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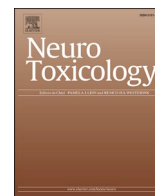
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## Associations between serum taurine concentrations in mothers and neonates and the children's anthropometrics and early neurodevelopment: Results from the Seychelles Child Development Study, Nutrition Cohort 2

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### ABSTRACT

**Background:** High concentrations of taurine are present in the developing human brain and maternal breast milk. Taurine is thought to influence fetal growth and brain development based on experimental rodent studies. As fish is an important dietary source of taurine, we investigated associations between taurine concentrations and child outcomes in a high fish consuming population.

**Objective:** To examine associations between maternal and cord serum taurine concentrations and birth anthropometric measures and cognitive development in children at 20 months of age.

**Methods:** Pregnant women were recruited between 2008 and 2011 as part of Nutrition Cohort 2 (NC2) of the Seychelles Child Development Study (SCDS). Maternal taurine serum concentrations were measured at 28 week's gestation and in cord serum. Child weight, length and head circumference were measured at birth and neurodevelopment was assessed using Bayley Scales of Infant Development II (BSID-II) at 20 months of age. Associations between taurine status, birth measures and neurodevelopmental outcomes were examined (n = 300) using regression models and adjusted for relevant covariates.

**Results:** Mean (SD) maternal and cord taurine concentrations were 124.9 (39.2)  $\mu\text{mol/L}$  (range 28.2–253.9  $\mu\text{mol/L}$ ) and 187.6 (60.0)  $\mu\text{mol/L}$  (range 55.0–417.4  $\mu\text{mol/L}$ ) respectively. We found no associations between maternal taurine concentrations and child anthropometric and neurodevelopmental measures (weight  $\beta = -0.001$ , SE=0.001; length  $\beta = -0.006$ , SE=0.006; head circumference  $\beta = -0.002$ , SE=0.002; MDI  $\beta = -0.005$ , SE=0.015; PDI  $\beta = -0.004$ , SE=0.016; all P > 0.05), or between cord taurine concentrations and outcomes (weight  $\beta = -0.001$ , SE<0.000; length  $\beta = -0.001$ , SE=0.004; head circumference  $\beta < 0.000$ , SE=0.002; MDI  $\beta = 0.004$ , SE=0.010; PDI  $\beta = -0.015$ , SE=0.012; all P > 0.05).

**Conclusion:** The Seychellois population have high maternal and cord taurine concentrations owing to their high fish intake and may be considered taurine replete compared to individuals who consume a Westernised diet. This high taurine status may explain why there were no significant associations between maternal and cord taurine concentrations and outcomes after adjusting for covariates.

**Abbreviations:** AA, arachidonic acid; ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder; CNS, central nervous system; BSID-II, Bayley Scales of Infant Development II; BMI, body mass index; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; LBW, low birth weight; MDI, Mental Developmental Index; MeHg, methylmercury; NC2, Nutrition Cohort 2; PDI, Psychomotor Development Index; PUFA, polyunsaturated fatty acid; SCDS, Seychelles Child Development Study; SES, socioeconomic status; WISC-R, Wechsler Intelligence Scale for Children.

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## 1. Introduction

Taurine is considered a conditionally essential amino acid which can be made endogenously during one carbon metabolism, except under certain conditions<sup>1</sup> (Huxtable et al., 1987). Endogenous production is limited in individuals with chronic hepatic, heart, or renal failure and those requiring long-term parenteral nutrition including premature infants and infants up to 1 year of age owing to insufficient synthesis and inability to conserve taurine in their immature kidneys (Lourenço and Camilo, 2002, Rigo and Senterre, 1977, Sturman, 1991, Zeljkovic et al., 1990). Taurine is most noted for its role in conjugating with bile acids to form water soluble bile salts for fat absorption (Ijare et al., 2005). It also functions as an antioxidant, anti-inflammatory agent, neuromodulator, calcium modulator and osmoregulator (Schaffer and Kim, 2018). Animal and human studies have suggested that deficiency of taurine leads to numerous adverse health outcomes including reduced life and health spans (McGaunn and Baur, 2023; Singh et al., 2023), cardiomyopathy (Sagara et al., 2015), inflammatory diseases (Marcinkiewicz and Kontny, 2014), retinal degenerative disorders (Castelli et al., 2021) and cognitive impairment (Chen et al., 2019).

