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# Timing of peripubertal steroid exposure predicts visuospatial cognition in men: Evidence from three samples

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ABSTRACT

Experiments in male rodents demonstrate that sensitivity to the organizational effects of steroid hormones decreases across the pubertal window, with earlier androgen exposure leading to greater masculinization of the brain and behavior. Similarly, some research suggests the timing of peripubertal exposure to sex steroids influences aspects of human psychology, including visuospatial cognition. However, prior studies have been limited by small samples and/or imprecise measures of pubertal timing. We conducted 4 studies to clarify whether the timing of peripubertal hormone exposure predicts performance on male-typed tests of spatial cognition in adulthood. In Studies 1 ($n$ = 1095) and 2 ($n$ = 173), we investigated associations between recalled pubertal age and spatial cognition in typically developing men, controlling for current testosterone levels in Study 2. In Study 3 ($n$ = 51), we examined the relationship between spatial performance and the age at which peripubertal hormone replacement therapy was initiated in a sample of men with Isolated GnRH Deficiency. Across Studies 1–3, effect size estimates for the relationship between spatial performance and pubertal timing ranged from.

−0.04 and −0.27, and spatial performance was unrelated to salivary testosterone in Study 2. In Study 4, we conducted two meta-analyses of Studies 1–3 and four previously published studies. The first meta-analysis was conducted on correlations between spatial performance and measures of the absolute age of pubertal timing, and the second replaced those correlations with correlations between spatial performance and measures of relative pubertal timing where available. Point estimates for correlations between pubertal timing and spatial cognition were −0.15 and −0.12 (both $p < 0.001$) in the first and second meta-analyses, respectively. These associations were robust to the exclusion of any individual study. Our results suggest that, for some aspects of neural development, sensitivity to gonadal hormones declines across puberty, with earlier pubertal hormone exposure predicting greater sex-typicality in psychological phenotypes in adulthood. These results shed light on the processes of behavioral and brain organization and have implications for the treatment of IGD and other conditions wherein pubertal timing is pharmacologically manipulated.

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## 1. Introduction

During pre- and perinatal development, androgens can permanently organize cognition, behavior, and physiology across a wide range of species (reviewed in Wallen, 2009; McCarthy, 2010). Experimental work on this organizing role of early androgen exposure has been carried out in a wide variety of taxa, including squamates, birds, rodents and nonhuman primates (Adkins-Regan, 2012; Hews et al., 1994; Pazol et al., 2009; Thornton et al., 2009; Wallen, 2005). Examination of 'natural experiments' in humans, or cases such as medical conditions in which reproductive hormone action is altered by genetic factors, has similarly indicated that early androgen exposure modulates sex typicality in adulthood across a wide range of phenotypes (Hines, 2010).

Puberty has been hypothesized to represent a second period of brain organization and sexual differentiation, as it is characterized by dramatic changes in hormone production, psychology, and behavior. Following a neonatal period of 'mini-puberty' in which the hypothalamic-pituitary-gonadal axis operates at nearly adult levels in the first several months of life, childhood levels of gonadotropins and gonadal hormones (androgens and estrogens) are virtually undetectable in both sexes. During the peripubertal reawakening of the hypothalamic-pituitary-gonadal axis, levels of the gonadotropins follicle stimulating hormone (FSH) and luteinizing hormone (LH) increase in both sexes (Apter, 1980; Lee and Migeon, 1975; Lee et al., 1976). Androgen production (Lee and Migeon, 1975; Lee et al., 1976), and particularly testosterone production (Handelsman et al., 2016), increases in both sexes, with post-pubertal and adult androgen levels in men typically exceeding those of women by an order of magnitude (Handelsman et al., 2016). Experimental research on laboratory animals and observational data in humans suggest that these pubertal hormones exert marked organizational effects on the brain and behavior. For example, male hamsters gonadectomized prior to puberty differed from males gonadectomized after puberty in their sexual (Bloch and Mills, 1995; Schulz et al., 2004), agonistic (De Lorme and Sisk, 2013; Schulz et al., 2006; Shrenker et al., 1985), and anxiety-related (Brown et al., 2015; Primus and Kellogg, 1989) behaviors. Similarly, female rodents gonadectomized or otherwise deprived of estradiol prior to puberty were less female-typical in their sexual (Bakker et al., 2002), play (Smith et al., 1998), defensive (Field et al., 2004), and maternal (Kercmar et al., 2014) behaviors.

Many human sex differences in psychological phenotypes either emerge or become exaggerated during puberty, and persist across adulthood (Berenbaum and Beltz, 2011; but see Herlitz et al., 2013). For example, depression and anxiety disorders are twice as common in women as in men (reviewed in Altemus et al., 2014), while substance abuse and risk-taking behaviors are higher in men (Becker and Hu, 2008; Byrnes et al., 1999), and these sex differences emerge at puberty. Though males outperform females in some measures of spatial cognition beginning as early as infancy (Moore and Johnson, 2008), some spatial cognitive sex differences increase significantly from childhood to adolescence and puberty (Geiser et al., 2008; for review, see Lauer et al., 2019) and are large in magnitude by adulthood (Voyer et al., 1995). Such differences are most pronounced for tasks of mental rotation specifically (Linn and Petersen, 1985). Performance on male-typed spatial tasks (i.e., tasks wherein males exhibit a performance advantage) also appears to be largely independent of current androgen levels in adulthood (Herlitz et al., 2013; Puts et al., 2010; Schultheiss and Zimni, 2015). That this cognitive sex difference is exaggerated at puberty and is seemingly unrelated to adult circulating androgens suggests that the underlying neural architecture may be organized by peripubertal hormone action.

An important question is whether gonadal steroids exert similar organizational effects throughout the pubertal window (termed the Constant Sensitivity Hypothesis; CSH; Fig. 1, panel A), or whether sensitivity to gonadal hormones declines with age resulting in eventual insensitivity in adulthood (termed the Decreasing Sensitivity Hypothesis; DSH; Fig. 1, panel B). The DSH was developed from work in rodents (Schulz et al., 2009a; Schulz and Sisk, 2016; Schulz et al., 2009b; Sisk and Zehr, 2005) and predicts that earlier puberty should result in higher sex-typicality on measures of behavior and psychology that sexually differentiate at puberty. In male Syrian hamsters gonadectomized before puberty, sexual behavior (mounts and intromissions) differed as a function of whether testosterone was reinstated early, on-time, or late within the peripubertal window, with earlier treatment organizing more male-typical sexual behavior (Schulz et al., 2009b).

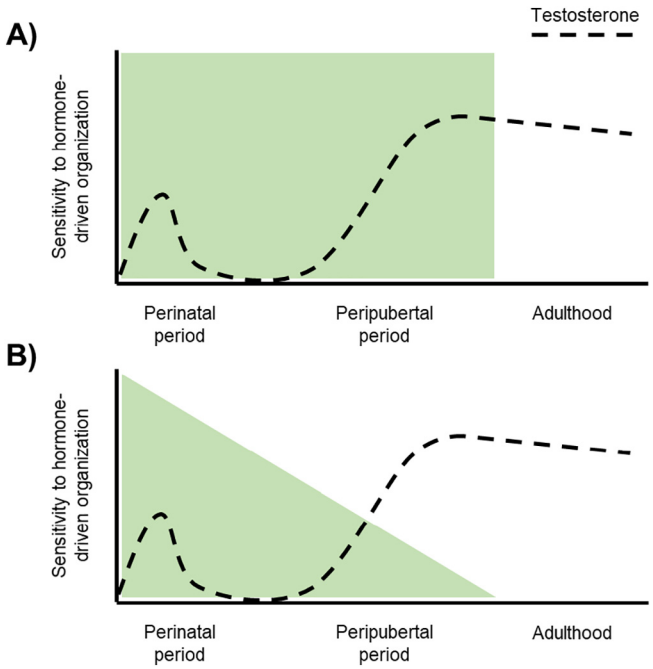


**Fig. 1.** Dotted lines reflect endogenous hormone production across development, while the shaded box represents sensitivity to hormone-driven organizational effects. It is possible that sensitivity to hormone-driven brain organization remains constant across perinatal and peripubertal development, the constant sensitivity hypothesis (CSH; panel A); alternatively, sensitivity to hormone-driven brain organization may decrease across this window, the decreasing sensitivity hypothesis (DSH; panel B). If so, earlier puberty should be associated with greater sensitivity to hormone-driven brain organization, and greater sex typicality in adulthood. Figure adapted from Schulz and Sisk (2016).

In humans, earlier recalled pubertal timing has predicted greater substance abuse (Copeland et al., 2010; Downing and Bellis, 2009; Graber et al., 1997; Hedges and Korchmaros, 2016; Tschann et al., 1994; Wilson et al., 1994), depression (Angold et al., 1998; Copeland et al., 2010; Graber et al., 1997; Kaltiala-Heino et al., 2003; Kaltiala-Heino et al., 2004), and anxiety (Zehr et al., 2007), and recent meta-analyses (Dimler and Natsuaki, 2015; Ullsperger and Nikolas, 2017) suggest that the effect of pubertal timing on these phenotypes is small-to-moderate in magnitude as defined by Cohen (1988) – for example, the effect of pubertal timing on externalizing behaviors reported in Dimler and Natsuaki (2015) was $r = 0.18$. Earlier pubertal timing may predict certain cognitive phenotypes as well. Waber (1976) suggested that earlier pubertal timing should predict lower spatial cognition in both sexes because, on average, girls both undergo puberty before boys and score lower on tests of spatial cognition (for review of mixed-sex studies, see Newcombe and Dubas, 1987). Investigations of the effect of pubertal timing (based on self-reports of pubertal timing) in adolescent boys and adult men have produced conflicting results, with some finding positive (Sanders and Soares, 1986), negative (Beltz and Berenbaum, 2013; Doll et al., 2016), and null (Geary and Gilger, 1989; Gilger and Ho, 1989; Herlitz et al., 2013; Vuoksimaa et al., 2012) results. The two published studies in which earlier pubertal timing predicted greater visuospatial cognition in men were both designed to test

the DSH (Beltz and Berenbaum, 2013; Doll et al., 2016), and all but two studies (Herlitz et al., 2013; Vuoksimaa et al., 2012) have relied on recalled pubertal timing.

