



Rhodiola and green tea, combined with magnesium and B-vitamins, may improve the brain's processing capacity under stress

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Stress can have a negative impact on cognitive functions. This secondary analysis from a randomized, double-blind, placebo-controlled study on moderately stressed healthy adults, showed the positive acute effects of a combination of magnesium, B vitamins (B₆, B₉, B₁₂), rhodiola and green tea extracts enriched in L-theanine on brain EEG theta activity during attentional task performance conducted under acute social stress conditions.

A novel combination could have a relieving effect under stressful conditions

Every third person worldwide feels affected by stress [1]. Stress has multiple consequences on health and quality of life, among which impaired cognitive functions are well described. Frontal theta activity has been implicated in numerous domains of cognitive functions, and heightened frontal theta activity is associated with executive function and working memory [2]. A recent double-blinded, randomized controlled study vs placebo in moderately stressed healthy adults showed that a combination of green tea enriched in L-theanine, rhodiola, and magnesium with B vitamins improved subjective stress, mood and arousal, and increased EEG resting state theta under acute psychosocial laboratory stress [3, 4].

Study examines effects on spectral brain activity in attentional tasks

In this secondary analysis of the same study, the objective was to examine the capacity of the combination to moderate spectral brain activity during attentional task performance after acute stress provocation. A total of 100 healthy volunteers aged in average 25 years were assigned to four treatment arms and each received a single dose of i) magnesium + B vitamins (B₆, B₉, B₁₂) + green tea + rhodiola (full combination), ii) magnesium + B vitamins + green tea (green tea), iii) magnesium + B vitamins + rhodiola (rhodiola), and iv) placebo. After supplementation, all participants were submitted to the Trier Social Stress Test [3], and participants were requested to complete attentional tasks. **Figure 1** visualises the study design.

Improved processing capacity during the execution of the attentional switching task

Oscillatory electrical brain activity refers to rhythmic changes in neuronal activity in the brain as measured by electroencephalogram (EEG). Oscillatory activity in the theta frequency band is particularly important for neuronal communication and is a marker for this analysis.

The ability to switch attention between different demands is an important competence. In the attentional switching task, subjects performed one task repeatedly and then switched to another task when prompted. Three sets of tasks were performed (Switch, Nested, Pre-switch) before switching to the new stimulus. In the third set of tasks (Pre-switch trial) the subjects were in a particular state of expectation and, interestingly, the results here showed significant differences between the combined treatment and the other study arms (see **Fig. 2B**).

The combination resulted in a significant increase in anterior midline theta scores compared to placebo (Switch trial, $p = 0.08$; Nested trial, $p = 0.07$; Pre-switch trial; $p = 0.02$) and rhodiola as a single treatment (Pre-switch trial, $p = 0.04$) [2]. Although the green tea treatment tended to slightly increase the frontal midline theta activity in response to switching tasks stimulus, the effect didn't reach statistical significance, in opposite to the combined treatment, which significantly increased the theta activity. Rhodiola alone had no effect (see **Fig. 2B**). This suggests that green tea and rhodiola have capacity to affect brain response when taken together rather than in isolation, highlighting the interest of the combination.

A double-blind, randomised, parallel (4 arms), placebo-controlled trial in moderately stressed healthy adults (N = 100)



Placebo (N=25)



Combination (N=25)
Green tea + Rhodiola (Teadiola®),
Mg, B vitamins (B₆, B₉, B₁₂)



Green tea (N=25)
Green tea, Mg,
B vitamins (B₆, B₉, B₁₂)



Rhodiola (N=25)
Rhodiola, Mg,
B vitamins (B₆, B₉, B₁₂)

Trier Social Stress Test



- **Primary endpoint**
Oscillatory brain activity (Theta, Alpha waves)
- **Secondary endpoints**
Subjective state, salivary cortisol, cardiovascular parameters, cognitive performance, attentional event related potentials

Attention switching tasks typically require respondents to repeatedly perform a task on some trials then switch to another task when cued to do so, thus requiring the effortful suppression of a dominant or distracting response.

Attentional bias tasks measure the degree to which attention is selectively focussed on a certain type of stimuli over another. Typically, threatening or rewarding stimuli are compared to neutral stimuli to determine the level of vigilance towards or avoidance of specific stimuli categories.

Fig. 1. Study design key points: 100 subjects in four study arms were requested to complete attentional switching and attentional bias tasks (left). Key conceptual notions for the study design (right)

