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Long-term effects of a maternal high-fat: high-fructose diet on offspring growth and metabolism and impact of maternal taurine supplementation

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Original Article

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Abstract

Objective: Maternal obesity is associated with obesity and metabolic disorders in offspring. However, there remains a paucity of data on strategies to reverse the effects of maternal obesity on maternal and offspring health. With maternal undernutrition, taurine supplementation improves outcomes in offspring mediated in part via improved glucose–insulin homeostasis. The efficacy of taurine supplementation in the setting of maternal obesity on health and well-being of offspring is unknown. We examined the effects of taurine supplementation on outcomes related to growth and metabolism in offspring in a rat model of maternal obesity.
Design: Wistar rats were randomised to: 1) control diet during pregnancy and lactation (CON); 2) CON with 1.5% taurine in drinking water (CT); 3) maternal obesogenic diet (MO); or 4) MO with taurine (MOT). Offspring were weaned onto the control diet for the remainder of the study.
Results: At day 150, offspring body weights and adipose tissue weights were increased in MO groups compared to CON. Adipose tissue weights were reduced in MOT versus MO males but not females. Plasma fasting leptin and insulin were increased in MO offspring groups but were not altered by maternal taurine supplementation. Plasma homocysteine concentrations were reduced in all maternal taurine-supplemented offspring groups. There were significant interactions across maternal diet, taurine supplementation and sex for response to an oral glucose tolerance test , a high-fat dietary preference test and pubertal onset in offspring.
Conclusions: These results demonstrate that maternal taurine supplementation can partially ameliorate adverse developmental programming effects in offspring in a sex-specific manner.

Introduction

It is now well established that, in addition to metabolic dysregulation and increased risk for a range of adverse pregnancy outcomes, maternal obesity has been shown to impact the long-term health of offspring via the process of developmental programming. Maternal obesity can perpetuate a cycle of obesity and related metabolic disorders across generations. Intervention strategies that can ameliorate or reverse the effects of developmental programming thus have the potential to break the cycle of obesity and related metabolic disorders.

Taurine (2-aminoethanesulfonic acid) is an amino acid produced endogenously in humans and rodents[1] and is the most abundant free amino acid in the human placenta.[2] Taurine exerts a wide range of functional roles including that as a neurotransmitter, a trophic factor in central nervous system development, an antioxidant and regulator of energy metabolism including altering transcription profiles of metabolism-related genes (for review, see Schaffer and Kim[3]). Taurine is conditionally essential in pregnancy and fetal tissues depend on taurine uptake from maternal blood[4] with taurine transporter activity in the placental syncytiotrophoblast mediating intracellular taurine concentration and maintaining a gradient that favours taurine efflux towards the fetus, where it is required for normal fetal growth and organ development.[5–7] It has recently been shown that maternal obesity is associated with a reduction in placental taurine transporter activity which potentially compromises placental development and function.[8] Several studies in experimental models have also demonstrated that taurine supplementation has potential as a regulator of insulin secretion and promotes insulin sensitivity in both the pregnant[9,10] and non-pregnant state.[11,12] Early work in the setting of a maternal low-protein diet has shown partial reversal of programming effects by maternal taurine, particularly as regards to restoration of pancreatic beta-cell function in offspring.[10,13,14] These beneficial effects on glucose homeostasis have recently been shown to persist in offspring into adult life in a

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sex-specific manner.[15] Maternal taurine supplementation has also been reported to confer beneficial effects on offspring outcomes in the setting of increased maternal alcohol consumption.[16]

We have developed a rat model, whereby a maternal high-fat: high-fructose diet results in maternal hyperinsulinemia, hyperleptinemia, increased plasma glucose and a pro-inflammatory phenotype.[17] Neonatal offspring of dams fed the obesogenic diet displayed a pro-inflammatory hepatic profile that was partially rescued in offspring of mothers supplemented with taurine.[17] However, to date, the long-term effects of maternal taurine supplementation in offspring following a maternal obesogenic (MO) diet have not been described. A maternal high-fat:high-fructose diet does not lead to a deficiency in circulating maternal taurine concentrations[17] – the present study was designed to investigate the impact of taurine supplementation in a taurine replete MO diet model on long-term growth and metabolic outcomes in adult offspring. The current study, therefore, aims to further evaluate the adverse effects of MO diet consumption during pregnancy and lactation on offspring outcomes, and to determine whether maternal taurine supplementation can reverse the metabolic disorders in adult offspring induced by maternal obesity.