Although it is a practical measure for retrospective studies (e.g., Beltz and Berenbaum, 2013; Doll et al., 2016), recalled pubertal timing may be prone to reporting error (Brooks-Gunn et al., 1987; Dubas et al., 1991; Shirtcliff et al., 2009), and the timing of observable pubertal changes does not necessarily correspond with the beginning of pubertal hormone exposure (Witchel and Plant, 2013). Experimental manipulation of peripubertal hormone exposure is obviously both unfeasible and unethical in humans. However, we have identified a human disease model in which a closely analogous "experiment of nature" occurs. Individuals with Isolated GnRH Deficiency (IGD) are unable to produce gonadal hormones due to nonfunctional or absent gonadotropin-releasing hormone (GnRH) neurons in the hypothalamus. About 50% of IGD patients meet diagnostic criteria for Kallmann Syndrome, which is characterized by IGD and anosmia and has an estimated prevalence of 1:30,000 male – 1:125,000 female live births (Laitinen et al., 2011). As GnRH-releasing neurons initiate gonadotropin secretion and then gonadal hormone synthesis, the lack of function or absence of these neurons necessarily means the absence of sex steroid hormone production (Han and Bouloux, 2012; Crowley and Pitteloud, 2017). It is notable however that hormone exposure of individuals with IGD is like that of typically developing males and females during the first trimester of gestation, when maternal human chorionic gonadotropin (hCG) acts as luteinizing hormone (LH) by binding to their shared receptor, stimulating the production of androgens and estrogens (Choi and Smitz, 2014; Seminara et al., 1998). As pregnancy progresses, hCG decreases, and individuals with IGD are thus unable to produce gonadal hormones secondary to their hypothalamic GnRH deficiency and consequent gonadotropin deficiency. Consequently, men and women with IGD not only lack reproductive hormone activity from after the first trimester to the 'mini-puberty' period during the first few months of early life, but they also then require gonadal steroid hormone replacement therapy (HRT) to initiate puberty and must continue a treatment regimen throughout adulthood. Puberty is usually induced in men through transdermal or injectable testosterone treatment, and in women, through oral or transdermal estradiol treatment (Boehm et al., 2015). Additional treatments include pulsatile GnRH therapy and gonadotropin therapy, though such treatments are often reserved for induction of fertility in adulthood (Boehm et al., 2015). Because individuals with IGD are not exposed to endogenous pubertal hormones prior to the initiation of HRT, it is possible to pinpoint the timing of pubertal hormone exposure in this human disease model and associate this age with cognitive phenotypes in adulthood. Of the existing studies of IGD, only one has assessed cognition (Hier and Crowley, 1982), some have assessed other aspects of psychology (Dwyer et al., 2014), but none has tested the association between age of HRT initiation and adult phenotypes.

The present research utilizes data from four studies to test the prediction of the DSH that earlier peripubertal exposure to gonadal steroids will lead to greater sex-typicality (i.e., higher scores) on male-typed tests of spatial cognition in adult men. We present data on two studies of typically developing men (Studies 1 and 2) and one study of men with IGD (Study 3) in which participants completed tests of spatial cognition on which there is an average male advantage. The timing of exposure to pubertal hormones was assessed via recalled pubertal timing in Studies 1 and 2, and from the recalled age of HRT initiation in Study 3. In Study 1, participants also completed cognitive tasks that do not typically exhibit significant sex differences, and in Study 2, participants provided saliva samples for testosterone assays. In Study 4, we meta-analyzed these results along with four previously published studies on pubertal timing and spatial cognition in humans.

**Table 1**
Demographic information for all studies.

| | Mean (standard error) or % (n) |
|---|---|
| Study 1 ($n$ = 1095) | |
| Age | 38.37 (0.39) |
| % Sex offenders | 95.5% (1046) |
| % White | 81.0% (997) |
| Age sexual preference[a] | −0.24 (0.05) |
| Gender sexual preference[b] | −1.92 (0.06) |
| Age of puberty | 12.92 (0.04) |
| FSIQ ($M$ = 100, $SD$ = 15) | 98.04 (0.40) |
| VIQ ($M$ = 100, $SD$ = 15) | 96.41 (0.42) |
| PIQ ($M$ = 100, $SD$ = 15) | 101.40 (0.41) |
| Information ($M$ = 10, $SD$ = 3) | 9.28 (0.09) |
| Similarities ($M$ = 10, $SD$ = 3) | 9.34 (0.08) |
| Digit span ($M$ = 10, $SD$ = 3) | 9.77 (0.08) |
| Arithmetic ($M$ = 10, $SD$ = 3) | 9.29 (0.09) |
| Block design ($M$ = 10, $SD$ = 3) | 10.88 (0.09) |
| Picture completion ($M$ = 10, $SD$ = 3) | 9.61 (0.08) |
| Study 2 ($n$ = 173) | |
| Age | 21.44 (0.43) |
| % Heterosexual | 91.8% (169) |
| % White | 78.8% (145) |
| Testosterone (pg/mL) | 52.17 (1.17) |
| Age of puberty | 13.86 (0.10) |
| MRT | 10.23 (0.37) |
| Study 3 (n = 51) | |
| Age | 37.50 (2.02) |
| % Heterosexual | 76.5% (39) |
| % White | 76.5% (39) |
| Age of HRT initiation | 19.66 (0.91) |
| MRT | 7.13 (0.51) |

FSIQ = Full Scale IQ, HRT = Hormone Replacement Therapy, MRT = Mental Rotation Task.

[a] Higher positive values indicate higher attraction to prepubescent and pubescent individuals relative to adults.

[b] Positive values reflect greater attraction to males, negative values reflect greater attraction to females, and zero reflects no gender preference.

## 2. Study 1

### 2.1. Participants & general procedure

Participants were drawn from 1398 men referred to the Kurt Freund Laboratory for the Centre for Addiction and Mental Health (CAMH; Toronto, Ontario, Canada). The purpose of all referrals to the Laboratory was to identify the participant's primary erotic preferences by means of phallometric assessment. The sources of referrals included participants' parole and probation officers, their lawyers, correctional institutions, their physicians, and a miscellany of other agencies. A second, smaller subset of men ($n$ = 49) had no involvement with the criminal justice system and initiated referrals to the Laboratory through their physicians (See Table 1 for demographic information). All men were typically developing insofar as they were not diagnosed with any disorders of sexual development or congenital disorders associated with alterations in hormone action (e.g., IGD, 5-alpha reductase deficiency). While all assessments were performed for clinical purposes, all participants included in the present analyses provided explicit permission for their data to be used for research purposes.

### 2.2. Measures of pubertal age

Pubertal age was collected along with personal and family demographic information via a self-administered questionnaire. This questionnaire included a single item on pubertal age: "At what age did you reach puberty? (*Males*: First sign of physical maturity—for example, pubic hair, voice change, first ejaculation)."

### 2.3. Measures of cognitive functioning

Participants' sexological assessments and questionnaires were supplemented by a brief neuropsychological screening battery (see Cantor et al., 2004, for further details). This battery included six subtests from the Wechsler Adult Intelligence Scale—Revised (WAIS–R; Wechsler, 1981): Information, Similarities, Digit Span, Arithmetic, Picture Completion, and Block Design. Full Scale IQ (FSIQ) was estimated from the subtests by the method detailed by Tellegen and Briggs (1967), using the age-scaled subtest scores and the intercorrelations between those subtests in the WAIS–R standardization sample. As the primary purpose of neuropsychological evaluations was to determine participants' IQ, more specialized tests of individual domains (e.g., mental rotation; see Section 3.3 below) were not administered in Study 1. Following the WAIS-R manual (Wechsler, 1981), we created a performance IQ (PIQ) composite by aggregating scores on the Block Design and Picture Completion subscales, both of which test aspects of visuospatial cognition and show a male advantage (Cohen's $d = 0.26$ and 0.17, respectively; Hines, 2003). We then created a verbal IQ (VIQ) composite by aggregating scores on the Information, Similarities, Digit Span, and Arithmetic subscales (Cohen's $d = 0.28$, 0.02, 0.00, and 0.32, respectively; Hines, 2003). Based on these effect size estimates, the average sex difference effect size should be generally small in magnitude (Cohen, 1988), but slightly larger for PIQ ($d = 0.22$) than for VIQ ($d = 0.16$). The inclusion of composites that differ in the magnitude of their sex differences is important to distinguish between the hypothesis that pubertal timing may affect cognitive sex-typicality, and the hypothesis that pubertal timing may affect cognition more broadly (see also Beltz and Berenbaum, 2013).

### 2.4. Data analysis

For the present analyses, we selected participants who had valid data on phallometric measures of the gender and age of their preferred sexual partners (i.e., completed these measures and had data that could be analyzed), age of puberty, age of learning English, race, age at examination, and FSIQ within the normal range (i.e., ≥70); participants who had missing values for any of these variables were excluded from analyses. Seventy-three participants were excluded because they had an FSIQ < 70, and an additional 185 were excluded because they did not have valid data on phallometric measures of gender and age preference of their desired sexual partners. This resulted in a final sample of 1095 men (see Table 1 for demographic information). Compared to participants who did not have valid phallometric data, participants who had valid phallometric data had PIQ and VIQ scores approximately 5 points higher (both $p < 0.01$), and were more likely to self-identify as white ($p < 0.01$). No other differences in variables included in analyses were statistically significant.

