



Cross-sex hormone treatment does not change sex-sensitive cognitive performance in gender identity disorder patients

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Abstract

Cognitive performance in untreated early onset gender identity disorder (GID) patients might correspond to their born sex and not to their perceived gender. As a current mode of intervention, cross-sex hormone treatment causes considerable physical changes in GID patients. We asked, as has been suggested, whether this treatment skews cognitive performance towards that of the acquired sex. Somatically healthy male and female early onset GID patients were neuropsychologically tested before, 3 and 12 months after initiating cross-sex hormone treatment, whereas untreated healthy subjects without GID served as controls (C). Performance was assessed by testing six cognitive abilities (perception, arithmetic, rotation, visualization, logic, and verbalization), and controlled for age, education, born sex, endocrine differences and treatment by means of repeated measures analysis of variance. GID patients and controls showed an identical time-dependent improvement in cognitive performance. The slopes were essentially parallel for males and females. There was no significant three-way interaction of born sex by group by time for the six investigated cognitive abilities. Only education and age significantly influenced this improvement. Despite the substantial somatic cross-sex changes in GID patients, no differential effect on cognition over time was found between C and GID participants. The cognitive performance of cross-sex hormone-treated GID patients was virtually identical to that of the control group. The documented test–retest effect should be taken into consideration when evaluating treatment effects generally in psychiatry. © 2005 Elsevier Ireland Ltd. All rights reserved.

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1. Introduction

Gender identity disorder (GID) in adults (DSM-IV 302.85; American Psychiatric Association, 1994) is characterized by a discrepancy between objective

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born sex and subjective gender identification, expressed as a feeling of being born in the wrong sex. Although both biological and psychological models have been proposed (Baker, 1969; Hoenig and Kenna, 1974; Person and Ovesey, 1974a,b; Stoller, 1979, 1985; Person and Ovesey, 1983; Blanchard, 1989; Johnson and Hunt, 1990; Brems, 1993; Blanchard et al., 1995; Zhou et al., 1995; Cohen and Ruiter, 1997), there is no established aetiology for the GID syndrome (Cohen-Kettenis and Gooren, 1999; Michel et al., 2001). Regardless of etiological controversy, evidence has been presented that the cognitive performance of GID patients' might be skewed towards that of their subjective gender (Cohen-Kettenis et al., 1998). Such skewing might originate from prenatal or postnatal hormonal influences. In favor of the former, a prenatal organizational effect of sex hormones on cognitive performance in early onset GID patients has been postulated from studies of prenatal endocrine disorders such as congenital adrenal hyperplasia (CAH). In some of these studies, adolescent female CAH patients display a cognitive performance skewed towards that of healthy males. So far, enhanced spatial ability (Resnick et al., 1986), a lower verbal and performance IQ and lower perceptual speed scores (Nass and Baker, 1991; Hampson et al., 1998), as well as enhanced right hemisphere development (Nass et al., 1987; Kelso et al., 1999), have been described. These cognitive differences of female CAH patients would be hypothetically based on their androgenized prenatal and perinatal hormone profile, while their postnatal profile is normalized by corticosteroid therapy. On the other hand, several other studies have failed to verify differences in cognitive brain function of women with CAH compared with their healthy siblings (McGuire and Omenn, 1975; McGuire et al., 1975; Helleday et al., 1994; Kelso et al., 2000).

As a current mode of intervention in adult GID patients, cross-sex hormone treatment causes considerable somatic changes. In the course of such treatment, several authors have suggested that the cognitive brain function of adult early onset GID patients might be activated towards that of the subjective gender, thus paralleling the endocrine and somatic changes observed during treatment (Miles et al., 1998; Slabbekoorn et al., 1999; Van Goozen et al., 1994). Hence, androgen-treated female GID patients

have been reported to improve in cognitive tasks generally favoring males ["mental rotation" (Van Goozen et al., 1994; Slabbekoorn et al., 1999)], but deteriorate in tasks favoring females ["verbal fluency" (Van Goozen et al., 1994)]. Conversely, male GID patients treated with estrogen reportedly showed a decrease in their performance on tasks favoring males ["mental rotation" (Slabbekoorn et al., 1999)], and an improvement in tasks favoring females ["verbal memory" (Miles et al., 1998)]. However, such an activating effect could not be replicated in a later study (Van Goozen et al., 2002).

The evidence for a hypothetically activating effect of cross-sex hormones in GID patients would appear to have support in cognitive studies of sex hormones substituted to elderly healthy males (Janowsky et al., 1994; Carlson et al., 1999; Maki et al., 2001), as well as postmenopausal women (Sherwin, 1988, 1997; Phillips and Sherwin, 1992; Yaffe et al., 2000) and female patients with dementia of the Alzheimer type (AD), in whom an improvement of cognitive performance has been reported (Henderson et al., 1996; Tang et al., 1996; Kawas et al., 1997). However, other studies of either healthy elderly females (Hackman and Galbraith, 1976; Ditkoff et al., 1991) or AD females have failed to observe such improvement (Henderson et al., 2000; Mulnard et al., 2000; Wang et al., 2000). Furthermore, some evidence for the activating hypothesis of cross-sex hormone is derived from studies of female cognitive function during different phases of their menstrual cycle (Hampson and Kimura, 1988; Saucier and Kimura, 1998), as well as from studies of testosterone fluctuations and their correlation to different cognitive functioning in men (Christiansen and Knusmann, 1987; Moffat and Hampson, 1996). However, other studies failed to support these observations (Gordon et al., 1986; McKeever et al., 1987).

The divergent results of the cognitive studies that address hormonal effects on brain function may be partly explained by the type of cognitive functions that were studied, the neuropsychological tests that were used, and the investigated confounders that were analyzed (e.g., education, health, mood) (Barrett-Connor and Kritz-Silverstein, 1993; McKeever, 1995; Teri et al., 1997; Wisniewski, 1998; Yaffe et al., 1998; Berenbaum, 2001; LeBlanc et al., 2001). For example, formal education and physical health status have been

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