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## Relationships of maternal plasma pro-vitamin A carotenoids and children's neurocognitive outcomes

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### Abstract

**Introduction:** Pro-vitamin A carotenoids namely  $\alpha$ -,  $\beta$ -carotene and  $\beta$ -cryptoxanthin have potential roles in neurocognitive development, but current literature on these carotenoids mainly focused on preventing cognitive decline in the elderly. This study examined the associations of maternal plasma pro-vitamin A carotenoids concentrations with offspring cognitive development up to 54 months in the GUSTO mother-offspring cohort study.

**Materials and Methods:** Maternal plasma pro-vitamin A carotenoids concentrations at delivery were determined by ultra-performance liquid chromatography. At age 24 months, the Bayley Scales of Infant and Toddler Development (BSID-III) was used to assess children's development for the following domains: cognitive, receptive and expressive language, and fine and gross motor. At age 54 months, the Kaufman Brief Intelligence Test (KBIT-2) was used to assess children's verbal and non-verbal intelligence. Associations of maternal pro-vitamin A carotenoids with offspring cognitive development at each time point were examined in 419 mother-offspring pairs using linear regressions adjusted for confounders (e.g. maternal demographics, antenatal mental health and breastfeeding duration).

**Results:** Median (IQR) maternal plasma concentrations (mg/L) were:  $\alpha$ -carotene 0.052 (0.032–0.081),  $\beta$ -carotene 0.189 (0.134–0.286), and  $\beta$ -cryptoxanthin 0.199 (0.123–0.304). In 24 months old infants, higher maternal  $\beta$ -cryptoxanthin (per SD increment) were associated with higher scores in most of BSID-III domains: cognitive [ $\beta$  0.18, (0.08, 0.28) SD], receptive language [ $\beta$  0.17 (0.07, 0.27) SD], fine motor [ $\beta$  0.16 (0.06, 0.27) SD], and gross motor [ $\beta$  0.16 (0.06, 0.27) SD]. Additionally, a 1-SD increment in maternal  $\beta$ -carotene concentrations were associated with 0.16 SD higher scores in BSID-III cognitive domain (95%: 0.04, 0.28), which was attenuated after adjusting for breastfeeding duration. No significant associations were observed between maternal  $\alpha$ -carotene concentrations and BSID-III in children at 24 months of age, or between maternal pro-vitamin A carotenoids and KBIT-2 in children at 54 months of age.

**Discussion:** Our study provides novel data suggesting a role of maternal pro-vitamin A carotenoids, especially  $\beta$ -cryptoxanthin, in offspring early cognitive development. This adds support to the importance of consuming sufficient amounts of red- and orange-coloured fruit and vegetables (rich sources of  $\beta$ -cryptoxanthin and  $\beta$ -carotene) during pregnancy. Further studies are required in other mother-offspring cohort with larger sample sizes, and intervention trials to confirm an effect of pro-vitamin A carotenoids on neurocognitive development.

### Conflict of Interest

Fabian Yap, Peter Gluckman, Keith Godfrey and Yap Seng Chong have received reimbursement for speaking at conferences sponsored by companies selling nutritional products. Peter Gluckman, Keith Godfrey and Yap Seng Chong are part of an academic consortium that has received research funding from Abbott Nutrition, Nestlé and Danone. Other authors declared: 'no conflict of interest'.