All analyses were performed using R. Data and code have been uploaded as electronic supplementary material. PIQ and VIQ were the outcome variables in our primary two multiple regression models. Included covariates for this study and for all subsequent studies in this paper were chosen based on prior literature and before analysis of our data. In the model with PIQ as an outcome, VIQ was included as a control, as different facets of cognition are highly correlated (Detterman and Daniel, 1989; Spearman, 1904; Wechsler, 1981). As age (Wechsler, 1981), gender sexual preference or sexual orientation (Gladue et al., 1990; Peters et al., 2007; Rahman and Wilson, 2003), age sexual preference (i.e., preference for the age of a sexual partner; Cantor et al., 2004; Cantor et al., 2005; Hucker et al., 1986), race (Barona et al., 1984; Kaufman et al., 1988), and sex offender status (Cantor et al., 2005) have been shown to predict neuropsychological performance, these variables were included as predictors of PIQ along with self-reported age of puberty. Race was assessed as either white or non-white via self-report, and gender and age sexual preferences were measured through phallometric testing. These same variables were used in the multiple regression predicting VIQ, with PIQ additionally entered as a control. Post-hoc models assessing the effect of pubertal timing on individual WAIS-R subtests were also run. Estimates presented are standardized regression weights (β), obtained using R's lm.beta package. We statistically compared models with only linear effects to models with both linear and quadratic effects of pubertal timing using ANOVAs; in all cases, model fit was not significantly improved with the inclusion of a quadratic term. Thus, results presented are of models including only a linear term, and not quadratic term, for pubertal timing.

### 2.5. Results

In a multiple regression with VIQ as the outcome variable, current age ($\beta = 0.14$, $t = 5.64$, $p < 0.001$), age sexual preference ($\beta = -0.06$, $t = -2.44$, $p = 0.015$), and PIQ ($\beta = 0.60$, $t = 23.43$, $p < 0.001$) significantly predicted VIQ; importantly, pubertal timing ($\beta = -0.03$, $t = -1.23$, $p = 0.218$; ESM Fig. 1) did not. In a multiple regression with PIQ as the outcome variable, race ($\beta = 0.09$, $t = 3.42$, $p = 0.001$, indicating higher PIQ in white versus non-white participants), gender sexual preference ($\beta = -0.07$, $t = -3.01$, $p = 0.003$, indicating a higher PIQ with greater attraction to females), VIQ ($\beta = 0.58$, $t = 23.43$, $p < 0.001$), and pubertal timing ($\beta = -0.07$, $t = -2.66$, $p = 0.008$) significantly predicted PIQ (Fig. 2, panel A). See ESM Table 1 for relationships between pubertal timing and individual subscales.

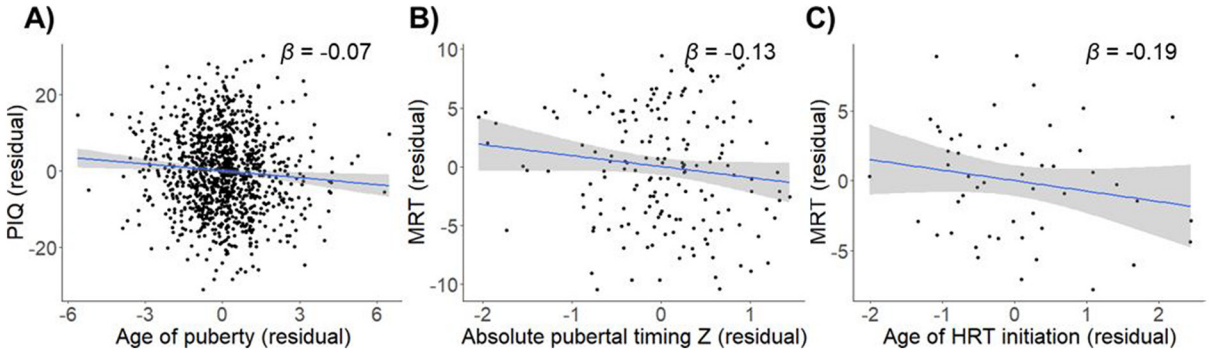


**Fig. 2.** Relationships between age of exposure to peripubertal androgens and performance on spatial cognitive tasks showing a male advantage. (A) Study 1: WAIS-R PIQ regressed on self-reported age of puberty in typically developing men (residuals after conditioning on age and gender preferences, current age, and race). (B) Study 2: MRT regressed on self-reported absolute pubertal timing in typically developing men (residuals after conditioning on sexual orientation, current age, race, and testosterone). (C) Study 3: MRT regressed on age of HRT initiation in men with IGD (residuals after conditioning on sexual orientation, current age, and race).

## 3. Study 2

### 3.1. Participants & general procedure

Two hundred twenty-six male participants were recruited as part of a study on the effect of pubertal timing on sexually differentiated phenotypes in adulthood conducted at the Pennsylvania State University. Recruitment materials were posted on various social media sites and a university-sponsored psychology study participant pool and advertised on the radio. All procedures were IRB-approved, and participants provided informed consent. Participants were compensated with either course credit or US$15. All test sessions were scheduled between 9:00 AM and 12:00 PM to control for diurnal fluctuations in testosterone production (Montanini et al., 1988). Upon arrival at the lab, participants provided trained research assistants with a first saliva sample via passive drool. Participants then completed a 45-minute online survey at a private computer workstation. A second saliva sample was taken before participants left. These two samples were then mixed for analyses to mitigate the effect of pulsatile release patterns of LH-induced testosterone secretion (Rose et al., 1972; Rowe et al., 1974).

### 3.2. Measures of pubertal age

Pubertal age was measured using a version of the male Pubertal Development Scale (PDS; Petersen et al., 1988) modified for retrospective use (Doll et al., 2016; Zehr et al., 2007; see ESM for full questionnaire). The modified PDS includes questions on the timing of general pubertal development, and specific questions about the timing of facial and body hair growth, vocal and skin changes, growth spurts, spontaneous erections, and wet dreams. As these pubertal changes occur at different ages (e.g., genital changes are typically observed before the beginning of facial hair growth; Witchel and Plant, 2013), composites including the timing of a range of pubertal development characteristics likely provide more precise and accurate estimations of pubertal timing, relative to measures of pubertal timing based on a single question alone, as in Study 1 (for further discussion of the effects of measuring pubertal timing with single questions versus composites, see Ullsperger and Nikolas, 2017). Questions on the PDS address both the recalled age of these events and when participants noticed these events relative to their peers (from *much earlier than peers* to *much later than peers*). The PDS includes 6 questions about absolute ages of pubertal changes. Of participants who completed the PDS, the mean number of questions answered was 4.67 (SE = 0.10). Responses to these questions were scaled and then averaged to create a composite measure of absolute pubertal timing, and this composite measure was used as a predictor in a multiple linear regression.

Responses to relative pubertal timing questions were also scaled and then averaged to create a composite measure of relative pubertal timing, with the exception of questions on timing of wet dreams and spontaneous erections. This is because men are less likely to recall when these events occurred relative to peers as these occur privately, and because they load onto another component in a principal components analysis (Beltz and Berenbaum, 2013; Doll et al., 2016). For further details on factor loadings of the PDS, see Doll et al. (2016). Here we present analyses using this composite measure; however, performing a principal components analysis and using the first principal component scores as the measure of relative pubertal timing as in Doll et al. (2016) did not significantly affect our results. Relative and absolute composite measures of pubertal timing correlated at $r = 0.53$, $p < 0.001$ (ESM Fig. 2).

### 3.3. Measures of cognitive functioning

Visuospatial cognition was assessed using a computerized 3D Mental Rotation Task (MRT). This task consisted of two four-minute blocks, each with 10 items (Vandenberg and Kuse, 1978). For each item, participants viewed a two-dimensional representation of a three-dimensional block figure (target figure) and four similar figures beneath it. Participants were instructed to select the two figures beneath the target that were rotated versions of the target figure and received a full point on that item if both correct responses were chosen. Total MRT scores could thus vary from zero to 20, and these total scores were used as the outcome variable.

### 3.4. Testosterone measures

Saliva samples were analyzed at the Nipissing University Biomarkers Lab (Nipissing University, North Bay, Ontario). Samples were quantified using commercially available enzyme immunoassay kits from DRG International. Sensitivity was 1.9 pg/mL, and intra- and inter-assay CVs were 6.4% and 4.9%, respectively. Testosterone values were standardized, and values greater than three standard deviations from the mean were dropped.

### 3.5. Data analysis

For the present analyses, we selected participants who had valid data on all covariates of interest. Forty-two participants did not provide saliva for testosterone assays, 17 did not answer any PDS questions, 2 did not provide data on self-identified race/ethnicity, and 1 did not provide data on sexual orientation. Excluding these participants resulted in a final sample of 173 men (see Table 1 for demographic information). Participants who were included versus excluded in these analyses did not significantly differ on any of these covariates or in their MRT scores and absolute pubertal timing scores.

Data and R scripts for this study can be found as described in Section 2.4 *Data analysis for Study 1*. As detailed above, neuropsychological performance is modulated by age, gender preference, and race. Thus, age, self-identified sexual orientation, and self-identified white or non-white race were included as covariates. As there is mixed support regarding an effect of circulating testosterone on mental rotation abilities, testosterone was included as a covariate. We ran two models to predict MRT: one using a composite measure of absolute age of pubertal timing, and a second using a composite measure of relative pubertal timing to predict MRT. The inclusion of a quadratic term for pubertal timing did not significantly improve model fit in either model; thus, the models we report on below include only linear effects of pubertal timing. We also tested for interactions between testosterone and pubertal timing; as these were not significant in the models with either absolute ($p = 0.966$) or relative ($p = 0.976$) pubertal timing, only main effects were included in the models reported below.

### 3.6. Results

In a multiple regression with the absolute measure of pubertal timing predicting MRT, race ($\beta = 0.19$, $t = 2.39$, $p = 0.018$, indicating higher MRT in white versus non-white participants) significantly predicted MRT, while circulating testosterone ($\beta = 0.09$, $t = 1.15$, $p = 0.252$) did not. The effect of absolute pubertal timing was moderate in size ($\beta = -0.13$, $t = -1.71$, $p = 0.090$; Fig. 2, panel B), though not statistically significant at $\alpha = 0.05$. In a multiple regression with relative pubertal timing and the covariates as predictors of MRT, only race ($\beta = 0.22$, $t = 3.00$, $p = 0.003$, indicating higher MRT in white versus non-white participants) significantly predicted MRT; testosterone ($\beta = 0.09$, $t = 1.17$, $p = 0.245$) and relative pubertal timing ($\beta = -0.02$, $t = -0.34$, $p = 0.735$; ESM Fig. 3) did not.

