DHEA ENHANCES WORKING MEMORY AND PREVENTS DISTRACTION – BEHAVIOURAL AND ERP EVIDENCE FROM AN AUDITORY-VISUAL DISTRACTION PARADIGM

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INTRODUCTION

Is DHEA relevant for working memory and distraction?

Dehydroepiandrosterone (DHEA) is much more abundant in humans than in other species and its sulphated form, dehydroepiandrosterone-sulphate (DHEAS), is the most abundant hormone in circulation. Yet, its physiological role is mostly unknown[1].

Several studies suggest DHEA and DHEAS [DHEA/DHEAS] may have memory enhancement effects and an anti-cortisol mechanism of action has been proposed to contribute to that relation, but results are inconsistent[2,3].

We studied DHEA/DHEAS and cortisol relations to working memory (WM) and distraction in humans at the performance and electrophysiological level. The hypotheses to test were: 1) if higher endogenous DHEA levels would be protective from involuntary distraction and enhance cognitive performance; 2) if that effect would be translated to the electrophysiological level; and 3) if DHEA effects would be antagonic from those of cortisol.

METHODS AND RESULTS

23 healthy female volunteers (18-26 years old) were presented a well-established auditory-visual distraction task protocol [4,5]. The electroencephalogram (EEG) was recorded during the performance of one task with WM load (WM1) and other without (WM0), while ignoring task-irrelevant sounds (80% standard – st; 20% novel – nov) – figure 1. The two tasks started 120min apart, with counterbalanced order across subjects.

Performance and Event Related Potentials (ERPs) were averaged for each auditory-stimulus trial type and WM condition. Performance was evaluated by hit rate (HR), error rate (ER) and reaction time (RT). Novelty-P3 (nov-P3) was identified in the nov minus st difference waveforms (dw). P300 elicited to the visual task was compared by using both WM conditions under st auditory stimuli. Salivary DHEA, DHEAS and cortisol were measured before each task and at 30 and 60min.

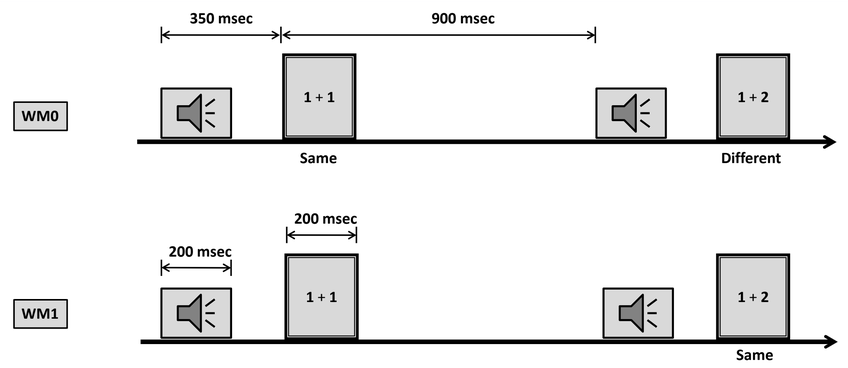

Figure 1: Example of trials stimulation sequence and correct responses for the two conditions, considering that in WM1 the subject had to compare the left digit.

Performance, ERP and Endocrine Results

WM load decreased the HR [F(1,21)=31.375, p<0.001, 84% in WM0 and 71% in WM1 condition] – figure 2. Distraction by novel sounds decreased the HR in WM1 condition [F(1,22)=8.697, p=0.007, 74% for st vs 65% for nov trials] and always increased the RT except when WM1 was the first task [p≤0.01 in all cases].

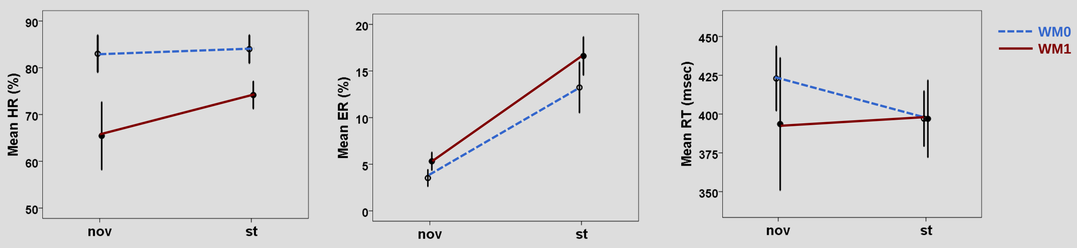

Figure 2: Performance for each condition and auditory stimulus type.

