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File: ■ Grapes (*Vitis vinifera*, Vitaceae)
■ Blueberries (*Vaccinium angustifolium*, Ericaceae)
■ Cognition

HC 062053-659

Date: February 26, 2021

RE: Grape and Blueberry Polyphenol-rich Extract Improves Mental Performance in Healthy Young Adults During Cognitive Exertion

Philip P, Sagaspe P, Taillard J, et al. Acute intake of a grape and blueberry polyphenol-rich extract ameliorates cognitive performance in healthy young adults during a sustained cognitive effort. *Antioxidants*. December 17, 2019;8(12):650. doi:10.3390/antiox8120650.

University students are under a high degree of pressure to perform well on exams, evaluations, and deadlines. Stress can adversely affect learning and memory and reduce quality of life. Students often seek ways to improve academic performance and productivity. Preliminary studies have shown a polyphenol-rich extract (PEGB) made from grape (*Vitis vinifera*, Vitaceae) fruit and wild blueberry (*Vaccinium angustifolium*, Ericaceae) fruit (and details of the actual flavonoid content are presented) was able to attenuate cognitive decline and improve neuronal function in aged mice. PEGB also improved working memory in patients with advanced cognitive decline. Flavonols in PEGB may improve flow-mediated dilation, positively affecting cerebral and peripheral vascular functions, and potentially translating to improved cognitive function. Hence, this randomized, double-blind, placebo-controlled, crossover study was conducted to evaluate the effect of acute PEGB on working memory and attention in students.

Healthy students (n = 30, aged 18-25 years) with exams at least every six months and attending lectures equivalent to at least two full days/week, were recruited at the University of Bordeaux (Bordeaux, France) between November 2017 and May 2018. Exclusion criteria included: high blood pressure (BP > 140/90 mmHg), body mass index (BMI) >30 kg/m^2, active smoking, psychiatric or neurologic disorders, presence of diabetes mellitus, dyslipidemia, cardiovascular disease, or thyroid disorders, restrictive/unbalanced diet, and excessive alcohol consumption (>15 units/week). Students were also excluded if they were taking prescription drugs or any dietary supplements aimed at improving memory, concentration, sleep, stress, anxiety, or contained ingredients derived from grape, cranberry (*Vaccinium* spp., Ericaceae), bilberry (*Vaccinium* spp., Ericaceae), tea (*Camillia sinensis*, Theaceae), coffee (*Coffea* spp., Rubiaceae), citrus (*Citrus* spp., Rutaceae), pine (*Pinus* spp., Pinaceae), olive (*Olea*

europeae, Oleaceae), omega-3 fatty acids, ginkgo (*Ginkgo biloba*, Ginkgoaceae), Asian ginseng (*Panax ginseg*, Araliaceae), multivitamin, or caffeine.

At the screening visit, participants completed a training session on the computerized cognitive demand battery (CDB) for habituation and detection of individual problems in the task. One week after the screening visit, following a 12-hour fast and 15-minute rest, BP and flow-mediated dilation (FMD) of the brachial artery were measured, and blood was drawn. Then participants ate a standard low flavonoid and glucose breakfast followed by consumption of an acute dose of either 600 mg PEGB (Memophenol™; Activ'Inside; Beychac et Caillau, France), or a placebo (pure maltodextrin, Maltrin M100; Roquette; Lestrem, France) containing no polyphenols. After a 90-minute rest period, participants underwent a 66-minute intensive and cognitively demanding test. This was followed by a 15-minute rest and collection for BP, FMD, and blood. Participants were instructed not to eat polyphenol-rich foods for 24 hours prior to each test session, and not to change their diet, sleeping, or exercise habits during the study. After a seven-day washout, participants were crossed-over to the alternate treatment. The cognitive assessment included the following tests: serial three subtraction task (STS), a serial seven subtraction task (SSS), a rapid visual information processing task (RVIP), and subjective ratings using visual analogical scales.

There was a significant effect of treatment on the STS, in the PEGB group, demonstrated by having more correct answers ($P = 0.001$). The difference between treatments on the RVIP task trended toward significance ($P = 0.058$). There was no significant effect on SSS scores. Self-perceived mental fatigue ($P < 0.001$) and anxiety ($P = 0.012$) were significantly increased and alertness was significantly decreased ($P < 0.001$) with multiple CDB repetitions. However, self-reported cognitive performance was significantly higher in the PEGB group than the placebo group with repetitions ($P = 0.033$). Analysis of plasma flavonol levels following PEGB consumption revealed circulating flavan-3-ols metabolites (epi)catechin-glucuronide, (epi)catechin-sulfate, and methyl(epi)catechin-sulfate isomers 3.5 hours post ingestion. Global cognitive performance was enhanced up to 2.5 hours after ingestion of PEGB; however, there was no significant difference between groups in FMD.

The authors conclude working memory and attention were improved following PEGB consumption in a student cohort, and participants felt an alteration in cognitive performance. Based on the results from this study, the cognitive enhancement may not occur via an increase in cerebral blood flow, although measurements were made peripherally (brachial artery). Hypothetically, the mechanism of action may be due to a direct effect on neurons. The authors attempted to eliminate confounding variables associated with dietary intake of polyphenols, and they report that compliance with food restrictions was good. Limitations of the study are that it only included 30 participants and that the benefit of PEGB was only seen on one cognitive outcome measure. The study was funded by Activ'Inside, the manufacturer of PEGB.

—Heather S. Oliff, PhD

Referenced article can be accessed at https://www.mdpi.com/2076-3921/8/12/650.