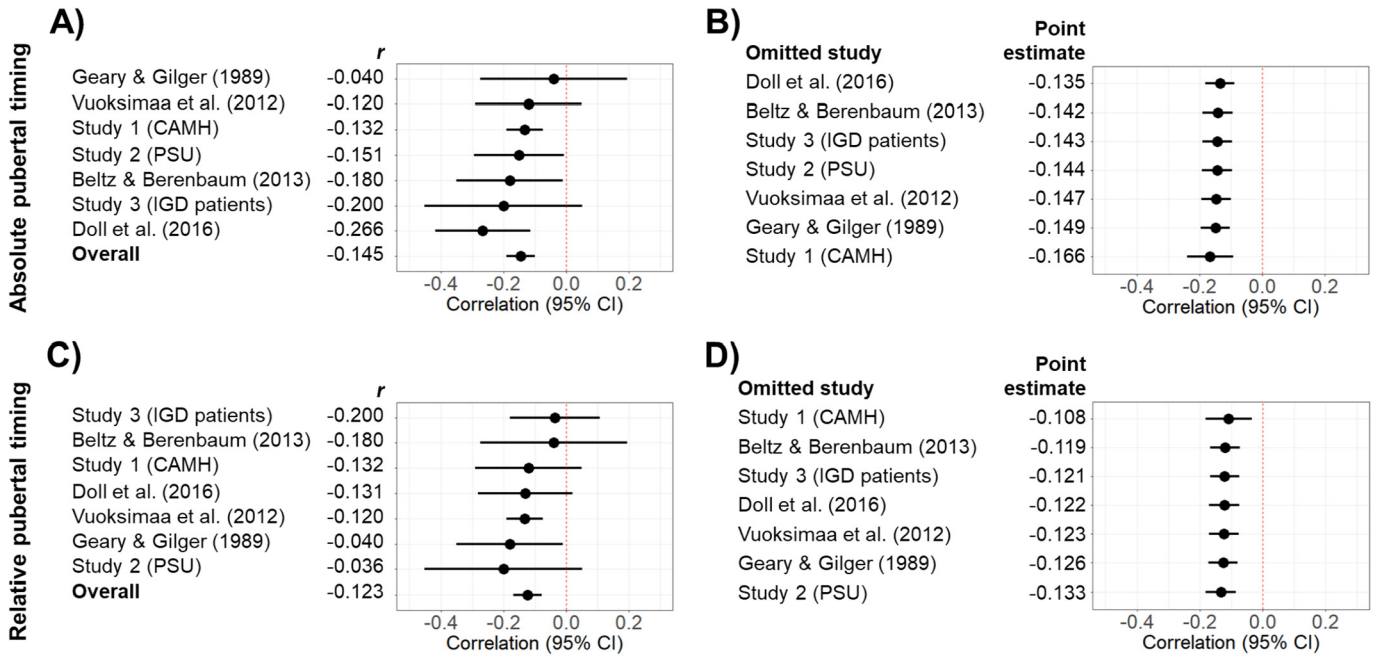


**Fig. 3.** Results of meta-analyses on the correlation between absolute (overall $r = -0.15$; panel A) and relative (overall $r = -0.12$; panel C) pubertal timing and spatial rotation, and of omit-one-study analyses ($-0.17 \leq r \leq -0.11$; panels B and D).

## 4. Study 3

### 4.1. Participants & general procedure

Sixty-two men with IGD were recruited as part of the same protocol described in Study 2. Men with IGD were referred by physicians at the Reproductive Endocrine Unit at Massachusetts General Hospital and the Reproductive Physiology and Pathophysiology group at the National Institute of Child Health and Human Development ($n = 30$). Men were also recruited through solicitations on IGD-specific email listservs, forums, and support groups ($n = 32$). All procedures were IRB-approved, and participants provided informed consent. Participants completed the same online survey as those in study 2 and were instructed to complete the survey in a single session at the time and location of their choosing. Compensation for survey completion was US $25. (See Table 1 for demographic information.)

### 4.2. Measures of pubertal age

Men with IGD completed a questionnaire about their HRT history. This questionnaire required participants to list when they first began HRT, and all subsequent changes in HRT regimens and gaps in HRT use. The measure of pubertal timing used as a predictor in subsequent analyses was self-reported age of HRT initiation, log-transformed to correct skew. In a subset of patients ($n = 17$) for whom physician records of HRT initiation were available, self-reported and physician recorded age of HRT initiation were significantly correlated ($r = 0.77$; $p < 0.01$).

### 4.3. Measures of cognitive functioning

The 3D MRT task as described in Study 2 was used to index mental rotation abilities in men with IGD.

### 4.4. Data analysis

Age, self-reported sexual orientation, self-identified white or non-white race, and age of HRT initiation were included as covariates to predict MRT. Age of HRT initiation was missing for 9 participants, race was missing for 2, and sexual orientation was missing for 1. Excluding participants with missing data resulted in a final sample of 51 men (see Table 1 for demographic information). Participants who were included versus excluded in these analyses did not significantly differ on any of these covariates or in their MRT scores and ages of HRT initiation. As in Studies 1 and 2, we tested for both linear and quadratic effects of age of HRT initiation. The inclusion of a quadratic term of HRT initiation did not significantly improve model fit and was dropped from the final model. We also tested whether MRT performance differed between men with IGD and control men in Study 2, and if so, whether this difference was mediated by absolute pubertal timing, measured as described in Section 3.2 above to facilitate comparisons between groups. Absolute pubertal timing correlated with age of HRT initiation at $r = 0.38$, $t = 2.90$, $p = 0.005$. Mediation was tested using R's psych package.

### 4.5. Results

In a multiple regression with log-transformed age of HRT initiation and the aforementioned covariates as predictors of MRT, no predictors significantly explained variance in MRT at $\alpha = 0.05$, though the effect size for age of HRT initiation ($\beta = -0.19$, $t = -1.3$, $p = 0.200$; Fig. 2, panel C) was moderate in size.

When controlling for age, sexual orientation, and race, group (i.e., IGD versus control) significantly predicted MRT ($\beta = -0.21$, $t = 2.65$, $p = 0.009$), with men with IGD scoring lower than controls. Absolute pubertal timing also differed significantly as a function of group when controlling for age, sexual orientation, and race ($\beta = 0.64$, $t = 10.81$, $p < 0.001$), as well as when these covariates were not entered ($\beta = 0.72$, $t = 16.65$, $p < 0.001$). Pubertal timing did not significantly mediate group differences in MRT ($\beta = -0.37$, $t = 0.78$, $p = 0.438$; see ESM Fig. 4).

## 5. Study 4: meta-analysis

We conducted two meta-analyses using data from Studies 1–3, and from other published studies assessing the link between pubertal timing and adult visuospatial abilities. Studies assessing stage of pubertal

development and neuropsychological function in adolescents, studies that recruited only women, and studies that report statistics for men and women analyzed jointly were excluded, as the goal of the present meta-analysis was to specifically evaluate the effect of pubertal timing on visuospatial abilities in adult men. PubMed search terms included puberty*, mental rotation*, pubertal timing, timing of puberty, sexual maturation, and spatial ability* (with asterisks indicating truncation). These search terms yielded a total of 31 studies, 23 of which were unique cases. Four studies met all our inclusion criteria and were included in our meta-analyses (for studies, see Fig. 3).

Correlation coefficients between measures of pubertal timing and measures of spatial ability were used as the effect size, and data were analyzed using random effects models in the Comprehensive Meta-Analysis software version 3 (Borenstein et al., 2005). A random effects model allows for the presence of systematic variance (e.g., moderator variables such as differences in the method of measuring spatial cognition or pubertal timing) in addition to random sampling error variance. In the first meta-analysis, we used correlations between spatial performance and measures of the absolute age of pubertal timing as our effect size. In computing the absolute measure of pubertal timing using data from Doll et al. (2016), we scaled and averaged responses to items targeting the absolute ages of pubertal changes as in Study 2. In the second meta-analysis, we replaced zero-order correlations between spatial performance and measures of absolute pubertal timing with those for relative pubertal timing where available (Doll et al., 2016 and Study 2). These analyses resulted in a total $n$ of 1749 for our meta-analysis using absolute measures and 1783 for our meta-analysis using relative pubertal timing measures. We subsequently conducted 'omit-one-study' analyses to determine whether the removal of any single study would change our meta-analysis results.

The population point estimate for the correlation coefficient between absolute pubertal timing and spatial abilities was $-0.15$ (95% confidence interval [CI] = $-0.19$, $-0.10$, $z = -6.08$, $p < 0.001$; Fig. 3, panel C). The exclusion of single studies in the omit-one-study analysis produced point estimates between $-0.17$ (when excluding Study 1) and $-0.14$ (when excluding Doll et al., 2016; Fig. 3, panel D). The 95% CI excluded a correlation coefficient of zero across all analyses, suggesting that observed relationship between pubertal timing and spatial performance does not depend upon the inclusion of any single study. The population point estimate for the correlation coefficient between relative pubertal timing and spatial abilities was $-0.12$ (95% CI = $-0.17$, $-0.08$, z = $-5.02$, $p < 0.001$; Fig. 3, panel A). The exclusion of single studies in the omit-one-study analysis produced point estimates between $-0.13$ (when excluding Study 2) and $-0.11$ (when excluding Study 1; Fig. 3, panel B). Again, the 95% CI excluded a correlation coefficient of zero across all analyses.