The auditory P3 in WM0 condition was enhanced by distraction [F(1,21)=60.894, p<0.001] and there was a trend for an additional enhancement with WM load [F(1,21)=3.439, p=0.078] – figure 3. The P300 to the visual task was enhanced in the second task [condition x task order – F(1,21)=10.184, p=0.004] – figure 4.

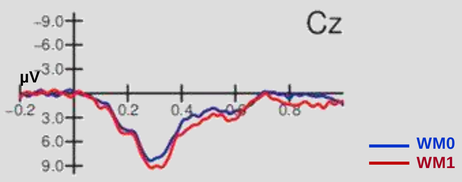

Figure 3: Grand average of dw.

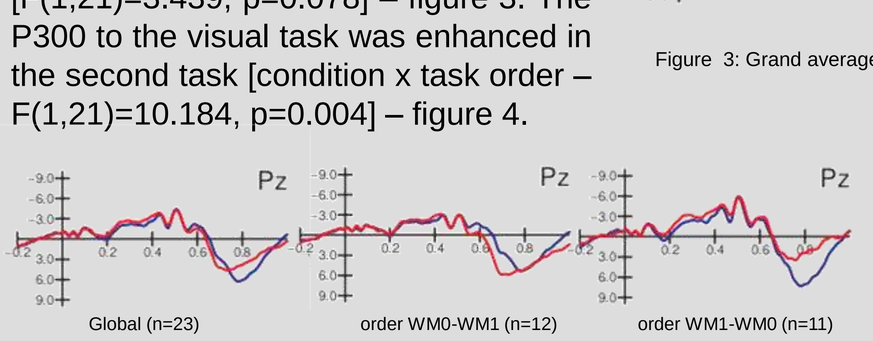

Figure 4: Standard ERP waveforms in WM0 and WM1 conditions.

DHEA levels increased with the second task [F(1,40)=9.839, p=0.002], more with WM load, so that the increase after WM1 as the second task was higher than that for WM0 as the first task [F(1,10)=10.676, p=0.008]. On the contrary, cortisol decreased when WM0 was the first task [F(2,22)=9.544, p=0.007]. DHEAS levels did not change.

Endocrine Relations to Performance and ERPs

In trials with simultaneous WM load and distraction, overall HR (figure 5) was inversely related to basal cortisol [F(1,22)=8.173, r=-0.529, p=0.009] and directly related to Δ DHEA30'/0' [F(1,21)=4.383, r=+0.424, p=0.049] and RT was inversely related to basal cortisol/DHEA ratio [F(1,21)=11.038, r=-0.596, p=0.003] and directly related to Δ DHEA30'/0' [F(1,21)=8.069, r=+0.536, p=0.01]. Those relations were the consequence of the relation between cortisol and DHEA reactivity and WM load costs and distraction costs on HR and RT (figure 6).

In WM1 condition, cortisol/DHEA ratio was related to novelty-P3 enhancement [F(1,21)=11.989, r=+0.612, p=0.002] while visP300 [F(3,22)=11.119, r=0.798, p<0.001] was directly related to visP300 amplitude in WM0 condition (partial r=+0.625, partial p=0.001), order (higher when it was the second task, r=0.616, partial p=0.002) and baseline DHEAS levels (partial r=+0.516, partial p=0.011) and changed due to WM load in direct relation to DHEA reactivity [F(1,20)=9.244, r=+0.562, p=0.006] – figure 7.

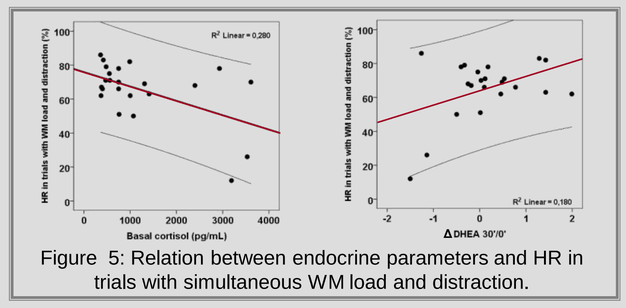

Figure 5: Relation between endocrine parameters and HR in trials with simultaneous WM load and distraction.

