Psychological stress and testicular function: a cross-sectional study of 1,215 Danish men

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Objective: To study the associations between self-reported psychological stress, semen quality, and serum reproductive hormones among young Danish men.
Design: Cross-sectional study.
Setting: University hospital-based research center.
Participant(s): Danish men (median age 19 years) from the general population were investigated from 2008 to 2012.
Intervention(s): Participants completed a questionnaire on health and lifestyle, including a four-item questionnaire about self-rated stress, had a physical examination performed, delivered a semen sample, and had a blood sample drawn.
Main Outcome Measure(s): Semen parameters (semen volume, sperm concentration, and percentages of motile and morphologically normal spermatozoa) and serum levels of reproductive hormones (LH, FSH, T, calculated free T, sex hormone–binding globulin, and inhibin B).
Result(s): Poorer semen quality was detected among men with self-reported stress scores above an intermediate stress level, in a dose–response manner. For example, men with the highest stress levels had 38% (95% confidence interval [CI] 3%; 61%) lower sperm concentration, 34% (95% CI 59%; 106%) lower total sperm count, and 15% (95% CI 1%; 27%) lower semen volume than men with intermediate stress levels. No significant associations between self-reported stress and levels of reproductive hormones were detected.
Conclusion(s): A negative association between self-reported stress and semen quality was detected. If causal, stress may be a contributing factor for suboptimal semen quality among otherwise healthy men. (Fertil Steril® 2015;■:■–■. ©2015 by American Society for Reproductive Medicine.)
Key Words: Stress, semen quality, sperm concentration, reproductive hormones, normal men

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Prospective studies of men from the general populations of several European countries have shown a high frequency of men with a non-optimal semen quality (1, 2). Approximately 40% of young Danish men have sperm counts at a level that may reduce fecundity (3). The underlying etiology for the majority of men with impaired semen quality is unknown. Poor semen quality is not only associated with a reduced likelihood of conception but also with increased all-cause mortality (4). A recent national survey, the Danish Work Environment and Health Cohort in 2012 and 2014, showed that psychological stress is common. Approximately 15% of Danish men and women consider themselves as having "high" or "very high" stress levels (5). Psychological stress has been linked to higher mortality and various diseases, including cardiovascular disease, obesity, and components of the metabolic syndrome (6–9).

Several studies have investigated associations between semen quality and stress due to different types of stressors: occupational stress, stressful life events, stress due to infertility, etc.

Received June 1, 2015; revised August 21, 2015; accepted September 10, 2015.
L.N. has nothing to disclose. T.K.J. has nothing to disclose. Å.M.H. has nothing to disclose. T.H.L. has nothing to disclose. A.K.B. has nothing to disclose. U.N.J. has nothing to disclose. M.B.J. has nothing to disclose. N.E.S. has nothing to disclose. N.J. has nothing to disclose.
This work was supported by Rigshospitalet (grant 961506336); European Union (grant FP7/2007-2013, agreement no. 212844), DEER (grant agreement 212844); The Danish Ministry of Health and The Danish Environmental Protection Agency; Kirsten and Freddy Johansen's Foundation (grant 95-103-72087); and Aase and Ejnar Danielsen's Fond, the Research Fund of Rigshospitalet (grant R42-A1326). The sponsors of the study had no role in study design, data collection, analysis, interpretation, or writing the article.
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Fertility and Sterility® Vol. ■, No. ■, ■ 2015 0015-0282/$36.00

http://dx.doi.org/10.1016/j.fertnstert.2015.09.016

(summarized in Table 1). Overall, these earlier studies provide evidence that semen quality is impaired by psychological stress. However, many studies were small and dealt with selected study populations, mostly infertile men, did not take into account confounding factors, or used a variety of different tools to assess stress, making comparison across studies difficult.

We undertook a cross-sectional study of young Danish men to elucidate whether stress might be a contributing factor that negatively affects semen quality in men who are unselected regarding fertility status and semen quality. On the basis of the literature, stress was expected to have a negative impact on testicular function.