## 6. Discussion

Building upon previous experimental and observational work, we hypothesized that earlier peripubertal exposure to gonadal steroids would increase performance on male-typed visuospatial cognitive tasks in men. Across a meta-analysis including six samples of typically developing men (Studies 1 and 2, Beltz and Berenbaum, 2013, Doll et al., 2016, Geary and Gilger, 1989, and Vuoksimaa et al., 2012) and a sample of men with Isolated GnRH Deficiency (IGD; Study 3), earlier peripubertal exposure to gonadal steroids predicted better performance on male-typed spatial cognitive tasks. This pattern was not observed for a cognitive measure that exhibits smaller sex differences (Study 1) and was not explained by current testosterone levels (Study 2). The point estimates for the correlation between pubertal timing and spatial abilities ($r = -0.15$ and $-0.12$) were robust to the exclusion of any single study in the meta-analyses and suggest a small-to-moderate (Cohen, 1988) population-level effect, and are similar in magnitude to correlations between pubertal timing and externalizing behavior (Dimler and Natsuaki, 2015) and psychopathology more broadly (Ullsperger and Nikolas, 2017). However, we note that these estimates reflect imprecision in estimating both the timing of pubertal steroid exposure and the underlying cognitive abilities putatively influenced by this timing. Hence, the results of our meta-analyses are likely to represent an underestimate of the true effect size. In Study 1, male-typed spatial cognition was assessed via a composite of the Block Design and Picture Completion subtests, which show smaller sex differences than the MRT (Hines, 2003) and hence are likely to more weakly reflect the influence of androgens. In addition, pubertal timing was assessed via a single self-report item. In Study 2, male-typed spatial cognition was assessed via the MRT, and pubertal timing was assessed via a more detailed self-report questionnaire. Finally, in Study 3, male-typed spatial cognition was assessed via the MRT, and pubertal timing was assessed most precisely via self-reported date of HRT initiation. We note a trend towards increasing effect size magnitudes with each presumed improvement in measurement precision. Precise measurement of both male-typed visuospatial performance and the age of onset of peripubertal hormone production in IGD patients may explain why the observed effect size estimate ($-0.19$) was greater in magnitude than all but one effect size observed across studies using less precise measures. The relatively large effect size in Study 3 may also in part be attributable to the high variation in pubertal onset among participants with IGD, which should mitigate effects of range restriction present in Studies 1 and 2 on associations between pubertal timing and visuospatial performance. These advantages of utilizing IGD as a disease model may have more than compensated for any decreased sensitivity to androgen as a result of IGD patients beginning puberty later, on average, than participants in Studies 1 and 2.

Our results support the hypothesis of Sisk and colleagues (Schulz and Sisk, 2016), which we have termed the DSH, that sensitivity to the organizational effects of gonadal hormones declines across the pubertal window (Fig. 1, panel B). By contrast, our results are inconsistent with the CSH (Fig. 1, panel A). However, the pattern of association between trait development and the timing of gonadal hormone exposure is likely to differ across psychological phenotypes and their underlying neural architectures. Neural sex differences that are organized by gonadal hormones may appear at different times during perinatal development (McCarthy et al., 2017). Thus, future work should examine a wide range of sexually differentiated cognitive, psychological, and behavioral phenotypes to determine their sensitivity to hormone-driven organization during the pubertal window. Future work should also aim to identify the mechanism that modulates putative differential sensitivity to the effects of gonadal hormones. Direct studies on this are critically lacking, but work from sexual imprinting in zebra finches suggests that changes in dendritic morphology occur at certain developmental periods in the presence of certain stimuli (Bischof and Rollenhagen, 1999). It is possible that in mammals, there are time-dependent changes in dendritic morphology, but that these changes are permanently modulated by timing of peripubertal gonadal hormone action (Schulz et al., 2009b).

We also note that declining sensitivity to pubertal sex hormones represents a possible developmental mechanism by which adult phenotypes may be linked to life history strategy (Del Giudice and Belsky, 2010; Del Guidice et al., 2016). Life history strategies are the age- and stage-specific patterns and timing of events in organisms' lives, such as birth, weaning, age of sexual maturation, and age of first reproduction (Flatt and Heyland, 2011). According to life history theory, species and individuals have been shaped by natural selection to vary in the relative amount of resources allocated to somatic maintenance, defense, and reproduction (Wells et al., 2017). Those with 'faster' life history strategies allocate more resources towards reproduction and should develop physiological and behavioral traits that allow them to do so, while those with 'slower' life history strategies allocate more resources towards somatic maintenance and defense, and parenting (Del Giudice and Belsky, 2010; Stearns, 1976). Age of reproductive maturity or pubertal timing is often examined as a marker of life history tempo, and

earlier pubertal timing predicts the development of sexually dimorphic physical characteristics indicative of a faster, more mating-focused life history strategy in young adult men (Doll et al., 2016). It follows that earlier pubertal timing may also predict cognitive phenotypes that may facilitate an emphasis on mating and reproduction. Functional hypotheses posit that spatial abilities could modulate mating success via enhanced mate location (Gaulin, 1992; Miner et al., 2014), targeting of same-sex competitors (Hill et al., 2017; Puts, 2010), and location of prey items used to provision potential mates (Hawkes, 1990), though tests of this hypothesis in humans are lacking. Nonetheless, incorporation of a life history framework in the study of pubertal timing and adult cognitive phenotypes may prove useful in predicting which phenotypes should be particularly sensitive to variation in pubertal timing, and their potential functions.

The study of natural quasi-experiments in humans, or people in whom hormone production or action is congenitally altered such as those with congenital adrenal hyperplasia (CAH; Hines, 2010; Hines et al., 2004; Puts et al., 2008) or androgen insensitivity syndrome (Hamann et al., 2014; Hines et al., 2003), have proved critical to our understanding of hormone-driven organization of the brain and behavior. This paper presents the first examination of a human disease model wherein pubertal timing can be objectively determined to study links between peripubertal hormone exposure and adult phenotypes. That the direction of the association between pubertal timing and visuospatial abilities was the same in typically developing and IGD men, and that the strength of this association was greater in IGD men than in all but one of the other effect sizes examined, suggests that the IGD disease model may prove to be particularly valuable in assessing sensitivity to hormone-driven organization for psychological traits that would be theoretically predicted to be affected by pubertal timing. Our results also suggest that IGD may be informative about the influence of early hormonal exposure. Men with IGD performed below controls on the MRT (see also Hier and Crowley, 1982), and this was not significantly mediated by pubertal timing. This suggests that the group difference in the timing of peripubertal androgen exposure is insufficient to explain the difference in MRT, and that the lower pre- and perinatal sex steroids presumed to characterize IGD may be responsible. Thus, while CAH has been studied to elucidate the effects of chronically high prenatal androgens on male-typed spatial tasks in females (Hampson et al., 1998; Resnick et al., 1986; see Puts et al., 2008 for meta-analysis), IGD may also clarify the effects of chronically low prenatal sex hormones.

### 6.1. Clinical considerations

Pubertal timing is medically altered across a range of conditions. GnRH agonists or antagonists may be used to block hormone production in children with precocious puberty (Comite et al., 1981; Mansfield et al., 1983), while exogenous hormones (e.g., Rosenfeld et al., 1982) or GnRH pumps (Boehm et al., 2015; Hoffman and Crowley, 1982; Nass et al., 2013) may be used in children with constitutionally delayed puberty or IGD to induce puberty. Puberty blockers may also be prescribed to gender nonconforming youth without congenital conditions of the hypothalamic-pituitary-gonadal axis (Vance et al., 2014). Physicians may prescribe, and patients may receive, such treatments without a thorough understanding of how pubertal timing may permanently affect a wide range of adult phenotypes (see Introduction). The present study suggests that in addition to the effects of pubertal timing on affective and externalizing disorders (Dimler and Natsuaki, 2015; Ullsperger and Nikolas, 2017), potential effects of pubertal timing on cognitive phenotypes should be considered.

### 6.2. Limitations and future directions

The present study investigated cross-sectional associations between measures of the timing of peripubertal androgen exposure and sexually differentiated aspects of cognition. Though our findings suggest a link between pubertal timing and spatial abilities in men, we are unable to draw conclusions about causation from cross-sectional data. Future studies, with both typically developing participants and participants with IGD, should thus utilize a longitudinal design, recruiting and testing participants before puberty, and repeating testing into young adulthood. Such studies would ideally document the progression of external physical changes that accompany puberty, and also measure hormone levels. The longitudinal documentation of physical and hormonal measures would effectively remove sources of measurement error that may accompany self-reported pubertal timing. One of three studies reported here measured cognitive phenotypes that both do and do not exhibit significant sex differences (PIQ and VIQ, respectively, in Study 1) and did not find an effect of pubertal timing on non-sexually differentiated aspects of cognition (see also Beltz and Berenbaum, 2013). Future work should utilize female-typed, male-typed, and sex-neutral cognitive measures to elucidate how pubertal timing may modulate sex typicality. As most rodent work showing an effect of pubertal timing on sex typicality has been conducted on males experimentally administered androgens at different times (Schulz et al., 2009a, b), it is unknown whether a similar mechanism is present in females. The inclusion of both females and females in experimental animal models, and the experimental administration of estrogens in addition to androgens, will provide a more comprehensive understanding of pubertal sensitivity to hormones across sexes, and can guide future translational work in humans. Brain imaging in such studies may elucidate the biological basis of the emergence and maintenance of sexually differentiated phenotypes. Though some work has examined the link between current pubertal development and neural structure (Herting et al., 2014; Peper et al., 2011a) and function (Peper et al., 2011b), it is unknown whether pubertal timing predicts sex typicality in the brain in adulthood. The sexual preference demographics of participants in Study 1 are not representative and some have suggested that atypical sexual preferences may result from prenatal pathologies (Cantor et al., 2005), potentially limiting the generalizability of that study's findings. In addition, Study 1 was also the only study not to use the MRT to assess visuospatial abilities. We note, however, that sexual preferences were statistically controlled in Study 1, and in our omit-one-study analyses, the effect of pubertal timing on visuospatial performance was robust to the exclusion of effect sizes from Study 1, suggesting that our overall results were not biased or significantly affected by the inclusion of the Study 1 sample. Finally, spatial abilities may be linked to variables we did not control for our analyses. Whereas some work finds an effect of education and academic program on mental rotation and visuospatial abilities (Peters et al., 2006), studies using the MRT specifically have failed to find an effect of education on performance (Vuoksimaa et al., 2012). Future work should thus aim to measure and statistically control for a wide range of variables that could potentially modulate cognitive performance.

### 6.3. Conclusion

Across the three studies reported here and four prior investigations of pubertal timing and cognition, earlier pubertal timing positively predicted sex-typicality on measures of male-typed spatial abilities in adult men, and the observed magnitude of the effect of pubertal timing on cognition is similar to those previously reported on psychopathology (Dimler and Natsuaki, 2015; Ullsperger and Nikolas, 2017). The association between pubertal timing and performance on sexually differentiated aspects of cognition is consistent with the DSH, suggesting that the sensitivity of the adolescent brain to the organizing effects of pubertal hormones decreases across the pubertal window.

