

## Study summary

### Neuravena® improves cognitive function in healthy adults

#### Background

Neuravena® is an extract prepared from a proprietary green oat (*Avena sativa* L.) variety. It was developed using a bioassay-guided approach focusing on its inhibitory effect on the enzymes monoamine oxidase B (MAO-B) and phosphodiesterase 4 (PDE4).

Previous research has demonstrated beneficial effects of Neuravena® on cognitive function in rodents and has shown that administration of a single dosage in humans can result in modulation of electrical brain activity (measured by EEG) and improved performance on the Stroop Test, a well-regarded cognitive assessment for attention and concentration. Chronic administration of 1500 mg Neuravena® per day has also been shown to improve peripheral and cerebral vasodilation.

#### Study design

The current placebo-controlled, double-blind, randomized cross-over study investigated the effects of 800 mg Neuravena® on the cognitive performance using the Computerized Mental Performance Assessment System (COMPASS), a battery of tests selected to allow assessments across the major cognitive domains, i.e. global functioning (speed, accuracy), attention, working memory, episodic memory and executive function.

The 42 participants were healthy adults (mean age 58.9) with self-reported age-associated cognitive decline. Exclusion criteria comprised chronic disease, sleep disturbance, the use of any dietary supplements/NSAIDs/prescribed medications, the presence of food allergies or a history of alcohol or drug abuse, smoking and a body mass index greater than 35. Cognitive performance/ mood were assessed prior to (baseline) and 1, 2.5, 4 and 6 hours after the consumption of a single dose of placebo or 800 mg of Neuravena®.

Each treatment was taken on two separate occasions and the assessments were separated by a 7 day wash-out period. Two measurements representing the overall speed and accuracy of performance across the entire battery were calculated. In addition, the outcomes from each individual test were analyzed.

#### Results

##### Global 'Speed of Performance' measurements:

The 'speed of performance' is a global reaction time outcome calculated from all the timed tasks within the battery of tests. Analysis of this global measure showed that participants taking 800 mg Neuravena® performed faster (i.e. decreased reaction times to stimuli in msec;  $p=0.019$ ) across the tasks within the test battery (Figure 1).

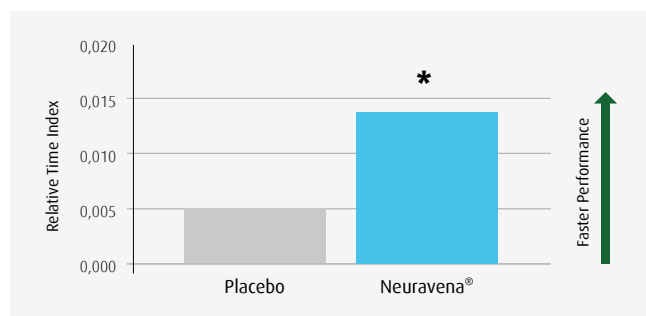


Fig. 1: Improvement of speed of performance in comparison to placebo (\* $p<0.05$ , significant differences between groups based on statistical analysis,  $n=40$ )



### Executive function – Peg & Ball task:

Peg & Ball task is an accepted model to measure accuracy, thinking time and speed of performance. Participants move colored balls on pegs using mouse and cursor to match a target display. Difficulty increases from problems requiring 3 moves, to 4 moves and 5 moves.

There was a significant effect of Neuravena® with regard to planning time (the time taken to plan the moves prior to commencing;  $p=0.004$ ; Figure 2A) as well as completion time (time to complete the moves;  $p=0.004$ ; Figure 2B) for the Peg & Ball task. Planning time was reduced across both visits and all post-dose assessments.

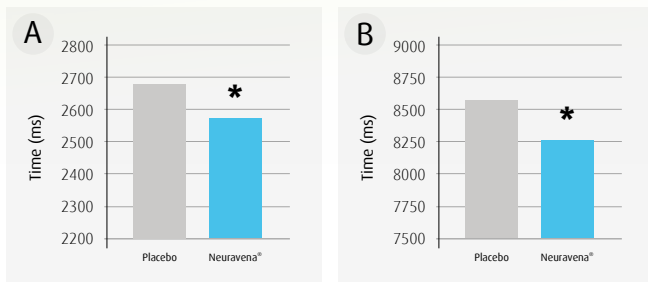


Fig. 2: In the Peg & Ball task Neuravena® showed a significant effect in comparison to placebo across visits/assessments for planning time (A) and completion time (B) (\* $p<0.05$ , significant differences between groups based on statistical analysis,  $n=38$ )

### Episodic memory – Delayed Word Recall task:

Participants study a list of words and are then prompted to recall them immediately and after a short distraction period. Delayed Word Recall task is an accepted model to measure episodic memory (i.e. memory of events, times, places) and accuracy.

A significant effect was measured on the number of errors made during the Delayed Word Recall task. Fewer errors were made following 800 mg Neuravena® treatment compared to placebo ( $p=0.021$ ) across both visits and all post-dose assessments (Figure 3).

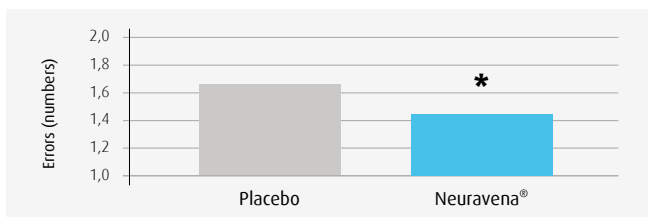


Fig. 3: In the Delayed Word Recall task, Neuravena® resulted in significantly fewer errors in comparison to placebo (\* $p<0.05$ , significant differences between groups based on statistical analysis,  $n=38$ )

### Working memory – Corsi Blocks task:

This test is a well-known model to assess subject's spatial memory span. A set of up to nine identical spatially separated blocks change in color, one by one, in a variable sequence on the screen. The subject must then reproduce the sequence in the same order as it was originally presented. The sequence starts simple using two blocks, but becomes more and more complex.

A significant effect was measured on the second occasion only, accuracy was improved compared to placebo ( $p=0.022$ ; Figure 4).

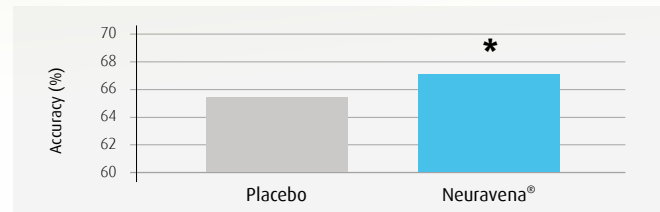


Fig. 4: Neuravena® resulted in better accuracy in the Corsi Blocks task in comparison to placebo (\* $p<0.05$ , significant differences between groups based on statistical analysis,  $n=42$ )

### Summary

The current study shows that the ingestion of a single dose of 800 mg of Neuravena® by healthy adults with self-reported age-associated cognitive decline leads to a number of significant benefits related to cognitive function.

Most notably, Neuravena® resulted in a significant improvement of the 'Speed of Performance' measure across all the timed tasks within the cognitive tests battery. This suggests a general benefit to brain function. In terms of individual tasks, this effect was also associated with improved executive function as evinced by faster performance in the Peg & Ball test; improved working memory performance as seen on the Corsi Blocks task (during the second visit only) and improved episodic memory, in terms of less incorrect words generated on the Delayed Word Recall task.

Overall, these findings confirm the previously demonstrated benefits of Neuravena® on acute improvement of cognitive function and demonstrate for the first time efficacy for an 800 mg dosage.

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