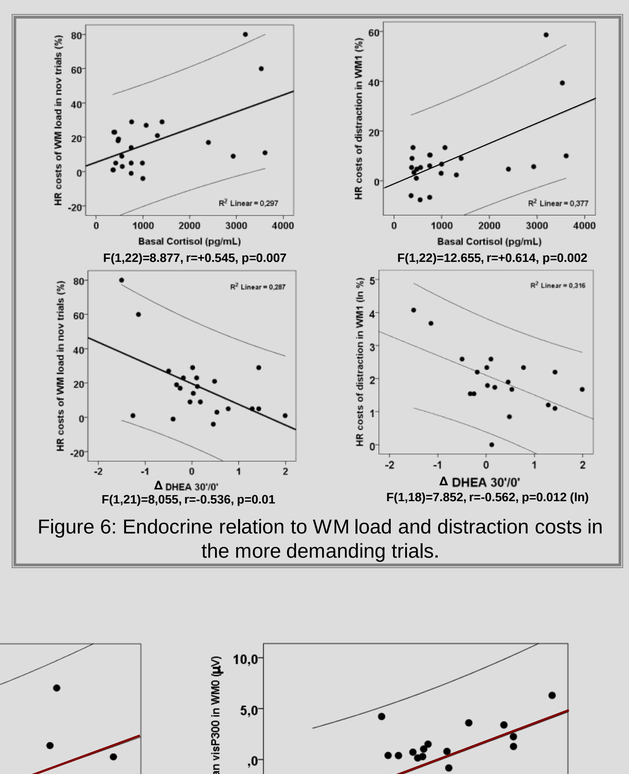

Figure 6: Endocrine relation to WM load and distraction costs in the more demanding trials.

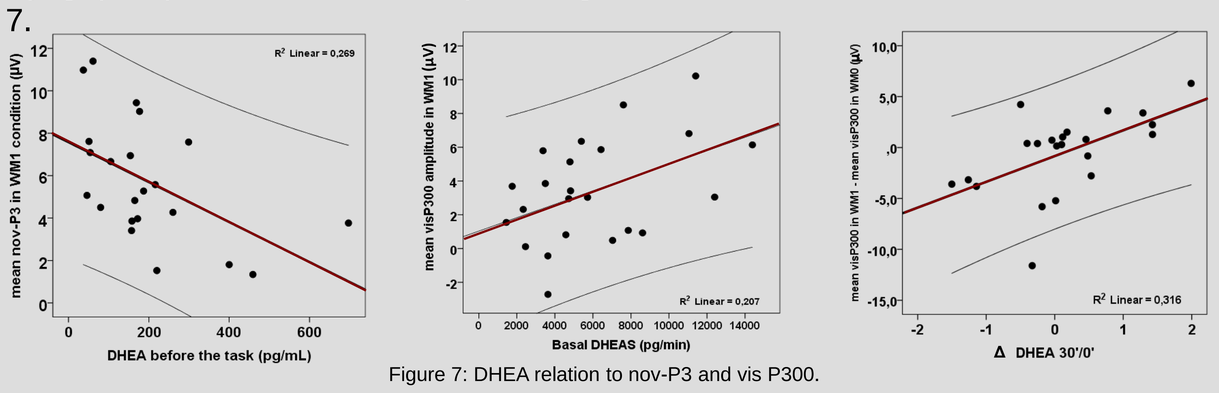

Figure 7: DHEA relation to nov-P3 and vis P300.

DISCUSSION

1. DHEA was related to WM load at the performance and electrophysiological level. DHEA relations to distraction became evident under WM load.
2. **In the more demanding situations (WM load and distraction), higher baseline cortisol was related to faster but less accurate answers while DHEA reactivity presented the opposite relations.**
3. **During WM load, baseline cortisol enhanced and DHEA prevented the processing of the distractor (nov-P3). On the other hand, DHEAS and DHEA reactivity enhanced the processing of the relevant to task stimuli.**

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