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SHORT COMMUNICATION

Hair testosterone and visuospatial memory in middle-aged men and women with and without depressive symptoms

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Summary
Background: Testosterone binds to androgen receptors, which can be found abundantly in the hippocampus. Associations between testosterone levels and visuospatial memory have been reported, albeit with inconsistent results. Previous studies have used point sampling of testosterone levels (blood, saliva) rather than long-term secretion measures. Hair analysis for steroids allows for retrospective ascertainment of cumulative steroid measures over several months. We examined hair testosterone and its association with verbal and visuospatial memory in middle-aged men and women with and without major depression.
Methods: We examined a total of 73 middle-aged individuals (35 depressed patients, and 38 age-, sex- and education-matched healthy subjects). We tested verbal (Auditory Verbal Learning Task) and visuospatial (Rey figure) memory and measured testosterone in the hair by liquid chromatography tandem mass spectrometry.
Results: Hair testosterone levels did not differ between patients and controls (mean 1.35 pg/mg vs. 1.40 pg/mg, SD 0.61 and 0.80, respectively). In men ($n = 24$) but not women ($n = 49$), hair testosterone was associated with visuospatial memory in a multiple regression analysis after controlling for age, education, body mass index, and depression (adjusted $R^2 = 0.56$).

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Conclusions: With the new method of testosterone measurement in hair allowing for long-term cumulative ascertainment of testosterone secretion, we extend recent results of a male-specific role for testosterone in visuospatial memory.

1. Introduction

Testosterone is an anabolic steroid hormone and belongs to the androgen group. It is secreted by the testicles in men and ovaries in women, and, in some part, by the adrenal glands. Testosterone exerts its effects in many parts of the body including muscles, bones, hematopoietic system, reproductive and sexual organs, and adipose tissue. In the brain, testosterone binds to androgen receptors, which can be found abundantly in the hippocampus (Beyenburg et al., 2000), a region of the brain closely involved in verbal and visuospatial memory.

Interestingly, studies using cell cultures and in vivo animal models showed that testosterone promotes neuroprotection including dendritic sprouting and increased expression of nerve growth factor in the hippocampus (see Hogervorst et al., 2010 for review). Consequently, studies have investigated associations between testosterone levels and hippocampus-dependent verbal and visuospatial memory, albeit with inconsistent results. Most rodent studies showed that gonadectomy leads to impaired memory performance in hippocampus-dependent tasks with restorage of memory performance through testosterone replacement in male rats (Kritzer et al., 2001; Edinger and Frye, 2004).

However, in humans results are equivocal. In line with rodent models, Moffat and colleagues demonstrated in large prospective studies with healthy elderly males that low baseline plasma testosterone levels were associated with worse performance on measures of visuospatial memory during follow-up (Moffat et al., 2002, 2004). Consistent with these results, Ackermann et al. (2012) demonstrated a role for testosterone in enhancing memory through increased brain activation in the amygdala during encoding. They found that higher salivary testosterone levels at encoding were associated with a greater number of freely recalled neutral pictures in men but not in women. Martin et al's cross-sectional study results, however, show poorer memory performance with higher testosterone levels in men over fifty years of age (Martin et al., 2007, 2008). In sum, the relationship between testosterone levels and memory function remains somewhat unclear.

There are a number of reasons why human studies on testosterone and its effect on memory may present with controversial results. First, the type of memory process that is being investigated may play an important role (e.g., hippocampus-dependent vs. other brain area-dependent memory functions). Second, the age range of the participants may be important because most studies investigated elderly men (e.g., Moffat et al., 2002, 2004; Martin et al., 2007, 2008). Third, health factors may be important to control for, especially in elderly samples (e.g. body mass index). Finally, so far, all studies have used blood or saliva sampling for ascertainment of testosterone levels. Blood and saliva samples represent point samples reflecting momentary testosterone levels, which undergo a circadian rhythm. Some criticize that salivary testosterone measurements are highly unreliable as cotton collection devices, storage time and temperature may bias testosterone levels (Wirth et al., 2012). Hence, for associations with compromised memory, a cumulative measure of testosterone may be of much greater importance.

Recently, hair analysis for steroids has been introduced to the field of biopsychology. Hair analysis allows for the retrospective ascertainment of cumulative steroid levels over several months (Dettenborn et al., 2012; Stalder and Kirschbaum, 2012; Russell et al., 2012). Here, we present for the first time, hair testosterone levels and their association to cognitive functioning in middle-aged men and women with and without depressive symptoms.

2. Methods

2.1. Subjects

As part of a larger study specifically designed to study hair steroids in depressed and non-depressed individuals, we recruited 35 in- and outpatients (24 women and 11 men, mean age 42.3, SD 11.6) from specialized depression clinics at the Department of Psychiatry and Psychotherapy and the Department of Psychosomatic Medicine, University Medical Center Hamburg (Germany) with a diagnosis of major depressive disorder, single or recurrent according to DSM-IV criteria and a minimum baseline score of 18 points on the Hamilton Rating Scale for Depression, 17-item version (HAMD-17). Patients were moderately depressed with a mean HAMD-17 score of 22.0 (SD 4.1) and a mean Beck Depression Inventory (BDI) score of 32.1 (SD 9.2). Whereas 17 patients were free of psychotropic medication, 18 patients were treated with SSRIs ($n = 7$), SNRI ($n = 1$), SSNRI ($n = 4$), Mirtazapin ($n = 2$), Agomelatine ($n = 1$), St. Johns Worth ($n = 2$), and Opipramol ($n = 1$). Criteria for exclusion were dementia, schizophrenia spectrum disorder, bipolar disorder, substance dependence < 6 months, serious medical conditions, pregnancy, and nursing.

A control group of 38 healthy subjects (25 women, 13 men, mean age 41.5 years, SD 10.5) matched for age, sex, and years of education were enrolled in the study. Subjects were free of former and present DSM-IV axis I disorders according to the MINI-interview, had no physical illness, and had been free of any medication at least 3 months prior to study entry.

The study was approved by the local ethics committee. After complete description of the study to the subjects, written informed consent was obtained.

2.1.1. Hormonal assessment

Hair strands of a total thickness of approximately 3 mm (diameter) were taken from the scalp — near posterior vertex position. Testosterone concentrations were determined from