lijkt het erop dat personeel in de gezondheidszorg (vooral huisartsen, medische specialismen en seksuologen) beter geïnformeerd dienen te worden over de rol van contraceptie op vrouwelijke seksualiteit. Wanneer contraceptiecounseling wordt aangeboden, dienen huisartsen en medische specialismen ermee rekening te houden dat het vinden van een geschikt preparaat waarover het paar tevreden is, meer kan zijn dan een proces van trial-en-error. Dit doctoraatsonderzoek bevestigt dat bepaalde contraceptieve preparaten vaker geassocieerd zijn met een een hoger of lager seksueel verlangen, zelfs na correctie voor verschillende biopsychosociale factoren.

Methodologische implicaties van de studies bij trans personen na GCB

Steekproefgrootte. Eerdere studies bij trans personen hebben zelden grote steekproeven bevraagd. Voor de huidige studies naar seksueel verlangen en GCB was het mogelijk om data verzamelen bij substantiële aantallen. Zeker gezien de relatieve zeldzaamheid van gender disforie (De Cuypere et al., 2007), heeft de beschikbaarheid van een interdisciplinair genderteam binnen één universitair ziekenhuis, met een

gestandaardiseerd behandelprotocol, ons de mogelijkheid gegeven om data te verzamelen in een ongewoon grote steekproef.

Tevens zijn er echter een aantal beperkingen aan de gepresenteerde studies bij trans personen. Eerst en vooral is het duidelijk dat het retrospectieve, cross-sectioneel onderzoeksopzet enkel correlationele bevindingen biedt en geen uitspraken kan doen omtrent causaliteit over GCB en veranderingen in seksueel verlangen. De huidige resultaten verdienen absoluut een bevestiging binnen een prospectief opzet met herhaalde metingen doorheen de GCB om het risico van sociaal wenselijke antwoorden en geheugeneffecten uit te sluiten. Hoewel de meeste deelnemers behandeld werden binnen één interdisciplinair genderteam, kan dit de generalisatie van de resultaten naar de ruimere populatie van trans personen belemmeren.

Klinische implicaties van de studies bij trans personen na GCB

Indien de gepresenteerde resultaten omtrent het verband tussen de GCB en seksueel verlangen bevestigd worden in een prospectief onderzoeksopzet, kunnen deze bevindingen potentieel zeer relevant worden voor de gehele transgender populatie. Hoewel het onderwerp seksualiteit lang stiefmoederlijk is behandeld, lijkt het erop dat de meerderheid van de trans personen een impact ondervinden van de GCB op hun seksueel verlangen, en uiteraard mogelijks op hun ruimere seksuele leven. Behandelaars van gender disfore individuen die zich aanmelden voor GCB dienen dan ook op de hoogte te zijn van de potentiële impact van deze behandeling (positief én negatief) opdat ze deze informatie vooraf kunnen bespreken en realistische behandeldoelen kunnen schetsen.

Toekomstig onderzoek

Gevalideerde meting van seksueel verlangen. De gepresenteerde studies hebben gebruik gemaakt van gevalideerde schalen om de frequentie en de intensiteit van zowel solitair als dyadisch seksueel verlangen te meten. Hoewel financiële en pragmatische overwegingen onderzoekers kunnen doen overwegen om één enkel item rond seksueel verlangen op te nemen, maken de huidige studies duidelijk dat een grondige meting van

dit concept opname in complexe modellen met biopsychosociale factoren mogelijk maakt. Gezien de recente bevindingen van het samen optreden van seksueel verlangen en seksuele opwinding, zou toekomstig onderzoek in zowel contraceptie-gebruiksters als trans personen baat kunnen ondervinden van het objectiveren van de overlap in deze twee aspecten van seksueel functioneren.

Longitudinaal onderzoek naar biopsychosociale factoren. Een tweede suggestie naar toekomstig onderzoek toe betreft het verder zetten van prospectieve, biopsychosociale onderzoeksopzetten bij HC starters, die controleren voor alle relevante baseline factoren. Bij deze vrouwen bestaat nog geen beïnvloeding van de attitudes omtrent en ervaringen met eerdere contraceptie. Zowel eerder als het gepresenteerde onderzoek kon helaas onvoldoende fondsen werven om dergelijke tijdsintensieve, dure en complexe studies op te zetten die ons meer begrip zouden opleveren over de biopsychosociale processen bij HC starters. Dergelijke onderzoeksopzetten zouden ons, bij voorbeeld, kunnen leren of in vrouwen met een natuurlijke cyclus, vooral het preparaat of de genetische androgeengevoeligheid de bovenhand heeft. Indien meer resultaten beschikbaar worden omtrent deze maat voor androgeengevoeligheid, zou deze maat mogelijks klinische implicaties kunnen verwerven, b.v. het voorschrijven van een preparaat met minder grote impact op hormoonspiegels aan vrouwen met een zeer laag aantal CAG repeats (en mogelijks gevoelig aan HC geïnduceerde veranderende hormoonspiegels).

Ook in trans personen zou longitudinaal onderzoek een beter begrip opleveren van het veranderend seksueel verlangen. Het zou onderzoekers in staat stellen om het relatieve belang te onderscheiden van biologische (androgeengevoeligheid, baseline en huidige hormoonspiegels), psychologische (afname van gender disforie, verbeterde zelfwaarde, positiever lichaamsbeeld, levenskwaliteit) en socio-relationele (betere partnerrelaties, meer voldoening gevend seksueel leven, ervaring van minderheidsstress) factoren op dit aspect van seksueel functioneren.

ALGEMENE CONCLUSIE

Veranderingen in seksueel verlangen zijn een onvermijdelijk en normaal onderdeel van elke persoonlijke en relationele context, en kunnen beïnvloed worden door vele inter- en intra-persoonlijke factoren. In dit doctoraatsonderzoek hebben we een reeks studies gepresenteerd die deze veranderingen in seksueel verlangen, en hun biopsychosociale correlaten, documenteren in contraceptie-gebruikende paren en trans personen na een GCB. Zoals verwacht, kan het seksueel verlangen in contraceptie-gebruiksters beïnvloed worden door het wijzigen van contraceptief preparaat. Verder spelen biologische (androgeengevoeligheid en contraceptief product), psychologische (stemming) en socio-relationele factoren (verlangen van de partner) allen een significante rol in deze optredende veranderingen. Bekeken binnen de contraceptieve cyclus, blijkt seksueel verlangen echter minder verbonden met het tijdstip van de cyclus, en meer met het positief affect bij de vrouw. In de context van een gender-confirmerende behandeling bleek een verandering in seksueel verlangen opgemerkt door zeven in tien trans personen, terwijl een minderheid van vooral trans vrouwen lijdensdruk rapporteerden van een verlaagd seksueel verlangen. Gezien veranderingen in seksueel verlangen in deze beide studie populaties nu beter gedocumenteerd is, hopen wij dat deze bevindingen verder fundamenteel en klinisch onderzoek kunnen stimuleren in het huidige veld.

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