Low Dehydroepiandrosterone Reflects Reduced Physical Vitality Beyond the Influence of Chronological Age

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Background
Dehydroepiandrosterone (DHEA) and its sulfated form (DHEAS), are the most abundant steroid hormones in human circulation, and are important precursors of androgen and estrogen biosynthesis. DHEAS and DHEA decline dramatically with age, and some studies indicate the decrease parallels age-related impairments in physical and mental abilities. Lower DHEAS/DHEA can also occur in early adulthood, and then may be associated with lower physical vitality. We determined whether DHEAS and DHEA were correlated with physical indices of vitality, including grip strength, gait speed and repetitive standing and self-reported pain symptoms.

Goals
Aim 1: Determine if age-related declines in DHEAS and DHEA are specifically associated with poorer physical vitality. Aim 2: Is this association present in middle age in addition to the possible effects later in the elderly.

Methods
- 1214 subjects participated in MIDUS II Biomarker Project (2004-2009)
  - 43.2% male
  - 19.1% African American
  - Age: 35-85 (M = 57)
- 2-Day stay at Clinical & Translational Research Centers
- DAY 1: Detailed medical history
  - Chronic Health conditions
  - Persistent Pain
  - Physical Assessment: Gait Speed, Grip Strength, & repetitive Chair Stand test
- DAY 2: Hormone levels determined from fasting blood sample
  - Analyses controlled for participant age, gender, BMI, and race

DHEAS/DHEA levels & Physical Function

<table>
<thead>
<tr>
<th>FEMALE</th>
<th>DHEAS (log nmol/l)</th>
<th>DHEA (log nmol/l)</th>
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<tbody>
<tr>
<td>Vitality Measure</td>
<td>N</td>
<td>Mean</td>
</tr>
<tr>
<td>49 &amp; Under</td>
<td>271</td>
<td>1.03</td>
</tr>
<tr>
<td>50-64</td>
<td>277</td>
<td>1.08</td>
</tr>
<tr>
<td>65 &amp; Over</td>
<td>142</td>
<td>0.98</td>
</tr>
</tbody>
</table>

Low DHEAS (<0.01) and DHEA (<0.01) co-occurred with a higher incidence of chronic illnesses.

Results
- The 426 individuals who self-reported chronic pain had both lower DHEAS (3.30 versus 3.37 log nmol/l, respectively; p<0.01) and DHEA (1.19 versus 1.23 log nmol/l; p<0.01) than those without pain.
- Lower scores on measures of physical functioning, including Rapidity of Chair Stands, Gait Speed, and Grip Strength, were each significantly associated with lower DHEAS and DHEA in circulation.
- Moreover, measures of physical function were more strongly linked with DHEA-S in men and women below 49 years of age than to older individuals.

Conclusions
- A more rapid and precipitous decline in DHEAS and DHEA appears to reflect early aging and physical senescence.
- Low levels are associated with lower vitality especially in middle-age.
- Conversely, the maintenance of higher levels conveys reduced risk for the physical weakness and ailments that precede frailty.
- Our findings highlight the value of evaluating the extent to which hormone levels deviate from age- and gender-typical norms (i.e., an age and gender adjusted residual, rather than the absolute concentration in blood). This measure is a more useful and sensitive correlate of vitality.

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