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Pubertal testosterone predicts mental rotation performance of young adult males

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Summary Robust sex differences in some spatial abilities that favor males have raised the question of whether testosterone contributes to those differences. There is some evidence for prenatal organizational effects of testosterone on male-favoring spatial abilities, but not much is known about the role of pubertal testosterone levels on adult cognitive abilities. We studied the association between pubertal testosterone (at age 14) and cognitive performance in young adulthood (at age 21—23), assessing male-favoring, female-favoring, and sex-neutral cognitive domains in a population-based sample of 130 male and 178 female twins. Pubertal testosterone was negatively associated with performance in the Mental Rotation Test in young adult men ($r = -.27$), while among women no significant associations between testosterone and cognitive measures were detected. The significant association among men remained after controlling for pubertal development. Confirmatory within-family comparisons with one-sided significance testing yielded a negative correlation between twin pair differences in testosterone levels and Mental Rotation Test performances in 35 male twin pairs ($r = -.32$): the twin brother with higher testosterone performed less well on the Mental Rotation Test. That association was evident in 18 pairs of dizygotic male twin pairs ($r = -.42$; analysis controlling for shared environmental effects). In contrast, the association of differences was not evident among 17 monozygotic male twin pairs ($r = -.07$; analysis controlling for shared genetic influences). Results suggest that pubertal testosterone levels are related specifically to male-favoring spatial ability and only among men. Within-family analyses implicated possible shared genetic effects between pubertal testosterone and mental rotation ability.

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1. Introduction

On average, males outperform females in some domains of spatial abilities. One such domain is mental rotation ability; the widely used Vandenberg and Kuse Mental Rotation Test (Vandenberg and Kuse, 1978) yields a large and robust sex difference with male mean scores about one full standard deviation higher than those of females (Voyer et al., 1995). Studies have investigated the hormonal basis in male favoring spatial abilities and have suggested a role for testosterone in creating these sex differences. The actions of testosterone on brain are usually considered to be either organizational or activational in nature (see e.g. McCarthy and Arnold, 2011). Organizational effects refer to permanent brain programming effects of testosterone during developmental stages of brain sexual differentiation, usually occurring during perinatal development, while reversible activational effects refer to temporary changes in brain and behavior activated by circulating testosterone levels at any time of life.

There has been a long-standing question of whether testosterone has sex specific effects on male favoring spatial abilities. Some studies have indicated a positive correlation between testosterone and male favoring spatial abilities in females, but a negative correlation among males, which raise the question of whether optimal levels of testosterone are requisite for good spatial abilities (Shute et al., 1983; Gouchie and Kimura, 1991; Moffat and Hampson, 1996). Nevertheless, other studies have reported a positive correlation between male favoring mental rotation ability and testosterone levels among males, as well (e.g. Silverman et al., 1999; Hooven et al., 2004). Recently, Puts et al. (2010) reviewed most, but not all studies of testosterone — spatial ability relationships, including mostly studies on young adults. They evaluated the relationship between male favoring spatial abilities and testosterone levels measured at the time of administration of spatial tests and concluded that there is no consistent evidence that testosterone has activational effects on spatial abilities (Puts et al., 2010). Further support for this conclusion was also reported in the same study by Puts et al. (2010), in which no significant association between activational testosterone levels and mental rotation performance was observed in a large new sample of young adults comprised of 160 females and 177 males.

Among elderly, testosterone substitution can enhance the performance in the domain of spatial abilities (see e.g. Beauchet, 2006). For example, improving effects of testosterone supplementation on spatial memory have been reported both among healthy men (Cherrier et al., 2001) and men with mild cognitive impairment and Alzheimer's disease (Cherrier et al., 2005). However, contradictory results have emerged among non-clinical samples of adult men over 35 years of age: two large-scale studies have indicated both negative (Yonker et al., 2006; $n = 450$) and positive (Thilers et al., 2006; $n = 1107$) associations between testosterone and visuo-spatial abilities.

As testosterone levels are highly heritable throughout life (Eriksson et al., 2005; Ring et al., 2005; Hoekstra et al., 2006; Kuijper et al., 2007), it is difficult to discriminate whether the testosterone levels measured in one time point reflect temporary activational or permanent organizational effects of testosterone. Different measures of spatial abilities and different types of hormone samples (saliva vs. blood) may also explain inconsistent results across studies.

Puts et al. (2010) have suggested that if there are effects of testosterone on spatial abilities, the timing of these effects must stem from the organizational effects that occur during perinatal or pubertal development when testosterone levels are highest before adulthood. Concerning organizational effects of testosterone, there is some evidence that the prenatal levels of testosterone are related to spatial abilities. Meta-analysis of individuals with congenital adrenal hyperplasia (CAH), a clinical condition exposing the fetus to excessive amounts of testosterone, offer support for sex-specific effects of testosterone on spatial abilities (Puts et al., 2008). Females with CAH had better spatial abilities than non-CAH individuals, and males with CAH were inferior to non-CAH individuals in their spatial abilities. Also, a recent twin study reported significantly better mental rotation test performance in females with a male co-twin compared to females with a female co-twin (Vuoksimaa et al., 2010). Having a male co-twin may be a possible source of prenatal exposure to higher levels of testosterone in females, although this result might also reflect postnatal socialization effects. Another twin study replicated this masculinization of mental rotation ability among females with a male co-twin, but found no masculinization among non-twin females with a slightly older brother compared to non-twin females with slightly older sister (Heil et al., 2011). These results were interpreted as support for the prenatal effects of testosterone rather than postnatal socialization effects. Finally, the relationship between the ratio of second and fourth digits (2d:4d, a putative marker of prenatal testosterone levels) and spatial abilities have been examined, but no consistent association has emerged neither in females or males (see Puts et al., 2008 for a meta-analysis). However, a large scale internet study of $>$200,000 participants (also included in the meta-analysis of Puts et al., 2008) found that low 2d:4d ratio (as a proxy for higher prenatal testosterone levels) was associated with better mental rotation performance both in females and males (Peters et al., 2007). Studies on transsexuals have yielded support to both organizational (van Goozen et al., 2002) and activational (Slabbekoorn et al., 1999) effects of testosterone on spatial abilities.

Beyond prenatal developmental effects, testosterone may have long lasting effects on cognitive functioning during pubertal development, a time when there is a substantial peak in testosterone production, especially among boys (Hiort, 2002). Sex hormones may have organizational effects on the developing human brain during pubertal development (for reviews, see Sisk and Zehr, 2005; Hines, 2011; Peper et al., 2011), and animal studies have suggested that it might be the last developmental stage in which brain organization is sensitive to sex hormones (Schulz et al., 2009).

To our knowledge, no large population-based studies have investigated the effects of pubertal testosterone levels on cognitive abilities in young adulthood. However, some research on the effects of pubertal development on cognitive abilities in adolescence does exist. Some 30 years ago, a group of studies investigated whether the rate of maturation during puberty has effects on cognition. A rationale for these studies stemmed from the observed cognitive sex differences during and after puberty and from the fact that pubertal