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## Appendix A. Supplementary data

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## References


Adkins-Regan, E., 2012. Hormonal organization and activation: evolutionary implications and questions. Gen. Comp. Endocrinol. 176 (3), 279–285. https://doi.org/10.1016/j.ygcen.2011.12.040.

Altemus, M., Sarvalya, N., Epperson, C.N., 2014. Sex differences in anxiety and depression: clinical perspectives. Front. Neuroendocrinol. 35 (3), 320–330. https://doi.org/10.1126/scitranslmed.aad1565.Inhibition.

Angold, A., Costello, E.J., Worthman, C.M., 1998. Puberty and depression: the roles of age, pubertal status and pubertal timing. Psychol. Med. 28 (28), 51–61. https://doi.org/10.1017/S003329179700593X.

Apter, D., 1980. Serum steroids and pituitary hormones in female puberty: a partly longitudinal study. Clin. Endocrinol. 12 (2), 107–120.

Bakker, J., Honda, S., Harada, N., Balthazart, J., 2002. The aromatase knock-out mouse provides new evidence that estradiol is required during development in the female for the expression of sociosexual behaviors in adulthood. J. Neurosci. 22 (20), 9104–9112. https://doi.org/10.1007/BF00832566.

Barona, A., Reynolds, C.R., Chastain, R., 1984. A demographically based index of premorbid intelligence for the WAIS–R. J. Consult. Clin. Psychol. 52 (5), 885–887. https://doi.org/10.1037/0022-006X.52.5.885.

Becker, J.B., Hu, M., 2008. Sex differences in drug abuse. Front. Neuroendocrinol. 29 (1), 36–47. Retrieved from. http://www.kup.at/cgi-bin/popup.pl?url=http://www.kup.at/dermann.

Beltz, A.M., Berenbaum, S.A., 2013. Cognitive effects of variations in pubertal timing: is puberty a period of brain organization for human sex-typed cognition? Horm. Behav. 63 (5), 823–828. https://doi.org/10.1016/j.yhbeh.2013.04.002.

Berenbaum, S.A., Beltz, A.M., 2011. Sexual differentiation of human behavior: effects of prenatal and pubertal organizational hormones. Front. Neuroendocrinol. 32 (2), 183–200. https://doi.org/10.1016/j.yfrne.2011.03.001.

Bischof, H., Rollenhagen, A., 1999. Behavioural and neurophysiological aspects of sexual imprinting in zebra finches. Behavioural Brain Researchral Brain Research 98, 267–276.

Bloch, G.J., Mills, R., 1995. Prepubertal testosterone treatment of male rats: defeminization of behavioral and endocrine function in adulthood. Neurosci. Biobehav. Rev. 19 (2), 177–186. https://doi.org/10.1016/0149-7634(95)00065-M.

Boehm, U., Bouloux, P.M., Dattani, M.T., De Roux, N., Dodé, C., Dunkel, L., ... Young, J., 2015. Expert consensus document: European Consensus Statement on congenital hypogonadotropic hypogonadism-pathogenesis, diagnosis and treatment. Nature Reviews Endocrinology 11 (9), 547–564. https://doi.org/10.1038/nrendo.2015.112.

Borenstein, M., Hedges, I., Higgins, J., Rothstein, H., 2005. Comprehensive Meta-analysis Version 2. Biostat, Englewood, NJ.

Brooks-Gunn, J., Warren, M.P., Rosso, J., Garguilo, J., 1987. Validity of self-report measures of girls' pubertal status. Child Dev. 58 (3), 829–841.

Brown, G.R., Kulbarsh, K.D., Spencer, K.A., Duval, C., 2015. Peri-pubertal exposure to testicular hormones organizes response to novel environments and social behaviour in adult male rats. Horm. Behav. 73, 135–141. https://doi.org/10.1016/j.yhbeh.2015.07.003.

Byrnes, J.P., Miller, D.C., Schafer, W.D., 1999. Gender differences in risk taking: a meta-analysis. Psychol. Bull. 125 (3), 367–383. https://doi.org/10.1037/0033-2909.125.3.367.

Cantor, J.M., Blanchard, R., Christensen, B.K., Dickey, R., Klassen, P.E., Beckstead, A.L., ... Kuban, M.E., 2004. Intelligence, memory, and handedness in pedophilia. Neuropsychology 18 (1), 3–14. https://doi.org/10.1037/0894-4105.18.1.3.

Cantor, J.M., Robichaud, L.K., Blanchard, R., Christensen, B.K., 2005. Quantitative reanalysis of aggregate data on IQ in sexual offenders. Psychol. Bull. 131 (4), 555–568. https://doi.org/10.1037/0033-2909.131.4.555.

Choi, J., Smitz, J., 2014. Luteinizing hormone and human chorionic gonadotropin: distinguishing unique physiologic roles. Gynecol. Endocrinol. 30 (3), 174–181.

Cohen, J., 1988. Statistical Power Analysis for the Behavioral Sciences. Routledge Academic, New York, NY.

Comite, F., Cutler, G.B., River, J., Vale, W.W., Loriaux, D.L., Crowley, W.F., 1981. Short-term treatment of idiopathic precocious puberty with a long-acting analogue of luteinizing hormone-releasing hormone. N. Engl. J. Med. 305, 1546–1550.

Copeland, W., Shanahan, L., Miller, S., Costello, E.J., Angold, A., Maughan, B., 2010. Outcomes of early pubertal timing in young women: a prospective population-based study. Am. J. Psychiatry 167 (10), 1218–1225. https://doi.org/10.1176/appi.ajp.2010.09081190.

Crowley, W.F., Pitteloud, N., 2017. Congenital hypogonadotropic hypogonadism. In: Winters, S.J. (Ed.), Male Hypogonadism: Basic, Clinical, and Therapeutic Principles. Humana Press, Totowa, NJ, pp. 81–100.

De Lorme, K.C., Sisk, C.L., 2013. Pubertal testosterone programs context-appropriate agonistic behavior and associated neural activation patterns in male Syrian hamsters. Physiol. Behav. 112–113, 1–7. https://doi.org/10.1016/j.physbeh.2013.02.003.

Del Giudice, M., Belsky, J., 2010. The development of life history strategies: toward a multi-stage theory. In: Buss, D.M., Hawley, P.H. (Eds.), Evolution of Personality and Individual Differences. Oxford University Press, pp. 154–176.

Del Guidice, M., Gangestad, S.W., Kaplan, H., 2016. Life history theory and evolutionary psychology. In: Buss, D.M. (Ed.), The Handbook of Evolutionary Psychology: Foundations. John Wiley & Sons, pp. 88–114.

Detterman, D.K., Daniel, M.H., 1989. Correlations of mental tests with each other and with cognitive variables are highest for low IQ groups. Intelligence 13 (4), 349–359. https://doi.org/10.1016/S0160-2896(89)80007-8.

Dimler, L.M., Natsuaki, M.N., 2015. The effects of pubertal timing on externalizing behaviors in adolescence and early adulthood: a meta-analytic review. J. Adolesc. 45, 160–170. https://doi.org/10.1016/j.adolescence.2015.07.021.

Doll, L.M., Cárdenas, R., Burriss, R.P., Puts, D.A., 2016. Sexual selection and life history: earlier recalled puberty predicts men's phenotypic masculinization. Adapt. Hum. Behav. Physiol. 134–149. https://doi.org/10.1007/s40750-015-0031-7.

Downing, J., Bellis, M.A., 2009. Early pubertal onset and its relationship with sexual risk taking, substance use and anti-social behaviour: a preliminary cross-sectional study. BMC Public Health 9 (446), 1–11. https://doi.org/10.1186/1471-2458-9-446.

Dubas, J.S., Graber, J.A., Petersen, A.C., 1991. A longitudinal investigation of adolescents' changing perceptions of pubertal timing. Dev. Psychol. 27 (4), 580–586. https://doi.org/10.1037/0012-1649.27.4.580.

Dwyer, A.A., Quinton, R., Morin, D., Pitteloud, N., 2014. Identifying the unmet health needs of patients with congenital hypogonadotropic hypogonadism using a web-based needs assessment: implications for online interventions and peer-to-peer support. Orphanet Journal of Rare Diseases 9 (1), 1–11. https://doi.org/10.1186/1750-1172-9-83.

Field, E.F., Whishaw, I.Q., Forgie, M.L., Pellis, S.M., 2004. Neonatal and pubertal, but not adult, ovarian steroids are necessary for the development of female-typical patterns of dodging to protect a food item. Behav. Neurosci. 118 (6), 1293–1304. https://doi.org/10.1037/0735-7044.118.6.1293.

Flatt, T., Heyland, A. (Eds.), 2011. Mechanisms of life history evolution: the genetics and physiology of life history traits and trade-offs. OUP Oxford.

Gaulin, S.J.C., 1992. Evolution of sex differences in spatial ability. Yearb. Phys. Anthropol. 35, 125–151.

Geary, D.C., Gilger, J.W., 1989. Age of sexual maturation and adult spatial ability. Bull. Psychon. Soc. 27 (3), 241–244.

Geiser, C., Lehmann, W., Eid, M., 2008. A note on sex differences in mental rotation in different age groups. Intelligence 36 (6), 556–563. https://doi.org/10.1016/j.intell.2007.12.003.

Gilger, J.W., Ho, H., 1989. Gender differences in adult spatial information processing: their relationship to pubertal timing, adolescent activities, and sex-typing of personality. Cogn. Dev. 4, 197–214.

Gladue, B.A., Beatty, W.W., Larson, J., Dennis Staton, R., 1990. Sexual orientation and spatial ability in men and women. Psychobiology 18 (1), 101–108. https://doi.org/10.3758/BF03327223.

Graber, J.A., Lewinsohn, P.M., Seeley, J.R., Brooks-Gunn, J., 1997. Is psychopathology associated with the timing of pubertal development? Child Adolesc. Psychiatry 36 (12), 1768–1776. https://doi.org/10.1097/00004583-199712000-00026.

