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Fatigue and cognition - hormonal perspectives

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ABSTRACT

Fatigue is a common complaint and considered a very challenging symptom to cope with in many different medical diseases. The assessment of fatigue is bound up with the problems of both conceptualization and definition. In addition, few studies have investigated suitable neuropsychological tests to examine fatigue and its consequences.

This thesis evaluates whether neuropsychological tests can elicit cognitive fatigue. It also investigates whether specific hormones and hormone replacement therapy influence fatigue as well as cognitive performance.

Study I examined and compared neuropsychological measures of cognitive fatigue with self-rated fatigue in patients with mild traumatic brain injury (mTBI). These patients scored significantly higher than controls on both self-rated and on test-derived measures of cognitive fatigue. Cognitive fatigue was best captured with a score derived from the WAIS Digit Symbol. From our findings we concluded that cognitive fatigue was independent of depression and sleep disorder. Self-rated fatigue, on the other hand, was highly correlated to depression.

Study II compared the effect of combined testosterone and estrogen replacement with estrogen treatment alone on subjective and objective measures of memory in oophorectomized women. Treatment with testosterone undecanoate 40 mg and estradiol 2 mg was associated with lower performance on immediate verbal memory compared to treatment with estrogen plus placebo. All other memory functions were unaffected.

Study III explored cognitive fatigue in oophorectomized women, and whether hormonal treatment regimens, as described in study II, were related to self perceived well-being, estrogen or testosterone serum levels. We found that cognitive fatigue was frequent in oophorectomized women and negatively associated to self-perceived health and positively associated to BMI. However, treatment with testosterone + estrogen or estrogen alone had no significant effect on cognitive fatigue.

Study IV investigated fatigue and cognitive performance in patients with Graves' disease (GD). As compared to controls, patients with GD scored significantly higher on self-rated fatigue and had a higher frequency on the cognitive fatigue. They also demonstrated lower performance on learning, memory, and various tests of executive functioning. Depression was associated with self-rated fatigue but not with the cognitive fatigue measure. High-free triiodothyronine (T3) levels were positively associated to better cognitive functions but negatively to self-rated everyday consequences of fatigue among the patients.

In conclusion: Cognitive fatigue measure, derived from Digit Symbol, could be a useful instrument to capture fatigue. It enables us to calculate an index of cognitive fatigue where neither depression nor sleep disturbance interfere with the result. Cognitive fatigue seems to be related to BMI and self-rated health but not directly related to hormonal levels. A curvilinear relation to sex hormones and the estrogen/testosterone ratio seem more likely. Indirect hormonal imbalances could influence subtle neuronal mechanisms leading to discrete neuropsychological dysfunctions.

Key words: fatigue, mild traumatic brain injury, oophorectomy, thyrotoxicosis, cognitive function, neuropsychological tests, estrogen, testosterone, thyroid hormones.