Dietary uptake is the major taurine supply for humans and can be obtained from foods such as meat and shellfish, but the main dietary source is fish (Gormley et al., 2007, Larsen et al., 2013). Infants must obtain taurine from their diet, and they achieve this through breast milk or formula supplemented with taurine (American Academy of Pediatrics, 1998; Mizushima et al., 1996). Currently, recommendations on taurine intake have only been established for full-term and preterm infant formulas (Heird, 2004). There are no set guidelines established for taurine dietary intakes in humans. There are few data on whether putative deficiency or optimal status would have consequential health outcomes in humans, including pregnant and lactating women (Wu, 2020).

During pregnancy the fetus obtains taurine from the maternal circulation via the placenta (Holm et al., 2018). Taurine is involved in the development and function of many organs (Huxtable, 1992) and appears to modulate various physiological functions (Huxtable, 1992) beginning at conception and continuing throughout life (Huxtable, 1992; Bouckenooghe et al., 2006, Sturman, 1993). Owing to taurine's function in fat absorption and its effect on the expression of growth promoting factors such as insulin-like growth factor-1 (IGF-1) (Moon et al., 2015), it has been proposed that taurine during pregnancy may be associated with infant anthropometric outcomes. The original research investigating associations between taurine and birth anthropometric outcomes was conducted in cats. It is an essential amino acid for felines as they are unable to endogenously synthesise it (Edgar et al., 1998; Rentschler et al., 1986). Results from cat studies found that taurine depleted pregnant cats had kittens with a significantly lower birth weight at full-term compared to those cats fed taurine supplemented diets (Sturman et al., 1985a). Other studies in animals have shown that taurine supplementation during pregnancy improved growth and weight gain in offspring compared to those receiving no supplement (Hayes et al., 1980, Hultman et al., 2007). Regarding human studies investigating the impact of perinatal taurine on birth anthropometric outcomes, the majority of studies have focused on infants with a low birth weight (LBW (<1500 g)) and the use of taurine supplementation to promote weight gain during the neonatal period (Verner et al., 2007).

Taurine is found abundantly in tissues throughout the human body, especially in the brain and particularly the neocortex (Hernández-Benítez et al., 2013; Lourenço and Camilo, 2002; Ripps and Shen, 2012), during fetal development and early infancy. The fetus has taurine concentrations four to five-fold higher in the brain compared to that of the developed human brain (Akahori et al., 1986). During the third trimester, there is an increase in placental transfer of taurine to the fetus, and this transfer coincides with high concentrations of taurine accumulating in the fetal brain (Aerts and Van Assche, 2002). Taurine is believed to affect the function of neurotransmitters (Santora et al.,

2013), regulate the volume of neurons (Massieu et al., 2004), and act as an antioxidant (Ananchapatana-Auitragoon et al., 2015, Baliou et al., 2021) and neurotrophic factor in central nervous system (CNS) development (Wu and Prentice, 2010). As taurine has numerous biological functions essential to neurodevelopment and function, deficiency during pregnancy may have a detrimental impact on fetal brain development and function. Studies using feline models have demonstrated the importance of taurine during pregnancy and cognitive outcomes in their offspring. Pregnant cats fed taurine-free diets were frequently unable to complete full-term pregnancies, whilst the kittens which did survive had neurological abnormalities (Sturman et al., 1985b, Sturman, 1991, Sturman et al., 1985a, Sturman et al., 1986, Sturman and Messing, 1992). In humans, studies have shown that taurine concentrations in adults are associated with cognitive function (Chen et al., 2019; Oh et al., 2020; Kim et al., 2003); however, limited research has been carried out investigating cognitive development and function in infants. Wharton et al. (2004) reported a positive correlation between neonatal taurine concentrations and neurodevelopmental outcomes at age 7 years in a study of 157 children (Wharton et al., 2004).

Overall, although there are limited data on humans, evidence from animal models supports the hypothesis that low taurine concentrations during pregnancy could adversely impact birth outcomes and neurodevelopment. This study aimed to investigate associations between maternal and cord serum taurine status at 28 weeks' gestation and infant birth anthropometric outcomes and neurodevelopmental outcomes in children at 20 months of age in the high fish-eating Seychellois population.