MATERIALS AND METHODS

Study Population

In Denmark all men, except those suffering from severe or chronic diseases (<15%), are required to attend a medical examination before being considered for military service. Men are called upon to present themselves at the age of 18–19 years, but some postpone this examination until completion of their education. Men attending the medical examinations are therefore considered representative of the general population of young men. In collaboration with the military health authority, men attending these medical examinations in the greater Copenhagen area of Denmark have since 1996 been invited to participate in the present study of testicular function, irrespective of whether they were declared fit for military service. Those men who consented to participate were given an appointment for examination at the Department of Growth and Reproduction at Rigshospitalet (Copenhagen, Denmark). Participants were instructed to abstain from ejaculation for at least 48 hours before attendance at Rigshospitalet, where each man returned a completed questionnaire, underwent a physical examination, and provided a semen sample. Participants received a financial compensation (approximately 65€).

In total, 1,215 men examined in the study from April 2008 to April 2012 were included in the present study, because the questionnaire they completed included information about stress. In that period 1,243 men had been examined, but 28 men were excluded from the present study for the following reasons: missing stress data from questionnaire (n = 6), missing data on total sperm count and sperm concentration (n = 2), ejaculatory duct obstruction (n = 5), diagnosis of testicular cancer during the study (n = 1), previous treatment of malignant diseases (n = 2), previous surgery of vas deferens (n = 1), and self-reported use of anabolic steroids (n = 10). None of the participants were treated with T for medical reasons. Participants did not differ from nonparticipants with regard to age, but they were generally better educated than nonparticipants (data not shown). A detailed description and other aspects of the study have previously been published (3).

Questionnaire

Before participation in the study the participants completed a questionnaire that included both specific stress questions and more general questions on lifestyle and health.

Stress questions. The questionnaire included four items about perceived stress during the 4 weeks before participation in the study. These four items constitute the stress-related part of The Copenhagen Psychosocial Questionnaire (10) and were chosen because of extensive validation in the Danish population (10). The questions were as follows: How often have you [1] "had problems relaxing," [2] "been irritable," [3] "been tense," and [4] "felt stressed"? Answer categories for each question were: "All the time" (100 points), "a large part of the time" (67 points), "rarely" (33 points), and "never" (0 points). Points were summed and divided by 4 to obtain a mean score per individual item, as described in the Copenhagen Psychosocial Questionnaire (10, 11). Thereafter, the men were classified into different stress groups according to their individual mean stress score, as described later.

General questions. The participants in the study also answered questions providing information on previous or current systemic and genital diseases, including inguinal hernia, varicocele, hydrocele, epididymitis, sexually transmitted diseases, cryptorchidism, hypospadias, testicular torsion or cancer, and mumps. Information on lifestyle factors, medication, number of years of schooling, and number of hours spent on light, medium, and hard exercise was also gathered. The estimated caffeine intake during the week before participation in the study was calculated from reported intake of caffeine-containing beverages and chocolate, as described elsewhere (12, 13). Alcohol intake within the week before participation was quantified as previously described (14). Cigarette smoking status was dichotomized into nonsmokers and smokers (including daily, weekly, and less than weekly smoking). Hashish and marijuana smoking and mother's smoking during pregnancy were dichotomized in the same way. Self-rated physical fitness was coded as three categories: good/very good, acceptable, and poor/very poor. Information about length of maternal education was coded as "less than 9 years," "9–10 years," and "more than 10 years." Information regarding fever above 38°C (100.4°F) within the previous 3 months was obtained.

Physical Examination

The physical examinations included evaluation of Tanner stage of pubic hair, genital development, testicular volume (determined by use of a Prader orchidometer), the possible presence of a varicocele (stage 1–3) or hydrocele, location of the testes, and consistency of the testis and epididymides. Scrotal ultrasound was performed on all men. Body weight and height was measured and body mass index (BMI) calculated as weight in kilograms divided by squared height in meters.

Semen Analysis

All men provided a semen sample by masturbation in a room close to the semen laboratory. The duration of ejaculation abstinence (time since last ejaculation) was recorded, and the sample was analyzed for volume, sperm concentration, total sperm count, motile spermatozoa, and morphologically