



A novel combination reduces objective measures and subjective stress perception

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Reducing harmful stress is a key challenge to preserve well-being. A recent, randomized, double-blind, placebo-controlled study in moderately stressed healthy adults (Clinicaltrials.gov: NCT03262376; 25/0817) demonstrates beneficial effects of a combination of magnesium, B vitamins (B6, B9, B12) and rhodiola and green tea extracts against objective and subjective indicators of stress. It was more effective than either extract alone.

Stress arguably is the most talked about harmful factor of the 21st century affecting 35% of the global population [1]. It may have become even more prevalent during the COVID-19 pandemic. Stress often leads to other conditions including anxiety, headache, poor sleep and can adversely affect cardiovascular risk. Removing stressful factors from the environment is the preferred approach, but often is beyond control of the stressed subject. This creates a need to otherwise alleviate the harmful impact of stress.

Magnesium, particularly when combined with B vitamins [2] and extracts of *Rhodiola rosea* [3] and of green tea [4, 5] have shown beneficial effects related to stress in animal models and/or clinical studies. Therefore, a recent placebo-controlled, double-blind study randomized 100 healthy volunteers aged approximately 25 years to receive a single dose of i) placebo, ii) magnesium + B vitamins (B6, B9, B12) + green tea (GREEN TEA), iii) magnesium + B vitamins + rhodiola (RHODIOLA), and iv) magnesium + B vitamins + rhodiola + green tea (Teadiola®, COMBINATION) as a remedy for stress [6]. After supplementation participants were exposed to the Trier Social Stress Test. The primary outcome parameter was treatment effects on α and θ oscillations in the electroencephalogram (EEG) during the rested state and during completion of attentional tasks under conditions of stress exposure. Secondary outcomes included validated psychometric questionnaires to evaluate subjects' perception (stress, mood, alertness, mental fatigue), heart rate variability and salivary cortisol responses after acute stress exposure.

While none of the treatments affected α oscillations, only the COMBINATION increased θ power (considered indicative of a relaxed, alert state) relative to placebo in the brain regions of interest, in the eyes open rested state (Fig. 1). The

combined treatment significantly attenuated subjective stress vs placebo during the recovery period (+115 min; -2.11 in the Stress Arousal Check List (SACL) score; $p = 0.04$) and by trend after stressor cessation (+65 min; -1.83 ; $p = 0.07$) and during the ambulatory period (+245 min; -1.74 ; $p = 0.08$). Similarly, the combined treatment significantly decreased tension-anxiety, anger-hostility, fatigue-inertia, and the total mood disturbance score and concomitantly increased vigor-activity; for some parameters, the effects of COMBINATION were significantly improved not only versus placebo but also versus GREEN TEA and/or RHODIOLA. Neither condition changed cortisol level or heart rate variability. The results suggest a temporal effect with the greatest functional benefits of the COMBINED treatment emerging up to 1 hr after stress and effects evident up to 5 and 7 hrs after stress exposure. Both magnesium and constituents of green tea and rhodiola may influence the production and activity of neural GABA

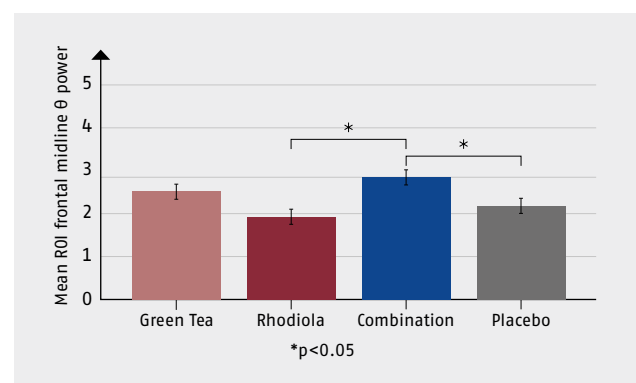


Fig. 1. Effects of the four treatments on the primary outcome parameter, θ power, as measured by EEG. ROI: region of interest. Reproduced with permission from [6].

(γ -aminobutyric acid), a main inhibitory neurotransmitter in the mammalian brain. Stress-reducing effect can occur via direct routes of action rather than being the indirect product of attenuated physiological responses (e.g. cortisol).

We conclude that a combination of magnesium, B vitamins and Teadiola® (rhodiola and green tea extracts) is promising to enhance coping capacity and offer protection from the negative effects of stress exposure in healthy adults. Importantly, the benefits of such supplementation were demonstrated by using both objective analysis of brain activity and validated psychometric questionnaires.

Literature

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