## 2. Methods

### 2.1. Study population

This study includes mother-child pairs who were recruited from 2008 to 2011 to the Nutrition Cohort 2 (NC2) of the Seychelles Child Development Study (SCDS). Details on recruitment of the NC2 have been previously described (Strain et al., 2015a). In brief, the SCDS is an ongoing longitudinal multi-cohort observational study conducted on the island of Mahé. Pregnant mothers were recruited during their first antenatal visit (from 14 weeks gestation onwards) across eight health centres. Inclusion criteria for NC2 included: being native Seychellois, being > 16 years of age, and having a singleton pregnancy, with no obvious health concerns. From NC2 (n = 1536) a subset of 300 mother-child pairs were randomly selected for this pilot study to determine taurine status in maternal and cord serum samples. Research protocols were reviewed and approved by the ethics boards from the University of Rochester and the Republic of the Seychelles Ministry of Health. Procedures were found to be in accordance with the Helsinki Declaration and participants gave written informed consent.

### 2.2. Blood collection

Non-fasting blood samples were collected at 28 weeks' gestation and cord blood was collected at delivery. Whole blood samples were processed to serum at the Public Health Laboratory at the Ministry of Health, Seychelles. All aliquots were stored at – 80 °C and were maintained at this temperature throughout the shipment to Ulster University, UK for biobanking.

### 2.3. Taurine analysis

Samples were shipped on dry ice to the Norwegian College of Fishery Science, UIT The Arctic University of Norway, for taurine analysis. Serum taurine was measured and quantified using a previously described method, with some modifications (Kristiansen et al., 2014, Elvevoll et al., 2008). A sample of 180 µL of maternal serum, 40 µL 1 mM nor-leucine (used as internal standard), and 25 µL of 35% sulfosalicylic

acid were centrifuged at 17,000 g for 3 min. The supernatant was analysed using a Biochrom 30 amino acid analyser (Biochrom Ltd) equipped with an ion exchange column and using ninhydrin as a post-column derivatisation agent. Taurine was detected at a wavelength of 540 nm and identified using A9906 Physiological amino acid standard from Sigma Aldrich. Serum taurine concentration was recorded in  $\mu\text{mol/L}$ .

#### 2.4. Anthropometric measurements

Data on the children's birth weight (kilograms), length (centimetres), and head circumference (centimetres), which were assessed by medical staff using routine clinical procedures and standardized scales at birth, were obtained for this study from medical records.

#### 2.5. Developmental assessments

At approximately 20 months of age (range: 15.9 – 28.4 months) the infants completed neurodevelopmental assessments using Bayley Scales of Infant Development II (BSID-II). Testing was conducted at the Child Development Centre in Mahé by specially trained child health care nurses. All study forms were shipped to the University of Rochester, USA, and double entered. Data from both the Psychomotor Development Index (PDI) and the Mental Developmental Index (MDI) BSID-II endpoints were scaled according to child age at testing. Inter-observer reliability for the BSID-II was determined for about 10% of the cohort by comparing the independent test scoring of 2 nurses. The median agreement on scored MDI and PDI items was 100%.

#### 2.6. Covariates

Data for all covariates were previously collected in this cohort and details have been previously described (Strain et al., 2015a, Davidson et al., 2008). Statistical models for birth anthropometric outcomes were adjusted for covariates that are known to be associated with these measurements including maternal age, parity, child sex, 20-month socioeconomic status (SES) and maternal body mass index (BMI) at 20 months ( $\text{BMI} = \text{weight (kg)} / \text{height (m)}^2$ ) and gestational age (Yeates et al., 2020).

All cognitive outcome statistical models were adjusted for covariates that are known to be associated with child cognitive development, including maternal age, child age at testing, child sex, 20-month SES, and family status (Strain et al., 2015a; Watson et al., 2013; Davidson et al., 2008).

Child sex and gestational age were obtained through hospital records, whereas Hollingshead Social Status index was obtained by questionnaire which was specifically designed for the SCDS population in the Republic of the Seychelles.

Furthermore, secondary analysis was conducted controlling for n6/n3 PUFA ratio, which has been previously measured in NC2 (Spence et al., 2022; Strain et al., 2015b) and has been shown to have beneficial effects on both neurodevelopmental and anthropometric measurements (Strain et al., 2021; Grootendorst-van Mil, 2018).