Hamann, S., Stevens, J., Vick, J.H., Bryk, K., Quigley, C.A., Berenbaum, S.A., Wallen, K., 2014. Brain responses to sexual images in 46,XY women with complete androgen insensitivity syndrome are female-typical. Horm. Behav. 66 (5), 724–730. https://doi.org/10.1016/j.yhbeh.2014.09.013.

Hampson, E., Rovet, J.F., Altmann, D., Hampson, E., Altmann, D., 1998. Spatial reasoning in children with congenital adrenal hyperplasia due to 21 - hydroxylase deficiency. Dev. Neuropsychol. 14 (2), 299–320. https://doi.org/10.1080/87565649809540713.

Han, T.S., Bouloux, P.M.G., 2012. Kallmann syndrome and other causes of hypothalamic hypogonadism and related development disorders. Handbook of Neuroendocrinology 597–617. https://doi.org/10.1016/B978-0-12-375097-6.10027-7.

Handelsman, D.J., Sikaris, K., Ly, L.P., 2016. Estimating age-specific trends in circulating testosterone and sex hormone-binding globulin in males and females across the lifespan. Ann. Clin. Biochem. 53 (3), 377–384. https://doi.org/10.1177/0004563215610589.

Hawkes, K., 1990. Why do men hunt? Benefits for risky choices. In: Cashdan, E. (Ed.), Risk and Uncertainty in Tribal and Peasant Economies. Westview Press, Boulder, pp. 146–166.

Hedges, K., Korchmaros, J., 2016. Pubertal timing and substance abuse treatment outcomes: an analysis of early menarche on substance use patterns. Journal of Child and Adolescent Substance Abuse 25 (6), 598–605. https://doi.org/10.1080/1067828X.2016.1171186.

Herlitz, A., Reuterskiöld, L., Lovén, J., Thilers, P.P., Rehnman, J., 2013. Cognitive sex differences are not magnified as a function of age, sex hormones, or puberty development during early adolescence. Dev. Neuropsychol. 38 (3), 167–179. https://doi.org/10.1080/87565641.2012.759580.

Herting, M.M., Gautam, P., Spielberg, J.M., Kan, E., Dahl, R.E., Sowell, E.R., 2014. The role of testosterone and estradiol in brain volume changes across adolescence: a longitudinal structural MRI study. Hum. Brain Mapp. 35 (11), 5633–5645. https://doi.org/10.1002/hbm.22575.

Hews, D.K., Knapp, R., Moore, M.C., 1994. Early exposure to androgens affects adult expression of alternative male types in tree lizards. Horm. Behav. 28, 96–115.

Hier, D.B., Crowley, W.F., 1982. Spatial ability in androgen-deficient men. N. Engl. J. Med. 306 (20), 1202–1205.

Hill, A.K., Bailey, D.H., Puts, D.A., 2017. Gorillas in our midst? Human sexual dimorphism and contest competition in men. In: Tibayrenc, M., Ayala, F.J. (Eds.), On Human Nature: Biology, Psychology, Ethics, Politics, and Religion. Academic Press, pp. 235–249.

Hines, M., 2003. Brain Gender. Oxford University Press.

Hines, M., 2010. Sex-related variation in human behavior and the brain. Trends Cogn. Sci.

