COGNITIVE OUTCOME OF PATIENTS WITH CLASSIC INFANTILE POMPE DISEASE RECEIVING ENZYME THERAPY

Gail A. Spiridigliozzi, James H. Heller, Priya S. Kishnani, Durham, NC: We would like to inquire whether glycogen impairs cognitive function. In addition, since enzyme replacement therapy (ERT) does not cross the blood–brain barrier, does cognitive function decline over time? The data of Ebbink et al.¹ suggest that glycogen in the CNS does not significantly impair cognitive function. This finding is consistent with an earlier report of 13 infants with infantile Pompe who responded positively to the first year of ERT and showed stable cognitive function at the lower end of the normal range.² Additionally, stable function was reported within the lower end of the normal range for 7 children treated with long-term ERT for 6.75 years, on average.³ Scores on a standardized measure of adaptive functioning, negatively affected by motor performance, were below IQ scores. Both research teams identified a particular weakness in processing speed and the need for developmental and educational support services, long-term cognitive surveillance, and neuroimaging studies.

Author Response: Ans T. Van der Ploeg, B.J. Ebbink, F.K. Aarsen, C.M. van Gelder, J.M.P. Van den Hout, Rotterdam, the Netherlands: Our study⁴ confirmed Spiridigliozzi et al.’s⁵ findings of normal or mildly delayed IQ scores in children with classic infantile Pompe disease treated with ERT. This is important because ERT cannot cross the blood–brain barrier. The longest follow-up reported by Spiridigliozzi et al.³ was 9 years and 11 months; ours was 12 years and 3 months.

CHOCOLATE CONSUMPTION AND RISK OF STROKE: A PROSPECTIVE COHORT OF MEN AND META-ANALYSIS

Matthew R. Walters, Catherine Williamson, Kathryn Lunn, Alison Munteanu, Glasgow, UK: Larsson et al.¹ investigated the association between chocolate consumption and risk of stroke in men, concluding that moderate chocolate consumption may lower the risk of stroke. We performed a prospective mechanistic study that may suggest a potential mechanism for this observation.

We investigated the acute effects of a bar (100 g) of dark or milk chocolate upon cerebrovascular reactivity in healthy volunteers. The flavanol content of the dark and milk chocolate was 104 mg and 32 mg of epicatechin, respectively. We found that dark chocolate, but not milk chocolate, increased cerebrovascular reactivity in healthy volunteers. This effect was mediated by the flavanols present in dark chocolate. These findings provide new insights into the potential mechanisms by which chocolate consumption may lower the risk of stroke.

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Although Spiridigliozzi et al.² found a correlation between cognitive and motor development, test limitations prevented them from determining whether lower cognition was caused by motor disabilities or weak cognition. Our more suitable nonmotor intelligence tests of 2 tetraplegic teenagers revealed the influence of severe motor disabilities on developmental scores. These teenagers previously had the lowest possible mental development scores during their first 4 years, but now scored normal or mildly delayed.

Similar to the findings of Spiridigliozzi et al.,² we also found delayed processing speed. Conceivably, these delays are explained by white matter changes like those on the MRIs we reported.

Although mild delays may develop over time, infantile Pompe disease differs substantially from other lysosomal storage diseases where progressive storage in the CNS and profound mental retardation occur at an early age.
respectively. Using a randomized double-blind crossover design, cerebral vasomotor reactivity was measured by transcranial Doppler ultrasound and calculated using breath-hold index (BHI).

Twenty-four fasted, healthy volunteers on no regular medication (12 female, 12 male, mean age 23.2 years [SD 3.29]) attended twice, each study visit at least 24 hours apart. Chocolate caused a significant change in BHI by −0.06 units 90 minutes after chocolate ingestion (BHI pre 1.3 [SD 0.16]; BHI post 1.24 [SD 0.14]; p = 0.015, n = 48). Dark chocolate caused a significant reduction in BHI from baseline by −0.07 units (SD 0.17; p = 0.05, n = 24), though the change in BHI between dark and milk chocolate was not significant (BHI dark −0.07 [SD 0.17]; BHI milk −0.04 [SD 0.13]; p = 0.431, n = 24). No differences in blood sugar, heart rate, or blood pressure were apparent between groups.

Acute ingestion of chocolate was associated with a measurable change in cerebral vasomotor reactivity. Regular consumption of cocoa polyphenols has been shown to reduce the risk of stroke, and antioxidant, antiplatelet, and anti-inflammatory effects, together with effects on lipid profile, have all been proposed as potential mediators of the effect.

Our data suggest that chocolate consumption is associated with an acute change in cerebral vasomotor reactivity, independent of metabolic and hemodynamic parameters. This acute effect may contribute to the observed relationship between long-term chocolate consumption and stroke risk, and is worthy of further investigation.

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