Psychiatry Research 229 (2015) 953–959

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Congenital Adrenal Hyperplasia, Polycystic Ovary Syndrome and criminal behavior: A Swedish population based study

Agnes Ohlsson Gotby [a,*], Anna Nordenström [b,c], Henrik Falhammar [b,d], Agneta Nordenskjöld [e,f,g], Angelica Linden Hirschberg [e,h], Louise Frisén [i,j], Mikael Landén [a,k], Paul Lichtenstein [a]

[a] Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, PO Box 281, SE-171 77 Stockholm, Sweden
[b] Departments of Molecular Medicine and Surgery, Karolinska University Hospital, Solna (L1:00), SE-171 76 Stockholm, Sweden
[c] Department of Pediatric Endocrinology, Astrid Lindgren Children Hospital, Karolinska University Hospital, SE- 171 76 Stockholm, Sweden
[d] Department of Endocrinology, Metabolism, and Diabetes, Karolinska University Hospital, SE-171 76 Stockholm, Sweden
[e] Department of Women's and Children's Health, Karolinska Institutet, SE-171 76 Stockholm, Sweden
[f] Center for Molecular Medicine, Karolinska Institutet, SE-171 76 Stockholm, Sweden
[g] Department of Pediatric Surgery, Astrid Lindgren Children Hospital, Karolinska University Hospital, SE-171 76 Stockholm, Sweden
[h] Department of Obstetrics and Gynaecology, Karolinska University Hospital, SE-171 76, Stockholm, Sweden
[i] Department of Clinical Neuroscience, Karolinska Institutet, SE-171 77 Stockholm, Sweden
[j] Child and Adolescent Psychiatry Research Center, Karolinska Institutet, SE-171 77 Stockholm, Sweden
[k] Institute of Neuroscience and Physiology, University of Gothenburg, Box 430, SE-405 30 Gothenburg, Sweden

ARTICLE INFO

Article history:
Received 24 October 2014
Received in revised form
15 June 2015
Accepted 5 July 2015
Available online 29 July 2015

Keywords:
Prenatal androgens
Androgens
Hyperandrogenism
Testosterone
Delinquency
Violent crime
Sex crime

ABSTRACT

Both prenatal and circulating testosterone and other androgens have been suggested to influence the individual's propensity to commit crime, but empirical evidence is limited and inconsistent. Congenital Adrenal Hyperplasia (CAH) and Polycystic Ovary Syndrome (PCOS) are both hyperandrogenic conditions but with an important difference; whereas subjects with CAH are exposed to high concentrations of androgens in utero, women with PCOS are subjected to high androgens in adulthood. Comparing these groups can therefore yield important insights of androgenic effects on behavior. In the current study, information on medical diagnoses and convicted crimes were gathered from Swedish population-based registers. The associations between diagnoses of CAH or PCOS and any crime, violent crime or sex crime were estimated with conditional logistic regression. Results showed that CAH in women and men did not predict criminality, whereas an increased risk for any crime and violent crime was found in PCOS women. Our findings indicate that female hyperandrogenism in adulthood, but not prenatal hyperandrogenism, is associated with risk for criminal behavior. Further research into hyperandrogenic conditions holds opportunities to deepen our understanding of the etiology of crime and psychopathology.

1. Introduction

Testosterone and other androgens affect not only physical but also behavioral masculinization (Cooke et al., 1998; Knickmeyer and Baron-Cohen, 2006; Hines, 2011). A possibility is that variations in androgen exposure can influence the individual's propensity to commit crime (Yildirim and Derksen, 2012b). However, empirical studies of the effect of testosterone and other androgens on crime-related outcomes have yielded inconsistent results. Circulating testosterone has been associated with antisocial behavior in young boys (Chance et al., 2000), delinquency in adolescent males (Maras et al., 2003; Fang et al., 2009), deviant behavior among male army veterans (Dabbs and Morris, 1990; Mazur, 1995), and with antisocial personality disorder or psychopathic traits in men (Virkkunen and Linnoila, 1993; Stalenheim et al., 1998; Rasanen et al., 1999; Aromaki et al., 1999, 2002). On the other hand, other studies have failed to show differences in testosterone levels between behaviorally disruptive boys (van Goozen et al., 1998; Dorn et al., 2009) or criminal subjects (Stalenheim et al., 1998) and healthy controls. Furthermore, one study found a negative association between testosterone and delinquency in girls, and no significant association in boys (Granger et al., 2003). Other androgens are less explored, but some studies have found associations between dehydroepiandrosterone sulfate (van Goozen et al., 2000; Golubchik et al., 2009), androstenedione (van Goozen et al.,

Abbreviations: CAH, Congenital Adrenal Hyperplasia; PCOS, Polycystic Ovary Syndrome; OAD, Other Adrenogenital Disorders

* Corresponding author.
E-mail address: agnes.gotby@ki.se (A. Ohlsson Gotby).

http://dx.doi.org/10.1016/j.psychres.2015.07.008
0165-1781/

1998; Dorn et al., 2009) and oppositional defiant disorder or conduct disorder in boys. However, a study of prepubertal boys (Constantino et al., 1993) and another study of adolescent girls (Pajer et al., 2006) found no such association.

A limitation in previous studies is that many have measured total testosterone only and not in association with sex hormone-binding globulin (e.g., Dabbs and Morris, 1990; Mazur, 1995), which can be affected by, for example, liver damage in contrast to the unbound bioavailable proportion of free testosterone. This may have confounded earlier result, considering that most studies have been conducted on criminal populations where alcohol and drug abuse might affect both total testosterone and risk for criminal offending (Aluja and Garcia, 2007).