14 (10), 448–456. https://doi.org/10.1016/j.tics.2010.07.005.
Hines, M., Ahmed, S.F., Hughes, I.A., 2003. Psychological outcomes and gender-related development in complete androgen insensitivity syndrome. Arch. Sex. Behav. 32 (2), 93–101. https://doi.org/10.1023/A:1022492106974.
Hines, M., Brook, C., Conway, G.S., 2004. Androgen and psychosexual development: core gender identity, sexual orientation, and recalled childhood gender role behavior in women and men with congenital adrenal hyperplasia (CAH). Journal of Sex Research 41 (1), 75–81. https://doi.org/10.1080/00224490409552215.
Hoffman, A.R., Crowley, W.F., 1982. Induction of puberty in men by long-term pulsatile administration of low-dose gonadotropin-releasing hormone. N. Engl. J. Med. 307, 1237–1241.
Hucker, S., Langevin, R., Wortzman, G., Bain, J., Handy, L., Chambers, J., Wright, S., 1986. Neuropsychological impairment in pedophiles. Can. J. Behav. Sci. 18 (4), 440–448. https://doi.org/10.1037/h0079965.
Kaltiala-Heino, R., Kosunen, E., Rimpelä, M., 2003. Pubertal timing, sexual behaviour and self-reported depression in middle adolescence. J. Adolesc. 26 (5), 531–545. https://doi.org/10.1016/S0140-1971(03)00053-8.
Kaltiala-Heino, R., Marttunen, M., Rantanen, P., Rimpelä, M., 2004. Early puberty is associated with mental health problems in middle adolescence. Soc. Sci. Med. 57 (6), 1055–1064. https://doi.org/10.1016/S0277-9536(02)00480-X.
Kaufman, A.S., McLean, J.E., Reynolds, C.R., 1988. Sex, race, residence, region, and education differences on the 11 WAIS-R subtests. J. Clin. Psychol. 44 (2), 231–248. https://doi.org/10.1002/1097-4679(198803)44:2<231::AID-JCLP2270440224>3.0.CO;2-J.
Kercmar, J., Snoj, T., Tobet, S.A., Majdic, G., 2014. Gonadectomy prior to puberty decreases normal parental behavior in adult mice. Horm. Behav. 66 (4), 667–673. https://doi.org/10.1016/j.yhbeh.2014.09.007.
Laitinen, E., Vaaralahti, K., Tommiska, J., Eklund, E., Tervaniemi, M., Valanne, L., 2011. Incidence, phenotypic features and molecular genetics of Kallmann Syndrome in Finland. Orphanet Journal of Rare Diseases 6 (41), 1–10.
Lauer, J.E., Yhang, E., Lourenco, S.F., 2019. The development of gender differences in spatial reasoning: a meta-analytic review. Psychol. Bull. 1–29.
Lee, P.A., Migeon, C.J., 1975. Puberty in boys: correlation of plasma levels of gonadotropins (LH, FSH), androgens (testosterone, androstenedione, dehydroepiandrosterone and its sulfate), estrogens (estrone and estradiol) and progestins (progesterone and 17-hydroxyprogesterone). Journal of Clinical Endocrinology & Metabolism 41 (3), 556–562.
Lee, P.A., Xenakis, T., Winer, J., Matsenbaugh, S., 1976. Puberty in girls: correlation of serum levels of gonadotropins, prolactin, androgens, estrogens, and progestins with physical changes. Journal of Clinical Endocrinology & Metabolism 43 (4), 775–784.
Linn, M.C., Petersen, A.C., 1985. Emergence and characterization of sex differences in spatial ability: a meta-analysis. Child Dev. 56 (6), 1479–1498.
Mansfield, M.J., Beardsworth, D.E., Loughlin, J.S., Crawford, J.D., Bode, H.H., River, J., ... Crowley, W.F., 1983. Long-term treatment of central precocious puberty with a long-acting analogue of luteinizing hormone-releasing hormone. New England Journal of Medicine 309, 1286–1290.
McCarthy, M.M., 2010. How it's made: organisational effects of hormones on the developing brain. J. Neuroendocrinol. 22 (7), 736–742. https://doi.org/10.1111/j.1365-2826.2010.02021.x.
McCarthy, M.M., Herold, K., Stockman, S.L., 2017. Fast, furious and enduring: sensitive versus critical periods in sexual differentiation of the brain. Physiol. Behav. 187 (October 2017), 13–19. https://doi.org/10.1016/j.physbeh.2017.10.030.
Miner, E.J., Gurven, M., Kaplan, H., Gaulin, S.J.C., 2014. Sex difference in travel is concentrated in adolescence and tracks reproductive interests. Proc. R. Soc. B Biol. Sci. 281, 1–8.
Montanini, V., Simoni, M., Chiossi, G., Baraghini, G.F., Velardo, A., Baraldi, E., Marrama, P., 1988. Age-related changes in plasma dehydroepiandrosterone sulphate, cortisol, testosterone, and free testosterone circadian rhythms in adult men. Horm. Res. 29, 1–6.
Moore, D., Johnson, S., 2008. Mental rotation in human infants. Psychol. Sci. 19 (11), 1067–1070. https://doi.org/10.1111/j.1467-9280.2008.02201.x.
Nass, R., Helm, K.D., Evans, W.S., 2013. Physiological and Pathophysiological Alterations of the Neuroendocrine Components of the Reproductive Axis. Yen and Jaffe's Reproductive Endocrinology: Seventh Edition (Seventh Ed). Elsevierhttps://doi.org/10.1016/B978-1-4557-2758-2.00021-4.
Newcombe, N., Dubas, J.S., 1987. Individual differences in cognitive ability: Are they related to timing of puberty? In: Lerner, R.M., Foch, T.T. (Eds.), Child psychology. Biological-psychosocial interactions in early adolescence. Lawrence Erlbaum Associates, Inc., pp. 249–302.
Pazol, K., Northcutt, K.V., Patisaul, H.B., Wallen, K., Wilson, M.E., 2009. Progesterone and medroxyprogesterone acetate differentially regulate α4 subunit expression of GABAA receptors in the CA1 hippocampus of female rats. Physiol. Behav. 97 (1), 58–61. https://doi.org/10.1016/j.physbeh.2009.01.021.
Peper, J.S., Hulshoff Pol, H.E., Crone, E.A., van Honk, J., 2011a. Sex steroids and brain structure in pubertal boys and girls: a mini-review of neuroimaging studies. Neuroscience 191, 28–37. https://doi.org/10.1016/j.neuroscience.2011.02.014.
Peper, J.S., van den Heuvel, M.P., Mandl, R.C.W., Pol, H.E.H., van Honk, J., 2011b. Sex steroids and connectivity in the human brain: a review of neuroimaging studies. Psychoneuroendocrinology 36 (8), 1101–1113. https://doi.org/10.1016/j.psyneuen.2011.05.004.
Peters, M., Lehmann, W., Takanashi, H., Takeuchi, J., 2006. Mental rotation test performance in four cross-cultural samples (n = 3367): overall sex differences and the role of academic program in performance. Cortex 42 (7), 1005–1014.
Peters, M., Manning, J.T., Reimers, S., 2007. The effects of sex, sexual orientation, and digit ratio (2D:4D) on mental rotation performance. Arch. Sex. Behav. 36 (2), 251–260. https://doi.org/10.1007/s10508-006-9166-8.
Petersen, A.C., Crockett, L., Richards, M., Boxer, A., 1988. A self-report measure of pubertal status: reliability, validity, and initial norms. Journal of Youth and Adolescence 17 (2), 117–133.
Primus, R.J., Kellogg, C.K., 1989. Pubertal-related changes influence the development of environment-related social interaction in the male rat. Dev. Psychobiol. 22 (6), 633–643. https://doi.org/10.1002/dev.420220608.
Puts, D.A., 2010. Beauty and the beast: mechanisms of sexual selection in humans. Evol. Hum. Behav. 31 (3), 157–175. https://doi.org/10.1016/j.evolhumbehav.2010.02.005.
Puts, D.A., McDaniel, M.A., Jordan, C.L., Breedlove, S.M., 2008. Spatial ability and prenatal androgens: meta-analyses of congenital adrenal hyperplasia and digit ratio (2D:4D) studies. Arch. Sex. Behav. 37, 100–111. https://doi.org/10.1007/s10508-007-9271-3.
Puts, D.A., Cárdenas, R.A., Bailey, D.H., Burriss, R.P., Jordan, C.L., Breedlove, S.M., 2010. Salivary testosterone does not predict mental rotation performance in men or women. Horm. Behav. 58 (2), 282–289. https://doi.org/10.1016/j.yhbeh.2010.03.005.
Rahman, Q., Wilson, G.D., 2003. Large sexual-orientation-related differences in performance on mental rotation and judgment of line orientation tasks. Neuropsychology 17 (1), 25–31. https://doi.org/10.1037/0894-4105.17.1.25.
Resnick, S.M., Berenbaum, S.A., Gottesman, I.I., Bouchard, T.J., 1986. Early hormonal influences on cognitive functioning in congenital adrenal hyperplasia. Dev. Psychol. 22 (2), 191–198. https://doi.org/10.1037/0012-1649.22.2.191.
Rose, R.M., Kreuz, L.E., Holaday, J.W., Sulak, K.J., Johnson, C.E., 1972. Diurnal variation of plasma testosterone and cortisol. J. Endocrinol. 54 (1), 177–178. https://doi.org/10.1677/joe.0.0540177.
Rosenfeld, R.G., Northcraft, G.B., Hintz, R.L., 1982. A prospective, randomized study of testosterone treatment of constitutional delay of growth and development in male adolescents. Pediatrics 69 (6), 681–687.
Rowe, P.H., Lincoln, G.A., Racey, P.A., Lehane, J., Stephenson, M.J., Shenton, J.C., Glover, T.D., 1974. Temporal variations of testosterone levels in the peripheral blood plasma of men. J. Endocrinol. 61 (1), 63–73.
Sanders, B., Soares, M.P., 1986. Sexual maturation and spatial ability in college students. Dev. Psychol. 22 (2), 199–203.
Schultheiss, O.C., Zimni, M., 2015. Associations between implicit motives and salivary steroids, 2D:4D digit ratio, mental rotation performance, and verbal fluency. Adapt. Hum. Behav. Physiol. 1 (4), 387–407. https://doi.org/10.1007/s40750-014-0012-2.
Schulz, K.M., Sisk, C.L., 2016. The organizing actions of adolescent gonadal steroid hormones on brain and behavioral development. Neurosci. Biobehav. Rev. 70, 148–158. https://doi.org/10.1016/j.neubiorev.2016.07.036.
Schulz, K.M., Richardson, H.N., Zehr, J.L., Osetek, A.J., Menard, T.A., Sisk, C.L., 2004. Gonadal hormones masculinize and defeminize reproductive behaviors during puberty in the male Syrian hamster. Horm. Behav. 45 (4), 242–249. https://doi.org/10.1016/j.yhbeh.2003.12.007.
Schulz, K.M., Menard, T.A., Smith, D.A., Albers, H.E., Sisk, C.L., 2006. Testicular hormone exposure during adolescence organizes flank-marking behavior and vasopressin receptor binding in the lateral septum. Horm. Behav. 50 (3), 477–483. https://doi.org/10.1016/j.yhbeh.2006.06.006.
Schulz, K.M., Molenda-Figueira, H.A., Sisk, C.L., 2009a. Back to the future: the organizational-activational hypothesis adapted to puberty and adolescence. Horm. Behav. 55 (5), 597–604. https://doi.org/10.1016/j.yhbeh.2009.03.010.
Schulz, K.M., Zehr, J.L., Salas-Ramirez, K.Y., Sisk, C.L., 2009b. Testosterone programs adult social behavior before and during, but not after, adolescence. Neuroendocrinology 150 (8), 3690–3698. https://doi.org/10.1210/en.2008-1708.
Seminara, S.B., Hayes, F.J., Crowley, W.F., 1998. Gonadotropin-releasing hormone deficiency in the human (idiopathic hypogonadotropic hypogonadism and Kallmann's syndrome): pathophysiological and genetic considerations. Endocr. Rev. 19 (5), 521–539.
Shirtcliff, E.A., Dahl, R.E., Pollak, S.D., 2009. Pubertal development: correspondence between hormonal and physical development. Child Dev. 80 (2), 327–337.
Shrenker, P., Maxson, S.C., Ginsburg, B.E., 1985. The role of postnatal testosterone in the development of sexually dimorphic behaviors in DBA/1Bg mice. Physiol. Behav. 35 (5), 757–762. https://doi.org/10.1016/0031-9384(85)90408-1.
Sisk, C.L., Zehr, J.L., 2005. Pubertal hormones organize the adolescent brain and behavior. Front. Neuroendocrinol. 26 (3–4), 163–174. https://doi.org/10.1016/j.yfrne.2005.10.003.
Smith, L.K., Forgie, M.L., Pellis, S.M., 1998. Mechanisms underlying the absence of the pubertal shift in the playful defense of female rats. Dev. Psychobiol. 33 (2), 147–156. https://doi.org/10.1002/(SICI)1098-2302(199809)33:2<147::AID-DEV5>3.0.CO;2-J.
Spearman, C., 1904. "General intelligence," objectively determined and measured. Am. J. Psychol. 15 (2), 201–292.
Stearns, S.C., 1976. Life-history tactics: a review of the ideas. Q. Rev. Biol. 51 (1), 3–47.
Tellegen, A., Briggs, P.F., 1967. Old wine in new skins: grouping Wechsler subtests into new scales. J. Consult. Psychol. 31 (5), 499–506.
Thornton, J., Zehr, J.L., Loose, M.D., 2009. Effects of prenatal androgens on rhesus monkeys: a model system to explore the organizational hypothesis in primates. Horm. Behav. 55 (5), 633–644. https://doi.org/10.1016/j.yhbeh.2009.03.015.
Tschann, J.M., Adler, N.E., Irwin, C.E., Millstein, S.G., Turner, R.A., Kegeles, S.M., 1994. Initiation of substance use in early adolescence: the roles of pubertal timing and emotional distress. Health Psychol. 13, 326–333.
Ullsperger, J.M., Nikolas, M.A., 2017. A meta-analytic review of the association between pubertal timing and psychopathology in adolescence: are there sex differences in risk? Psychol. Bull. 143 (9), 903–938.
Vance, S.R., Ehrensaft, D., Rosenthal, S.M., 2014. Psychological and medical care of gender nonconforming youth. Pediatrics 134 (6), 1184–1192. https://doi.org/10.1542/peds.2014-0772.

Vandenberg, S.G., Kuse, A.R., 1978. Mental rotations, a group test of three-dimensional spatial visualization. Percept. Mot. Skills 47 (2), 599–604.
Voyer, D., Voyer, S., Bryden, M.P., 1995. Magnitude of sex differences in spatial abilities: a meta-analysis and consideration of critical variables. Psychol. Bull. 17 (2), 250–270.
Vuoksimaa, E., Kaprio, J., Eriksson, C.J.P., Rose, R.J., 2012. Pubertal testosterone predicts mental rotation performance of young adult males. Psychoneuroendocrinology 37 (11), 1791–1800. https://doi.org/10.1016/j.psyneuen.2012.03.013.
Waber, D., 1976. Sex differences in cognition: a function of maturation rate? Science 192 (4239), 572–574.
Wallen, K., 2005. Hormonal influences on sexually differentiated behavior in nonhuman primates. Front. Neuroendocrinol. 26 (1), 7–26. https://doi.org/10.1016/j.yfrne.2005.02.001.
Wallen, K., 2009. The organizational hypothesis: reflections on the 50th anniversary of the publication of Phoenix, Goy, Gerall, and Young (1959). Horm. Behav. 55 (5), 561–565. https://doi.org/10.1016/j.yhbeh.2009.03.009.
Wechsler, D., 1981. WAIS-R Manual: Wechscler Adult Intelligence Scale-revised. Psychological Corporation, New York, NY.
Wells, J.C.K., Nesse, R.M., Sear, R., Johnstone, R.A., Stearns, S.C., 2017. Evolutionary public health: introducing the concept. Lancet 390, 500–509. https://doi.org/10.1016/S0140-6736(17)30572-X.
Wilson, D., Killen, J.D., Hayward, C., Robinson, T.N., Hammer, L.D., Kraemer, H.C., ... Taylor, C.B., 1994. Timing and rate of sexual maturation and the onset of cigarette and alcohol use among teenage girls. Archives of Pediatrics and Adolescent Medicine 148, 789–795.
Witchel, S.F., Plant, T.M., 2013. Puberty: Gonadarche and Adrenarche. Yen and Jaffe's Reproductive Endocrinology: Seventh Edition (Seventh Ed). Elsevierhttps://doi.org/10.1016/B978-1-4557-2758-2.00018-4.
Zehr, J.L., Culbert, K.M., Sisk, C.L., Klump, K.L., 2007. An association of early puberty with disordered eating and anxiety in a population of undergraduate women and men. Horm. Behav. 52 (4), 427–435. https://doi.org/10.1016/j.yhbeh.2007.06.005.