Methods

Animal model

All procedures described were approved by the Animal Ethics Committee at the University of Auckland (Approval R888). The experimental model of a MO diet and taurine supplementation has previously been described by our group.[17]

Virgin Wistar rats were time-mated at 100 days of age using an estrous cycle monitor (EC-40; Fine Science Tools, San Francisco, CA, USA). Day 1 of pregnancy was determined by the presence of spermatozoa after a vaginal smear. Pregnant rats were then housed individually with free access to food and water and maintained at 25°C and a 12 h light: 12 h darkness cycle. Animals were randomly assigned to one of four nutritional groups: control group (CON) fed a standard chow diet (Diet 2018, 24% calories from protein, 18% from fat, 58% from carbohydrate; Harlan Teklad, Oxon, UK) ($n = 9$); control taurine group (CT) fed a standard chow diet with additional 1.5% w/v taurine supplementation in drinking water[17] ($n = 7$); MO diet group fed a high-fat:high-fructose diet (20% calories from protein, 45% from fat, 35% from carbohydrate (including 26% from fructose); Diet D03101602; Research Diets, New Brunswick, NJ, USA; $n = 8$); MO diet and taurine group (MOT) fed the obesogenic diet with additional 1.5% w/v taurine supplementation in drinking water ($n = 8$). Diets were fed *ad libitum* throughout pregnancy and lactation. As a high-fat:high-fructose diet can potentially affect water intake, taurine concentrations in the MOT group were adjusted where necessary according to the previous day's water intake. This was essential to ensure that the taurine doses were equivalent across both CT and MOT groups. At birth, litter size was adjusted to eight pups per litter (four male and four female) to ensure standardised nutrition until weaning. Offspring were weaned at day 22 and housed two per cage under standard conditions and fed the standard control diet *ad-libitum* for the remainder of the study (150 days). At day 150, animals were fasted overnight and killed by decapitation following anaesthesia with pentobarbitone (60 mg/kg, IP). Blood was collected into heparinised vacutainers, kept on ice and centrifuged for collection of supernatant (2500 g/10 min/4°C). Plasma samples were stored at −20°C until subsequent analysis. Adipose tissue was immediately excised and weighed.

Assessment of pubertal onset

From postnatal day 24 (P24) onwards, female offspring were examined daily by the same research staff for vaginal opening (VO). On the day when VO was observed, age and body weight were recorded. From postnatal day 35 (P35), male offspring were examined daily for balanopreputial separation.[18] All pubertal observations were performed by the same research investigator between 0900 and 0930.

Food preference

A food preference test was performed in offspring at day 130 to assess food preference and body weight responsiveness to obesogenic diets. Two hundred grams of the standard chow diet and 200 g of the MO diet were placed side by side in each cage each day for a period of 10 days. Animals had free choice to select which diet they preferred. Body weight and food intakes were recorded daily during this period.

Plasma analysis

Fasting plasma insulin and leptin concentrations were measured using rat specific commercial ELISAs (Catalogue #90060 and #90040, respectively; CrystalChem, Elk Grove Village, IL, USA). Plasma homocysteine (HcY) was measured via immunoassay (Abbott AxSYM System, Abbott Park, IL, USA). Each kit was performed as per manufacturer's provided protocol. In general, plasma samples were thawed on ice and centrifuged for 3 min at 2500 rpm at 4°C prior to performing the kits to remove fibrous clots which are common in rodent plasma. Where multiple plates were needed for one marker, samples were performed in a randomised order which was generated via an Excel database to avoid time-of-day effects and inter-assay effects. All intra- and inter-assay coefficients of variation were <5%.

