ORIGINAL RESEARCH—INTERSEX AND GENDER IDENTITY DISORDERS

Specific Cerebral Activation due to Visual Erotic Stimuli in Male-to-Female Transsexuals Compared with Male and Female Controls: An fMRI Study

Elke R. Gizewski, MD,* Eva Krause, MD,† Marc Schlamann, MD,* Friederike Happich, MD,† Mark E. Ladd, PhD,* Michael Forsting, PhD,* and Wolfgang Senf, PhD†

*Department of Diagnostic and Interventional Radiology and Neuroradiology, University Hospital Essen, Essen, Germany; †Department of Psychosomatic Medicine and Psychotherapy, University Hospital Essen, Essen, Germany

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ABSTRACT

Introduction. Transsexuals harbor the strong feeling of having been born to the wrong sex. There is a continuing controversial discussion of whether or not transsexualism has a biological representation. Differences between males and females in terms of functional imaging during erotic stimuli have been previously described, revealing gender-specific results.

Aim. Therefore, we postulated that male-to-female (MTF) transsexuals may show specific cerebral activation differing from their biological gender.

Main Outcome Measure. Cerebral activation patterns during viewing of erotic film excerpts in functional magnetic resonance imaging (fMRI).

Methods. Twelve male and 12 female heterosexual volunteers and 12 MTF transsexuals before any treatment viewed erotic film excerpts during fMRI. Additionally, subjective rating of sexual arousal was assessed. Statistics were performed using the Statistical Parametric Mapping software.

Results. Significantly enhanced activation for men compared with women was revealed in brain areas involved in erotic processing, i.e., the thalamus, the amygdala, and the orbitofrontal and insular cortex, whereas no specific activation for women was found. When comparing MTF transsexuals with male volunteers, activation patterns similar to female volunteers being compared with male volunteers were revealed. Sexual arousal was assessed using standard rating scales and did not differ significantly for the three groups.

Conclusions. We revealed a cerebral activation pattern in MTF transsexuals compared with male controls similar to female controls compared with male controls during viewing of erotic stimuli, indicating a tendency of female-like cerebral processing in transsexualism. **Gizewski ER, Krause E, Schlamann M, Happich F, Ladd ME, Forsting M, and Senf W. Specific cerebral activation due to visual erotic stimuli in male-to-female transsexuals compared with male and female controls: An fMRI study. J Sex Med 2009;6:440–448.**

Key Words. fMRI; Transsexual; Emotional

Introduction

Transsexuals experience themselves as being of the opposite sex, despite having the biological characteristics of one sex [1]. This circumstance is an immense and dominating problem in the life of transsexuals. The technical possibility of surgical sex change has opened up a debate concerning the legitimacy and utility of carrying out such an intervention. Diagnostic, psychological, medical, and ethical arguments have been brought forth, both for and against. Regardless, surgical anatomical transformation has become an increasingly common practice, as the frequency of serious

gender identity disorders has steadily risen [2]. The increasing incidence is probably due to a better acceptance of transsexuals in the population, but influences of hormonal and environmental substances have also been discussed in the literature [3].

The origins of transsexualism are still unclear [1]. Certain prenatal factors seem to be associated with transsexualism, but it is still unclear to what extent cross-gender identity is due to the pre- and perinatal organizing effects of sex hormones on the brain [3–5]. Empirical evidence for a relationship between prenatal hormonal influences and certain aspects of gender-typical cognitive functions, e.g., in visuospatial tasks, has been demonstrated in pre- and postpubertal clinical samples. The results of various cognitive and emotional tests showed that gender differences were pronounced, and that the two transsexual groups (male-to-female [MTF] and female-to-male) occupied a position in between the two heterosexual gender groups (male and female), thus revealing a pattern of cognitive performance for the transsexuals departing from their biological sex [6]. A previous study has also demonstrated that 3 months of cross-sex hormone treatment clearly influenced cognitive functioning in transsexuals [7].

Swaab et al. found that genetic factors and prenatal hormone levels contributed to the determination of sexual orientation, such as heterosexuality, bisexuality, or homosexuality; postnatal social factors, on the other hand, did not [5]. Animal studies have revealed that prenatal exposure to the anticonvulsant drugs phenobarbital and phenytoin alters steroid hormone levels, which consequently leads to disturbed sexual differentiation, and there are first experiences regarding hormone influences in human groups [8].

First anatomic brain differences between transsexuals and nontranssexuals were described by Kruijver and Zhou [9,10]. Therefore, it seems evident that gender-specific cortical activation patterns could be of great scientific and clinical interest and might reveal further differences or similarities in transsexuals compared with male or female volunteers, as well as being a possible ancillary tool for clinical investigation, especially preceding gender-change surgery.

Gender differences with respect to erotic stimuli have been the subject of investigation for many years. Besides social factors that influence gender-specific behavior, genetic, and hormonal influences have also been discussed [11,12]. Cortical activation patterns of sexual arousal were first investigated by Stoleru et al. using H_2O positron emission tomography (PET) [13]. They utilized erotic film excerpts in male subjects, which revealed activations of the right orbitofrontal cortex and anterior cingulate cortex, and hypothalamus for the autonomic portion, as well as Brodmann areas 9 and 32 for the emotional aspect of the task. Another PET study found that sexual arousal was mainly associated with activation of bilateral, predominantly right, inferoposterior extrastriate cortices of the right inferolateral prefrontal cortex, and of the tegmentum in heterosexual men [14]. Redoute et al. described activations in the anterior cingulate gyrus, orbitofrontal cortex, in the striatum, and in the posterior hypothalamus [15]. The number of imaging studies has increased in recent years, and these methods have become an important tool in sexual research [16]. Gender differences for the neural correlates of sexual arousal have also been discussed in a few functional magnetic resonance imaging (fMRI) studies examining brain response to sexual stimulation in heterosexual males and females. These studies identified activated brain regions and revealed gender differences in brain response to sexual stimulation and arousal: men compared with women revealed a higher level of brain activation and a superior activation in the amygdala and hypothalamus, whereas women did not reveal any specific activation [17,18].

However, transsexual orientation has not been the focus of neural functional imaging studies to date. In this study, we used fMRI to explicitly examine the influence of transsexual orientation on brain response to visual sexual stimuli in MTF transsexuals. We postulated that MTF transsexuals before hormonal therapy may show specific cerebral activation, differing from their biological gender.

Materials and Methods

Subjects

Twelve male (mean age 29 years, range 22–53) and 12 female (mean age 29 years, range 17–55) healthy heterosexual volunteers as well as 12 MTF transsexuals (mean age 36 years, range 20–55) were studied. The MTF were non-autogynephilic. All subjects were right-handed. The female volunteers were scanned outside the menstrual phase. No subject revealed any brain tissue abnormality on structural MRI, and no subject had a history of neurological or psychiatric disease.