#### 2.7. Statistical analysis

Statistical analysis was conducted using the statistical software package R (version 3.0.2; The R Foundation for Statistical Computing). The cohort characteristics were examined in descriptive analyses including means, standard deviation (SD), minimum (min) and maximum (max) values. Regression models investigated the relationships between maternal and cord taurine concentrations and outcomes. Analysis models were controlled for relevant covariates as described earlier. Separate regression models were created to investigate the relationship between taurine and birth outcomes (weight, length, and head circumference) and between taurine and cognitive outcomes (BSID-II MDI and PDI). Except for child sex and family status, all model

covariates and outcomes were treated as continuous variables. A statistically significant association was considered with a two-sided  $p \leq 0.05$ .

### 3. Results

Of the 300 mother-child pairs who were randomly selected for this pilot study, 6 were missing data on maternal and cord taurine concentrations. One extreme maternal taurine value was also excluded. A total of 225 cord and 285 maternal samples were available for the birth anthropometric outcomes statistical analysis models. At 20 months a further 3 children were excluded (seizures  $n = 2$ , deceased  $n = 1$ ). A total of 224 cord and 283 maternal samples were available for the neurodevelopmental outcome's statistical analysis models.

Mean (SD) maternal taurine concentration at 28 weeks' gestation was 124.9 (39.2)  $\mu\text{mol/L}$  with a range of 28.2–253.9  $\mu\text{mol/L}$ , excluding an extreme maternal taurine value ( $\mu\text{mol/L}$ ). Mean (SD) cord taurine concentration was 187.6 (60.0)  $\mu\text{mol/L}$  with a range of 55.0–417.4  $\mu\text{mol/L}$ . There were 128 female and 166 male infants, and their mean (SD) gestational age was 38.9 (1.7) weeks (Table 1). For birth outcomes, the mean (SD) birth weight was 3.2 (0.5) kg, birth length 51.4 (3.7) cm, and head circumference 33.9 (1.7) cm. For developmental outcomes at 20 months, the mean (SD) results were MDI 88.5 (9.8) and PDI 96.1 (10.4) (Table 1).

There were no statistically significant associations between maternal taurine concentrations and any of the birth outcomes or between cord taurine concentrations and birth length and head circumference. A significant negative association was observed between cord taurine concentrations and birth weight ( $\beta = 0.001$ ,  $\text{SE} = 0.001$ ,  $P = 0.02$ ), but did not remain significant when analysis was adjusted for covariates (Table 2).

There were also no statistically significant associations between maternal or cord taurine concentrations and any of the neurodevelopmental outcomes at 20 months (Table 3).

Supplementary tables 1–6 show associations between taurine and child anthropometric and neurodevelopmental outcomes controlling for all covariates including n6/n3 PUFA ratio. Results did not differ when n6/n3 PUFA was included as a covariate in models.

### 4. Discussion

There were no significant associations between maternal taurine concentrations at 28 weeks' gestation and anthropometric measures or with cord taurine concentrations and birth length and head circumference. However, a significant negative association was observed with birth weight, but this did not remain significant when analysis was adjusted for covariates including n6/n3 PUFA ratio. Neither maternal nor cord taurine concentrations were associated with child BSID endpoint at 20 months.

In this study, the population consumed a large quantity of fish, averaging 8.5 meals per week (Strain et al., 2015a). As fish is the main dietary source of taurine, the taurine concentrations observed in the current study were expected to be higher than a population who consume a more Westernised diet. The average maternal serum taurine concentrations in this study (124.9 (39.2)  $\mu\text{mol/L}$ ) were similar to those of other fish-eating populations, such as from a Korean fish farming area where the non-pregnant women had a mean (SD) serum taurine concentration of 169.7 (41.5)  $\mu\text{mol/L}$  (Kim et al., 2003). In our study, a minimum concentration of 28.2  $\mu\text{mol/L}$  was observed in the maternal samples which is lower compared to that observed in studies of non-pregnant European populations (Elvevoll et al., 2008). However, physiological changes of pregnancy may influence concentrations and cannot be directly compared to non-pregnant individuals. In the current study, cord taurine concentrations (187.6 (60.0)  $\mu\text{mol/L}$ ) were higher than those observed in the maternal samples. This finding was also observed in another study where higher cord plasma taurine

**Table 1**

Summary statistics for maternal characteristics, infant birth outcomes and neurodevelopmental outcomes at 20 months of age, and model covariates.

