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File: ■ Cocoa (*Theobroma cacao*)
■ Neurovascular Coupling
■ Cognition

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RE: Cocoa Improves Cognitive Functioning in Older Adults with Neurovascular Compromise

Sorond FA, Hurwitz S, Salat DH, Greve DN, Fisher NDL. Neurovascular coupling, cerebral white matter integrity, and response to cocoa in older people. *Neurology*. 2013;81(10):904-909.

Neurovascular coupling is the relationship between neuronal activity and cerebral blood flow; an increase in neuronal activity increases the demand for glucose and oxygen, so cerebral blood flow increases. The relationship between neurovascular coupling and cognition and aging is unknown. Cocoa (*Theobroma cacao*), which is rich in flavanols, may improve endothelial and cognitive function. The purpose of this randomized, double-blind, placebo-controlled study was to determine whether neurovascular coupling is associated with lower cognitive function, whether impaired coupling is associated with cerebral white matter disease, and whether cocoa can modify coupling.

Subjects (n = 60, aged > 65 years) were recruited from local advertisements near Boston, Massachusetts. Included subjects had hypertension (systolic blood pressure [SBP] > 140 mmHg or diastolic blood pressure [DBP] > 90 mmHg on repeated occasions, or treatment with antihypertensive medication) and/or well-controlled type 2 diabetes mellitus. Excluded subjects had absent temporal acoustic windows; intracranial stenosis; history of stroke, chest pain, or heart attack in the last 6 months; stage 2 high blood pressure not controlled by medication (> 160/100 mmHg); serum creatinine > 2 mg/dL; or diagnosis of dementia. Subjects received cocoa powder (Mars, Inc.; McLean, Virginia) in packets to be mixed with water and were instructed to consume 2 cups of cocoa daily either as flavanol-rich cocoa (609 mg flavanols/serving) or flavanol-poor cocoa (13 mg flavanols/serving) for 30 days.

Subjects continued with regular medications and were instructed to eliminate 100 kcal from the diet to prevent weight gain or worsening of diabetes. They were told to refrain from eating chocolate and not to consume caffeine on the study days. Cerebral blood flow velocity was measured at the middle cerebral artery via transcranial Doppler ultrasonography at baseline and after 30 days of treatment at rest, in response to cognitive tasks (N-back tasks), and before and after cocoa consumption. Magnetic

resonance imaging (MRI) was conducted on 24 subjects to determine volumes of normal and abnormal brain white matter.

Subjects with intact neurovascular coupling had significantly better scores on the Trails B Cognitive test ($P = 0.002$) and the 2-Back Task ($P = 0.02$). There was no significant association between neurovascular coupling and the mini-mental state examination score. On MRI, abnormal white matter appears as hyperintensities, and tissue microstructure is measured with fractional anisotropy and mean diffusivity. As would be expected, greater neurovascular coupling occurred in subjects with less white matter macro- and microstructure damage (smaller volume of hyperintensities and higher fractional anisotropy, $P = 0.02$).

After both 24 hours and 30 days of cocoa consumption, cerebral blood flow and blood pressure did not significantly differ between high- and low-flavanol treatment groups, so both groups were combined for analysis. Blood pressure significantly decreased after 1 day of cocoa compared with baseline (SBP: 3.2 ± 13.4 mmHg, $P = 0.07$; DBP: 3.0 ± 9.6 mmHg, $P = 0.02$); however, at 30 days there was no significant effect on blood pressure. At rest, there was no significant difference between treatment groups for neurovascular coupling. During cognitive testing, 89% of subjects with impaired coupling at baseline had a significant improvement in coupling after 30 days of cocoa compared with 36% of those with intact baseline coupling ($P = 0.0002$). In those subjects with impaired baseline coupling, cocoa consumption was associated with 10.6% ($P = 0.0001$) and 8.3% ($P < 0.0001$) increases in coupling at 24 hours and 30 days, respectively. Cocoa resulted in very little change in coupling in subjects with intact coupling at baseline. Also, Trails B performance significantly improved in response to 30 days of cocoa consumption in those with impaired coupling at baseline ($P < 0.007$).

The authors conclude that neurovascular coupling is related to cognitive performance and cerebral white matter structural integrity in elderly subjects with vascular risk factors. In addition, they conclude that neurovascular coupling can be modified by cocoa. Cocoa had an effect irrespective of the amount of flavanols, indicating that there is something else in cocoa that is producing the benefit or that coupling is so sensitive to flavanols that even the small amount in the flavanol-poor group was enough to produce a benefit. It should be noted that this study population had vascular disease, so the effect of cocoa on healthy populations may be different. The authors do not discuss other forms of cocoa, for example, a chocolate bar, which may be preferable to drinking daily hot cocoa especially in warmer months.

—Heather S. Oliff, PhD

The American Botanical Council has chosen not to reprint the original article.