Oral glucose tolerance test (OGTT)

An oral glucose tolerance test (OGTT) was performed 1 week before cull in a subset of adult offspring ($n = 6$ per group). Rats were fasted overnight in clean cages. Rats were gavaged with a glucose solution (2 g/kg body weight) and tail blood samples were taken repeatedly at 0, 5, 10, 20, 30, 60, 90 and 120 min. Blood glucose concentrations at each time point were determined using a glucose meter (Optium Xceed; Abbott Laboratories, Auckland, New Zealand). Tail snip was performed only once for each animal to reduce the stress as sequential blood can be obtained from the same wound. The first drop of blood was discarded, and the second drop of blood was used for glucose measurement.

Statistics

The study design represented a balanced $2 \times 2 \times 2$ factorial design with maternal diet, taurine supplementation and sex as factors. With the exception of puberty and OGTTs, data were analysed by three-way ANOVA with post hoc corrections for multiple comparisons (SigmaStat, San Jose, CA, USA). Puberty data were analysed by two-way factorial ANOVA with maternal diet and taurine as factors. OGTT data were measured using repeated measures ANOVA. Data are shown as means SEM unless otherwise stated and differences were considered significant at the $P < 0.05$ level.

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Table 1. Absolute body weights, NA lengths and bloodHcY, glucose and ketone concentrations in M and F adult offspring at postnatal day 150. Data are means ± SEM, $n = 7–9$ l represented per group[a]

	M-CON	M-CT	M-MO	M-MOT	F-CON	F-CT	F-MO	F-MOT
BW (g)#*	669 ± 12	672 ± 13	736 ± 18	681 ± 17	360 ± 11	340 ± 12	373 ± 10	369 ± 14
NA (mm)*	271 ± 1.5	272 ± 2.0	274 ± 1.9	271 ± 1.4	231 ± 2.1	230 ± 2.3	232 ± 2.5	236 ± 2.2
HcY (μmol/l)*$	6.82 ± 0.2	6.10 ± 0.2	6.26 ± 0.4	5.98 ± 0.3	7.82 ± 0.4	7.21 ± 0.2	7.89 ± 0.4	6.67 ± 0.7
Glucose (mmol/l)*	7.55 ± 0.13	7.52 ± 0.12	7.33 ± 0.14	7.81 ± 0.11	6.99 ± 0.12	6.75 ± 0.13	7.22 ± 0.12	7.09 ± 0.14
Ketones (mmol/l)*	1.16 ± 0.04	1.10 ± 0.06	1.07 ± 0.04	1.07 ± 0.05	1.33 ± 0.09	1.55 ± 0.10	1.49 ± 0.08	1.49 ± 0.07

BW, bodyweight; CON, control; CT, control taurine group; F, female; HcY, homocysteine; M, male; MO, maternal obesogenic diet; MOT, MO with taurine; NA, nose–anus length; SEM, standard error of the mean.
#$P < 0.05$ for effect of maternal diet, *$P < 0.001$ for effect of sex, $$P < 0.005$ for effect of taurine.
[a]There were no statistical interactions across any of the measures reported.

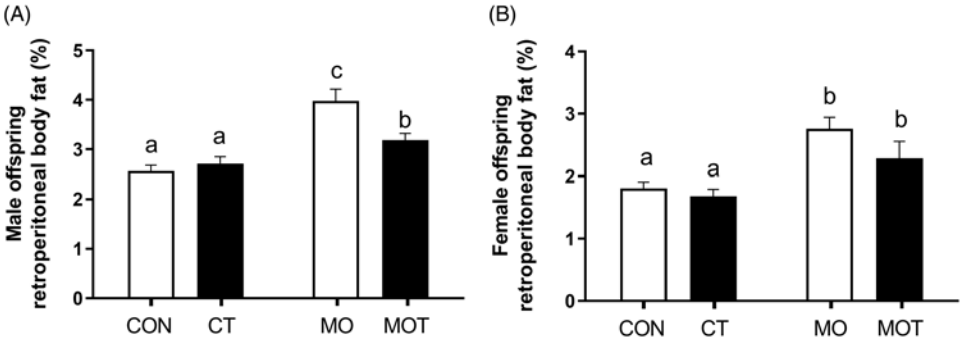

Fig. 1. Retroperitoneal fat mass (expressed as percentage body weight) in male (A) and female (B) adult offspring at day 150. Data are means ± SEM, $n = 7–9$ l represented per group. Letters that are different from each other represent statistically significant differences.