Variables	N	Mean (SD)	Median	25th percentile	75th percentile	Min	Max
Total participants	300						
Male	166						
Maternal measures at 28 weeks' gestation							
Maternal Taurine 28 weeks ( $\mu\text{mol/L}$ )	285	124.9 (39.2)	122.7	99.3	150.4	28.2	253.9
Maternal age at delivery (years)	284	27.7 (6.6)				16.8	44.2
Prenatal MeHg (ppm)	280	3.4 (2.6)	2.9	1.4	4.7	0.01	16.2
AA (mg/mL)	292	0.2 (0.1)	0.2	0.2	0.3	0.04	0.4
DHA + EPA (mg/mL)	292	0.2 (0.1)	0.2	0.2	0.3	0.1	0.5
n6/n3 ratio	291	4.4 (1.4)	4.1	3.5	4.9	1.9	10.8
Birth Measures							
Taurine cord ( $\mu\text{mol/L}$ )	225	187.6 (60.0)	179.8	148.4	221.5	55.0	417.4
Gestational age (weeks)	292	38.9 (1.7)	39.0	38.0	40.0	32.0	41.0
Weight (kg)	294	3.21 (0.5)	3.2	2.9	3.6	1.56	4.40
Length (cm)	287	51.4 (3.7)	52.0	49.5	54.0	32.0	59.0
Head circumference (cm)	286	33.9 (1.7)	34.0	33.0	35.0	28.0	38.0
20 months measures							
BSID-II MDI score	282	88.5 (9.8)	88.0	82.0	94.8	53.0	116.0
BSID-II PDI score	283	96.1 (10.4)	97.0	90.0	104.0	50.0	121.0
Maternal BMI ( $\text{kg/m}^2$ )	271	27.3 (6.8)	26.6	22.2	31.5	14.8	47.4
SES	287	32.3 (11.4)	31.5	23.0	40.3	11.0	63.0
Child age at testing (months)	284	20.8 (1.1)	20.9	20.0	21.0	16.9	24.9

Abbreviations: AA, Arachidonic acid; BSID-II, Bayley Scales of Infant Development II; BMI, body mass index; cm, centimetres; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; kg, kilograms;  $\text{kg/m}^2$ , kilogram per square metre; Max, maximum; MDI, Mental Developmental Index; MeHg, methylmercury; mg/mL, milligrams per millilitre; Min, minimum; n, number of observations; PDI, Psychomotor Developmental Index; PPM, parts per million; SD, standard deviation; SES, socioeconomic status;  $\mu\text{mol/L}$ , micromoles per litre. Original to this manuscript.

**Table 2**Main effects models for prenatal taurine exposure and birth outcomes <sup>a</sup>.

Variables	Birth Weight (g)				Birth Length (cm)				Head Circumference (cm)			
	n	$\beta$	SE	P	n	$\beta$	SE	P	n	$\beta$	SE	P
Maternal Taurine	277	0.000	0.001	0.839	273	-0.002	0.005	0.779	272	0.000	0.002	0.893
Maternal Taurine + Covariates	253	-0.001	0.001	0.275	249	-0.006	0.006	0.286	248	-0.002	0.002	0.406
Cord Taurine	223	-0.001	0.001	0.024*	221	-0.004	0.004	0.333	221	-0.001	0.002	0.571
Cord Taurine + Covariates	203	-0.001	0.000	0.114	201	-0.001	0.004	0.713	201	0.000	0.002	0.898

<sup>a</sup> Estimated regression coefficients and P values are shown. \*Significant associations,  $P < 0.05$ . Abbreviations:  $\beta$ , beta coefficient; cm, centimetres; g, grams; n, number of observations; SE, standard error. Covariates: Maternal age (years), parity, child sex, 20-month socioeconomic status (SES), maternal body mass index (BMI) ( $\text{kg/m}^2$ ), gestational age (weeks). Original to this manuscript.

**Table 3**Main effects models for prenatal taurine exposure and the Bayley Scales on Infant Development II MDI and PDI at 20 months of age<sup>a</sup>.