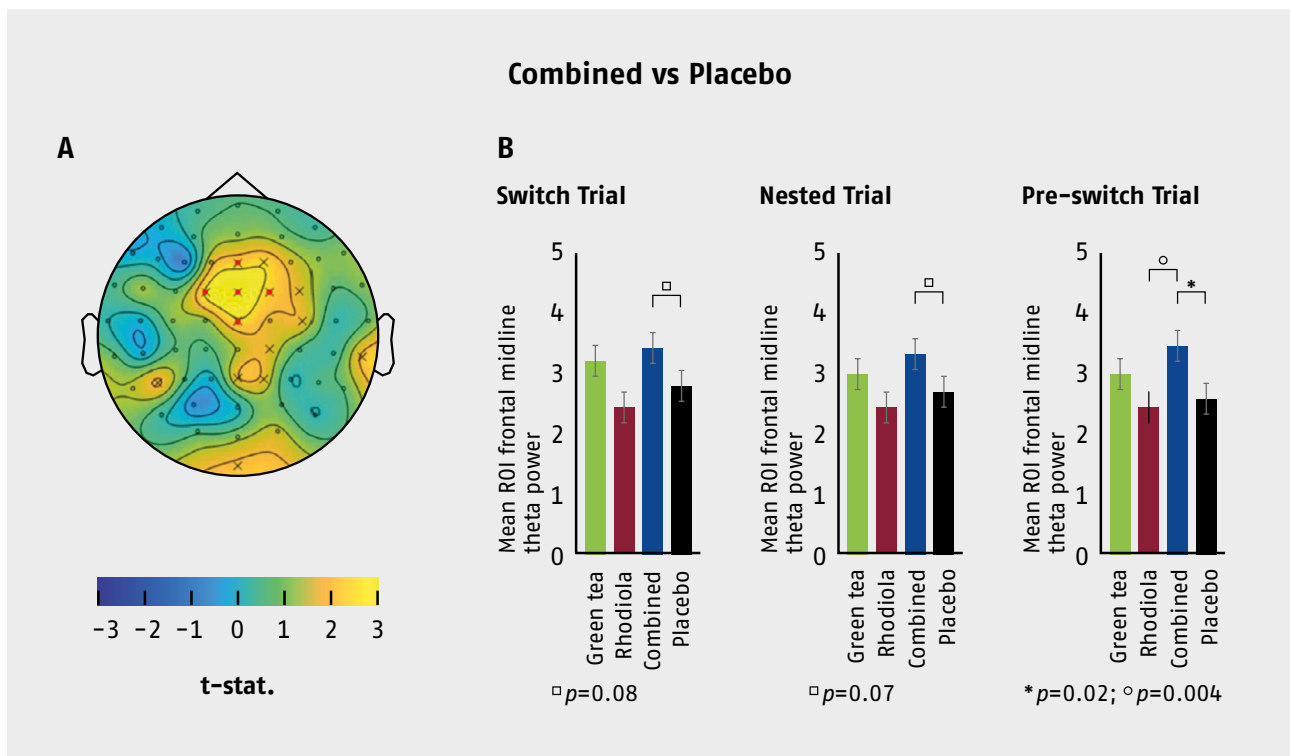


Fig. 2. (A) Map of t-statistic comparison of oscillatory theta band activity during attention switching task in combination vs. placebo treatments (positive values indicate combination > placebo in comparison). A priori defined ROI midline frontal electrodes shown in map by ●. (B) Mean averaged ROI (SEM) frontal midline theta for each attention switching trial by treatment. [2] ROI: region of interest

This increased frontal midline theta in the treatment with the combination indicates enhanced processing capacity during performance of the attentional switching task. Stress may have an unfavorable effect on performance in attentional switching tasks. The positive effect under treatment with the combination may be due to its previously demonstrated ability to induce a relaxed focused state and reduce subjective ratings of stress and anxiety [2].

Improved attentional processing function during an emotionally threatening attentional task

In attention bias tasks, the combination significantly increased contralateral theta activation in relation to viewing emotionally threatening images compared to placebo and rhodiola alone (left parietal theta: emotional threat provided from the left, $p < 0.05$; left parietal theta: emotional threat provided from the right, $p < 0.02$). Combined treatment seemed to enhance attentional processing function during an emotionally threatening attentional task [2]. Attentional vigilance to threatening stimuli is increased by stress states. Thus, stress induction narrows attentional processes toward threat salient stimuli.

Summary

In conclusion, the study demonstrated the capacity of the combination of these ingredients to modulate theta activity during the execution of two distinct attentional tasks. In everyday life, situations that require optimal presence are often associated with increased stress levels. Reducing stress levels while improving cognitive performance is desirable. The combination showed increased theta brain activity during the execution of two distinct attentional tasks, indicating improved attentional capacity under stressful conditions and may have potential benefits for brain cognitive functions in stressful situations (e. g., exams).

Literature

1. Gallup. Global Emotions Report. Washington DC, 2019.
2. Boyle NB, Dye L, Lawton C, Billington J. A Combination of Green Tea, Rhodiola, Magnesium, and B Vitamins Increases Electroencephalogram Theta Activity During Attentional Task Performance Under Conditions of Induced Social Stress. *Front Nutr.* 2022;9:935001, <https://doi.org/10.3389/fnut.2022.935001>.
3. Boyle NB, Billington J, Lawton C, Quadri F, Dye L. A combination of green tea, rhodiola, magnesium and B vitamins modulates brain activity and protects against the effects of induced social stress in healthy volunteers. *Nutrit Neurosci.* 2021;25(09):1845–59. [Online ahead of print]. doi: 10.1080/1028415X.2021.1909204.
4. Noah, L. A novel combination reduces objective measures and subjective stress perception. *Evid Self Med* 2022;2:220041, <https://doi.org/10.52778/efsm.22.0041>.

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