Results

Body and adipose tissue weights

Maternal and neonatal data have been reported by our group previously.[17] In brief, a MO diet resulted in maternal hyperinsulinemia and hyperleptinemia and increased plasma glucose, glutamate and TNF-α concentrations. Maternal plasma TNF-α and glutamate concentrations were normalised in MOT animals. MO neonates displayed a hepatic pro-inflammatory profile which was partially rescued in MOT offspring.[17] Conversely, a pro-inflammatory phenotype was observed in MOT mothers suggesting a possible maternal trade-off to protect the neonate. Of note, despite the protective effects of maternal taurine supplementation in MOT offspring, neonatal mortality was increased in CT neonates, indicating possible early adverse effects of taurine in the setting of normal pregnancy.[17]

In the present study investigating effects in adult offspring, final body weights were significantly increased in male and female offspring of mothers fed the MO diet but there was no effect of taurine supplementation (Table 1). Retroperitoneal fat pad weights were significantly increased in adult male and female offspring of MO mothers (Fig. 1A, 1B). There was a significant maternal diet x taurine interaction in male offspring, whereby maternal taurine supplementation reduced retroperitoneal adipose tissue weights in MO offspring but not in CON offspring (Fig. 1A).

Pubertal onset

Male offspring: Pubertal onset in male offspring was significantly earlier in CT, MO and MOT groups when compared with CON (Fig. 2A, 2C). MO resulted in an overall earlier age of pubertal onset but there was no significant effect of taurine supplementation. There was a significant interaction between maternal diet and taurine on age of onset of puberty where CT offspring entered puberty earlier compared to CON animals (Fig. 1C). Similarly, MO resulted in an overall reduced body weight at the time of pubertal onset but there was no overall significant effect of taurine supplementation. There was a significant interaction between maternal diet and taurine on male body weight at onset of puberty being reduced in CT compared to CON animals but no effect of taurine in MO groups (Fig. 2E).

Female offspring: Although there was no overall effect of maternal diet, post hoc tests showed that pubertal onset was earlier in MO compared to CON females (Fig. 2B, 2D). Although there was an overall effect of maternal taurine on reducing age of pubertal onset, this was only significant in CON animals as evidenced by a significant maternal diet × taurine interaction (Fig. 2D). There was an overall effect of MO on a lower body weight at pubertal onset in MO and MOT animals compared to CON. There was a maternal diet × taurine interaction on body weight at time of pubertal onset with taurine leading to a lower body weight in CON animals versus CT but this was not evident in MO animals (Fig. 2F).

Plasma glucose, insulin, leptin, HcY and ketones

Fasting plasma insulin concentrations in adult males were increased in offspring of MO mothers and were not altered as a result of maternal taurine supplementation (Fig. 3A). Similarly, plasma leptin concentrations in adult males were increased in offspring of MO mothers and were not altered as a result of maternal taurine supplementation. As with males, female offspring of MO mothers had increased plasma leptin and insulin concentrations compared to CON offspring and were not affected by maternal taurine supplementation (Fig. 3B).

Plasma HcY concentrations in adult offspring were not altered as a result of maternal diet (Table 1). There was a significant overall effect of maternal taurine in lowering HcY concentrations