Variables	BSID-II MDI				BSID-II PDI			
	n	$\beta$	SE	P	n	$\beta$	SE	P
Maternal Taurine	273	-0.002	0.015	0.871	274	0.000	0.016	0.985
Maternal Taurine + Covariates	273	-0.005	0.015	0.763	274	-0.004	0.016	0.807
Cord Taurine	217	0.005	0.010	0.599	217	-0.012	0.012	0.289
Cord Taurine + Covariates	217	0.004	0.010	0.718	217	-0.015	0.012	0.204

<sup>a</sup> Estimated regression coefficients and P values are shown. \*Significant associations,  $P < 0.05$ . Abbreviations:  $\beta$ , beta coefficient; BSID-II, Bayley Scales of Infant Development II; MDI, Mental Developmental Index; n, number of observations; PDI, Psychomotor Developmental Index; SE, standard error. Covariates: Maternal age (years), child age at testing (months), child sex, 20-month socioeconomic status (SES), family status. Original to this manuscript.

concentrations in twins ( $256 \pm 28 \mu\text{mol/L}$  and  $239 \pm 25 \mu\text{mol/L}$ ) was reported, compared to their maternal taurine concentrations ( $134 \mu\text{mol/L}$ ) (Bajoria et al., 2001) which may be owing to the different time-points that the maternal blood samples were taken and the fluctuations in taurine that can be observed in the mother throughout pregnancy (Zaima, 1984). As previously mentioned, a decrease in taurine concentrations is seen towards the end of gestation in the mother as an increase of taurine is transported to the fetus. This increased transport may result in cord samples having higher taurine concentrations than those of the mother during the third trimester.

Although no optimal taurine status or safe upper limit for adults, children or pregnant women have currently been established, the higher-than-average taurine concentrations observed in the current

study did not have detrimental impacts on either neurodevelopmental or birth outcomes in the offspring. No human studies have investigated associations between cord taurine status and anthropometric outcomes in children, making it difficult to compare the results observed in this study to other populations.

Efficient absorption of fat from the diet is important for energy supply, growth, and development throughout life (Uauy and Castillo, 2003). During the neonatal period, and particularly in the case of prematurity, a considerable part of dietary fat is not absorbed from the intestine but is excreted via the faeces (Signer et al., 1974, Verkade et al., 1991), and may have detrimental effects on infant's growth and development, and, therefore, taurine may be essential for infant fat absorption and anthropometric outcomes. Two systematic reviews and

meta-analyses on taurine supplementation and growth outcomes in LBW have previously been carried out (Verner et al., 2007; Cao et al., 2018). Both studies found no significant effects of taurine supplementation on child growth; however, (Verner et al., 2007) suggested that taurine may only be essential in very preterm LBW or critically ill infants who were unable to maintain taurine tissue concentrations, as most participants in the studies investigated clinically stable infants. These studies were carried out during the postnatal period, and there is currently limited research on the effects of human maternal taurine concentrations during pregnancy and infant anthropometric birth outcomes. Any infant who had a birth weight < 1500 g was excluded in the current study making it difficult to extrapolate results to those within this birthweight range. Furthermore, after the inclusion criteria were applied and owing to the mean (SD) gestational age in this study being 38.9 (1.6) weeks with a minimum of 32 weeks, most infants were full-term healthy infants, and this may have also contributed to the lack of significant associations observed.

In animal studies, taurine has been shown to be essential for fetal brain development (Ripps and Shen, 2012; Kim et al., 2014); however, research investigating taurine concentrations during pregnancy in humans and associations with child neurodevelopmental outcomes are limited. Infants mean (SD) score for both PDI 95.9 (10.4) (range 50.0–121.0), and MDI 88.5 (9.76) (range 53.0–116.0) were above 85, suggesting that few infants displayed any severity of developmental delay. The lack of associations observed between maternal and cord taurine concentrations and neurodevelopmental outcomes may be owing to the lack of very preterm LBW infants and to the exclusion of any infants with severe cognitive disability. Furthermore, the high taurine concentrations observed in this high fish-eating population may also contribute to the lack of significant associations. A study in humans by Wharton et al. (2004) found that low neonatal taurine was associated with lower scores on the BSID MDI at 18 months and the Wechsler Intelligence Scale for Children (WISC-R) arithmetic subtest at 7 years. The infants in this study were preterm (mean gestational age 31 weeks) and had a LBW (mean birth weight 1398 g), again supporting the hypothesis that associations are only evident in very preterm LBW infants.

