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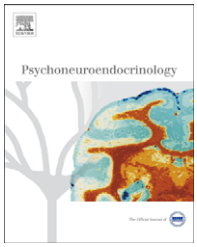

Associations between sex steroid hormone levels and depressive symptoms in elderly men and women: Results from the Health ABC study

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Summary
Introduction: Sex steroid hormone levels decline with age and in some studies this decline has been linked with depressive symptoms. This study investigates the association between total testosterone, free testosterone, and DHEAS levels with depressive symptoms in a well-functioning elderly population.
Methods: Data are from 2855 well-functioning elderly men and women, 70–79 years of age, participating in the Health, Aging, and Body Composition study. Depressive symptoms were measured using the Center for Epidemiologic Studies Depression scale. Total testosterone, free testosterone, and DHEAS levels were assessed after an overnight fast.
Results: In men and women, DHEAS levels and depressive symptoms were inversely associated after adjustment for covariates (men: $\beta = -0.059$, $p = 0.03$, women: $\beta = -0.054$, $p = 0.05$). In addition, free testosterone levels in women, but not in men, were inversely associated with depressive symptoms (adjusted $\beta = -0.079$, $p = 0.004$). Men, but not women, in the lowest total testosterone quartile reported significantly more

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depressive symptoms than men in the other total testosterone quartiles (adjusted $\beta = -0.166$, $p = 0.04$).
Discussion: Our study is consistent with the idea that testosterone and DHEAS levels may play a role in mechanisms underlying depressive symptoms in old age.

1. Introduction

Neuroendocrine dysfunction plays an important role in the pathogenesis of depression. Although most attention of existing research has focused on the role of cortisol (Parker et al., 2003), several studies suggest that testosterone and the adrenal androgen dehydroepiandrosterone-sulfate (DHEAS) may also be important in the development of depression (Berr et al., 1996; Heuser et al., 1998; Yaffe et al., 1998; Schweiger et al., 1999; Barrett-Connor et al., 1999a b; Weber et al., 2000; Morrison et al., 2001; Seidman et al., 2001, 2002; Kaneda and Fujii, 2002; Breuer et al., 2002; Erdincler et al., 2004; Shores et al., 2005; T'Sjoen et al., 2005).

Animal studies have shown that dehydroepiandrosterone (DHEA) and its sulfated conjugated metabolite DHEAS have anti-depressant effects through their modulation of neurotransmitter systems in the brain (Majewska et al., 1990; Majewska, 1992). Consistent with this, epidemiological studies in men and women have shown inverse associations between serum levels of DHEAS and depressive symptomatology (Berr et al., 1996; Yaffe et al., 1998; Barrett-Connor et al., 1999a; Morrison et al., 2001). However, other studies show a positive relationship (Heuser et al., 1998; Weber et al., 2000; Morrison et al., 2001; T'Sjoen et al., 2005) or no relationship (Breuer et al., 2002; Erdincler et al., 2004), which may reflect age differences in the study samples. For example, Morrison et al. (2001) found that the link between DHEAS and depressive symptoms was inverse in old age, but positive in younger persons.

Estradiol and its precursor testosterone have been shown to increase neurotransmitter function, due to synaptogenesis, receptor function, and neurotransmitter metabolism, which favorably affects mood (McEwen, 1991). Consistent with this premise, lower levels of testosterone in older men have been associated with more depressive symptoms (Schweiger et al., 1999; Barrett-Connor et al., 1999b; Shores et al., 2005) which seem to disappear with testosterone hormone treatment (Wang et al., 1996; Perry et al., 2002). For women, in contrast, either a positive association between testosterone levels and depressive symptoms has been found (Weber et al., 2000) or no association was uncovered (Barrett-Connor et al., 1999a; Breuer et al., 2002; Erdincler et al., 2004).

Of the studies that investigated the association between sex steroid hormone levels and depressive symptoms (Berr et al., 1996; Heuser et al., 1998; Yaffe et al., 1998; Schweiger et al., 1999; Barrett-Connor et al., 1999a, b; Weber et al., 2000; Morrison et al., 2001; Seidman et al., 2001, 2002; Kaneda and Fujii, 2002; Breuer et al., 2002; Erdincler et al., 2004; Shores et al., 2005; T'Sjoen et al., 2005), only a few studies included a large sample (e.g. more than 200 participants), (Berr et al., 1996; Yaffe et al., 1998; Barrett-Connor et al., 1999a b; Morrison et al., 2001; Seidman et al., 2001; T'Sjoen et al., 2005). Furthermore, most of these studies had a wide age range, and thus included participants at different stages during their menopause or andropause. Especially with age the sex steroid hormone levels tend to decrease and therefore it is important to investigate whether these lower levels are accompanied with higher depressive symptoms (for a review see Lamberts et al., 1997). Also, several studies included men or women only, which gives little insight into the consistency of the association between sex steroid hormones or DHEAS and depression across gender. Berr et al. (1996) investigated sex steroid hormone synthesis in both men and women, but they only considered DHEAS and no other sex steroid hormones.

The primary aim of the present study was to investigate the associations between depressive symptoms with DHEAS, total testosterone (Total T) and free testosterone (Free T) levels in older (70–79 years) men and women in a large, well-functioning population. Since racial differences have been found for the association between depressive symptoms and sex steroid hormone levels (Morrison et al., 2001), this study also explores potential race interactions.

2. Methods

2.1. Subjects

Data are from the Health, Aging and Body Composition (Health ABC) study, a prospective cohort study of 3075 well-functioning elderly, aged 70–79 years at baseline. Between April 1997 and June 1998, participants were recruited from Medicare-eligible adults residing in the areas surrounding Pittsburgh, Pennsylvania and Memphis, TN. Selected subjects were able to communicate with the interviewer and were free of functional limitations, defined as difficulty walking $\frac{1}{4}$ mile or walking up 10 steps without resting and difficulty with activities in daily living. Exclusion criteria were an active cancer treatment in the past 3 years or plan to move out of the area within the next 3 years.

Participants were excluded from the analyses if they had missing Center for Epidemiologic Studies Depression (CES-D) scale data ($n = 24$), no sex hormone data ($n = 33$), or were using inhaled or oral steroid hormones ($n = 134$). Women with extremely high Total T values (above 130 ng/dl) were also excluded ($n = 29$), because these women probably had (subclinical) disease, were using androgens, or had erroneous hormone assay results that may lead to these high levels. Finally, we maintained 2855 participants for the present analysis. Excluded persons were more likely to be women, but did not differ by age or education.