It is also unclear if exposure to prenatal levels of androgens influence crime propensity. Hormonal effects are often classified as organizational (permanent changes that occur early in development) or activational (later effects that are transient and superimposed on earlier changes; Phoenix et al., 1959). However, prenatal androgens are difficult to investigate directly in humans and the association between prenatal androgens and criminal behavior has, until recently, been scarcely studied (Yildirim and Derksen, 2012b). Nonetheless, some studies have shown associations between low second-to-fourth digit ratio (2D:4D; a proxy for exposure to androgens in utero) and criminality (Hanoch et al., 2012, Hoskin and Ellis 2014), traffic violations (Schwerdtfeger et al., 2010) and self-reported criminal behavior (Ellis and Hoskin, 2013). However, other studies have not been able to show this effect (Blanchard and Lyons, 2010; Anderson, 2012). Moreover, the digit ratio is not a direct measurement of exposure to androgens in utero and its reliability has been discussed (Putz et al., 2004). Therefore, it is important to corroborate the indications of associations between prenatal effects and criminality by other methods. One possibility is to compare individuals who have been differentially exposed to androgens in utero because of disorders of sex development, so called experiments of nature. Yet, this has not been done previously.

The aim of this study was to investigate the association between prenatal hyperandrogenism or hyperandrogenism in adulthood and criminal behavior, by comparing individuals with congenital adrenal hyperplasia (CAH, associated with increased prenatal androgens) or polycystic ovary syndrome (PCOS, associated with hyperandrogenism in adulthood) with unaffected population-based controls. CAH is most often caused by mutations in the *CYP21A2* gene that leads to an impaired synthesis of cortisol and aldosterone, shunting cortisol precursors through the androgen synthetic pathway leading to a prenatal excess of androgens. After diagnosis, the child is treated with glucocorticoids, which normalize androgen levels (Merke and Bornstein, 2005). PCOS, by contrast, is characterized by excessive androgen production, polycystic ovaries, and chronic anovulation and is a frequent endocrine disorder in women of reproductive age (Norman et al., 2007). Neither CAH nor PCOS are the result of hepatic insufficiency due to alcohol or illicit drug use; thereby we overcome limitations in earlier studies measuring total testosterone. We hypothesized increased rates of convictions among individuals diagnosed with both (a) disorders of prenatal hyperandrogenism (i.e., CAH) and (b) disorders of hyperandrogenism in adulthood (i.e., PCOS), that is both organizational and activational effects.

2. Methods

2.1. National registers

The study was conducted by linkage of several longitudinal nationwide population-based registers in Sweden: the *National Patient Register* (held by the National Board of Health and Welfare) contains nearly all inpatient and day surgery records since 1964 and outpatient records since 2001; the *Medical Birth Register* (National Board of Health and Welfare) holds information about all births in Sweden since 1973; the *National CAH Register* (held by the Swedish screening laboratory) encompasses most patients with confirmed *CYP21A2* deficiency born since 1910; the *Multi-Generation Register* (Statistics Sweden) contains information about relationships between people born after 1932, and nationally registered after 1961, and their parents or adoptive parents; *Migration Records* (Statistics Sweden) contains registered migrations since 1901; the *Integrated Database for Labor Market Research* (Statistics Sweden) has data of income, education, occupation, employment status, social transfers, and so forth since 1990; the *Register of Education* (Statistics Sweden) holds information about highest finished education level for the years 1985–1989; the *Population and Housing Census* (Statistics Sweden) contains individual, household and dwelling data for year 1960–1990; the *National Crime Register* (Swedish National Council for Crime Prevention) covers all registered convictions since 1973 and the *Cause of Death Register* (National Board of Health and Welfare) contains all registered deaths since 1952 and their causes. In the present study, information until the end of year 2009 was used.

In Sweden, every resident receives a unique ten-digit personal identity number. This constitutes a key to interconnect different records, and enables register research on non-identifiable data.

2.2. Identification of study cases

The study has a population-based matched cohort design. Patients with CAH ($n=572$) were identified in the National CAH register (Gidlöf et al., 2013). Additionally 748 people diagnosed with CAH were identified in the National Patient and Medical Birth Registers. Women with a PCOS diagnose ($n=16\ 218$) were abstracted from the National Patient Register (Fig. 1).

In addition, we identified 915 people that had received the diagnose other adrenogenital disorders (OAD) in the National Patient Register. OAD is an unspecific diagnose for conditions were circulating androgens are increased without any known cause. These patients were included as a separate group to corroborate potential findings in PCOS women.

In the National Patient Register and the Medical Birth Register, discharge diagnoses are coded according to the International Classification of Diseases (ICD). Diagnostic codes of interest were grouped as CAH, PCOS, and OAD according to the International Classification of Disease-10 manual (see Table 1).

2.3. Exclusions

CAH is a serious condition that requires lifelong medication with glucocorticoids. Thus several notations in the National Patient Register are expected. Therefore, CAH patients diagnosed with CAH less than three times and without confirmed *CYP21A2* deficiency were excluded ($n=568$; Fig. 1). The 180 patients that remained from the Medical Birth Register and the National Patient Register were further scrutinized. Those who had subsequently been given other diagnoses (i.e., Addison's disease, Cushing's syndrome, acromegaly), or had received glucocorticoid treatment due to malignancies were excluded ($n=137$). Twelve patients in the National CAH Register had incomplete personal identification number, 13 cases were not identified in the Multi-Generation Register, and additionally two cases had personal identification number that had been reused. These patients ($n=27$) were consequently excluded. This process has been described in detail previously (Falhammar et al., 2014).

Cases that had received more than one diagnosis ($n=150$) were