Furthermore, a study on rhesus monkeys reported endogenous taurine synthesis after 6–12 months of age and noted a significant decline in dependence on dietary taurine suggesting that taurine concentrations in infants older than one year old may not be reflective of maternal taurine obtained from the mother during pregnancy (Sturman et al., 1991). In the current study, cognitive testing was conducted at 20 months of age and scores may be influenced more by the infant's concurrent taurine concentrations, which was not measured, rather than prenatal concentrations. Whilst no association was observed with MDI or PDI scores, taurine has been shown to influence other cognitive impairments not assessed in this study such as autism spectrum disorder (ASD) (Park et al., 2017; Zheng et al., 2017), Angelman syndrome (Guzzetti et al., 2018), Fragile X syndrome (Neuwirth et al., 2015) and attention deficit hyperactivity disorder (ADHD) (Chen et al., 2017). A recent review by Jakaria et al. (2019) suggested therapeutic use of taurine against these neurological disorders and for maintaining neuronal health. Future research should include cognitive testing on infants 12 months or younger with prenatal taurine concentrations and should take into consideration the infants current taurine concentrations if testing is carried out at an older age.

Our study has a number of strengths. It is a random sample from the well-established Seychelles Child Development Study, enabling the issue of confounding by other variables to be considered in secondary statistical models. The taurine concentrations were analysed using Biochrom 30 (Biochrom Ltd), the gold standard of amino acid analysis. Taurine was also measured at 28 week's gestation, which may be representative of third trimester, a time-point during pregnancy which is important for brain development and growth of the fetus (Bouyssi-Kobar et al., 2017; Clark et al., 2003). Our study also has some limitations. Whilst the taurine concentrations were measured in serum, other authors suggest

that analysis in plasma and/or whole blood samples enable a more accurate measurement (Gray et al., 2016; Trautwein and Hayes, 1990). Furthermore, serum concentrations make comparisons with other studies which have used plasma for analysis difficult as there is a low correlation between the two matrices (Yu et al., 2011). Additionally, the cohort only investigated healthy children with a normal birth weight, while a majority of literature investigated taurine improving birth weight and other outcomes in very preterm LBW or clinically ill infants. Also, serum taurine concentrations were only measured at one time-point during pregnancy and may not be representative of taurine concentrations throughout pregnancy, particularly as the fetus accumulates taurine at a higher rate towards the end of gestation (Ghisolfi, 1987).

## 5. Conclusion

We observed no associations between either maternal or cord taurine concentrations and children's birth length and head circumference or their neurodevelopmental outcomes at 20 months of age. There was one statistically significant association between cord taurine and birth weight with a very small beta in an adverse direction; albeit this did not remain significant after adjusting for relevant covariates. In this high fish-eating population, there were no clinically significant associations between maternal or cord taurine and birth anthropometrics or 20-month neurodevelopment outcomes. Further research is needed to investigate prenatal taurine status and a range of neurodevelopmental outcomes in preterm infants.

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## CRediT authorship contribution statement

**Laura A Beggan:** Methodology, Validation, Investigation, Writing – original draft, Writing – review & editing. **Maria S Mulhern:** Methodology, Validation, Investigation, Writing – original draft, Writing – review & editing, Supervision. **Hanne K. Mæhre:** Formal analysis, Investigation, Writing – review & editing. **Emeir M McSorley:** Methodology, Validation, Investigation, Writing – original draft, Writing – review & editing, Supervision. **Alison J Yeates:** Methodology, Validation, Investigation, Writing – original draft, Writing – review & editing, Supervision. **Alexis Zavez:** Formal analysis, Writing – original draft, Writing – review & editing. **Sally W Thurston:** Formal analysis, Validation, Writing – original draft, Writing – review & editing. **Conrad Shamlaye:** Conceptualization, Methodology, Writing – review & editing. **Edwin van Wijngaarden:** Conceptualization, Methodology, Validation, Writing – review & editing, Supervision. **Philip W Davidson:** Conceptualization, Methodology, Writing – review & editing. **Gary J Myers:** Conceptualization, Methodology, Writing – review & editing. **JJ Strain:** Conceptualization, Methodology, Writing – review & editing, Supervision. **Edel O Elvevoll:** Conceptualization, Formal analysis, Investigation, Writing – original draft, Writing – review & editing.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Data Availability

Data will be made available on request.

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## Conflict of Interest

No conflict of interest.

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## Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.neuro.2023.08.004](https://doi.org/10.1016/j.neuro.2023.08.004).

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