Chapter 17
Dehydroepiandrosterone Administration in Treating Medical and Neuropsychiatric Disorders

High Hopes, Disappointing Results, and Topics for Future Research

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Abstract Studies have shown that dehydroepiandrosterone (DHEA) influences multiple systems and disease processes in animals and humans. Many researchers around the world have explored the therapeutic role of DHEA. This chapter provides the main facts on biological effects of DHEA administration followed by review of recently reported findings from DHEA clinical trials in schizophrenia. Alterations in DHEA metabolism in schizophrenia are not well understood. Despite higher hopes after preliminary randomized and placebo-controlled cross-sectional trials, a crossover study failed to find any significant effect of DHEA administration on both positive and negative symptoms, on side effects of antipsychotic agents, or on quality of life measures. However, while still preliminary, there is evidence regarding improvement in some neurocognitive functions due to DHEA administration. This chapter also examines the influence of DHEA administration on blood concentrations of neuroactive steroids, symptomatology, neurocognitive functions, side effects and quality of life measures in schizophrenia. A special section of the chapter addresses the association between serum DHEA(S) concentrations on performance of neurocognitive task in schizophrenia patients during the DHEA trial. Deficit in the current knowledge in this area are identified, and suggestions for future research are provided.

Keywords Dehydroepiandrosterone, dehydroepiandrosterone sulfate, schizophrenia, treatment, cognition, side effects, depression, anxiety, medical disorders

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Abbreviations  AIMS abnormal involuntary movement scale; ATPase adenosine triphosphatase; BMD bone mineral density; BMI body mass index; CGI-S clinical global impression scale-severity; CGI-I clinical global impression-improvement; CDSS Calgary depression scale for schizophrenia; DHEA dehydroepiandrosterone; DHEAS dehydroepiandrosterone sulfate; DHEA(S) both DHEA and DHEAS; EPS medication-induced extrapyramidal symptoms; ESRS extrapyramidal symptom rating scale; FGAs first-generation antipsychotic agents; HDRS Hamilton depression rating scale; LHA life history of aggression; NMDA N-methyl-d-aspartate; PANSS positive and negative symptom scale; PMW postmenopausal women; SANS scale for the assessment of negative symptoms; SAS Simpson–Angus extrapyramidal symptom scale; SGAs second-generation antipsychotic agents; Q-LES-Q quality of life enjoyment and satisfaction questionnaire; QLS quality of life scale for rating the schizophrenic deficit syndrome; CANTAB Cambridge automated neuropsychological test battery; BLC big/little circle; RTI reaction time; MTS matching to sample visual search; DMS delayed matching to sample; PRM pattern recognition memory; SRM spatial recognition memory; SSP spatial span; PAL paired associates learning; RVP rapid visual information processing; SWM spatial working memory; IED intra/extra dimensional set shift; SOC stockings of Cambridge; VMS visual/movement skills index; AM attention/memory index; EE executive functions index; GCI global cognitive index

17.1 Introduction

Dehydroepiandrosterone (DHEA) and its sulphate form (DHEAS) [both DHEA(S)] are the most abundant circulating neurosteroids. Although the physiological roles of DHEA(S) are still not fully understood, they have many functions associated with neuronal excitability and synaptic plasticity, stress, mood and neurocognitive performance. DHEA is increasingly available commercially as a supplement aimed at slowing aging processes, and improving various medical and neuropsychiatric conditions. However, there is scant evidence to support the use of DHEA for this purpose.

Two treatment models have been applied in the DHEA administration studies:

- A replacement model with physiological (25–50mg) or near-physiological (100mg) daily doses of DHEA.1–5
- A pharmacological model of treatment using more than 100mg/day DHEA. Few reports are available regarding the use of higher DHEA doses (up to 1,600mg/day),6 and supraphysiologic doses (1,600mg–2.25g).7

It should be noted that the perception of DHEA differs around the world. In the USA it is considered only a mere dietary supplement and is sold “over the counter”, while in many European countries it is considered a “true hormone” that has yet to be approved for use as a hormonal treatment by the European health authorities.8