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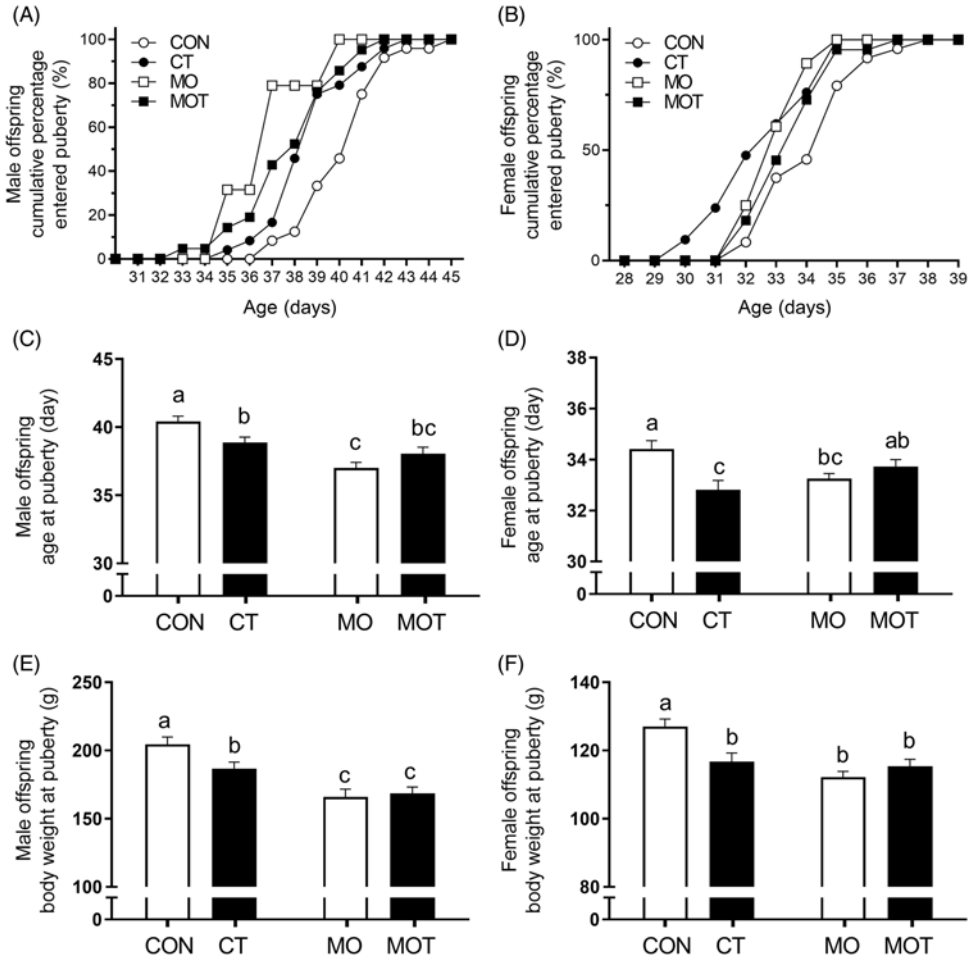

Fig. 2. Pubertal outcomes in offspring of mothers fed an obesogenic diet and supplemented with or without taurine. Percentage of male (A) and female (B) offspring entering puberty over time. Age at puberty in males (C) and female (D). Body weight at onset of puberty in males (E) and females (F). Data are means ± SEM, $n = 7$–9 l represented per group. Letters that are different from each other represent statistically significant differences.

($P < 0.005$), and HcY concentrations were higher overall in females compared to males ($P < 0.001$). There were no differences in fasting plasma glucose concentrations across any of the maternal diet or taurine groups (Table 1), although glucose concentrations were slightly but significantly lower in females compared to males. Similarly, there were no overall effects of maternal diet or taurine supplementation on plasma ketone concentrations with the only significant effect being sex with higher plasma ketone concentrations in females compared to males (Table 1). There were no significant interactions present for any of the plasma measures examined.

OGTT

The overall response to glucose load and calculated area under the curve (AUC) was increased in MO male and female offspring, and glucose concentrations were lower in females compared to males (Fig. 4A, 4B, 4C, 4D). There was an effect of taurine supplementation on improving glucose response in male MO offspring compared to CON groups with a maternal diet x taurine interaction, whereby glucose response was directionally dependent upon prior maternal nutritional status (Fig. 4A, 4C). In females, there was no effect of maternal taurine supplementation on AUC but there was an increase in the glucose response in the AUC in MO and MOT offspring compared to the CON and CT groups (Fig. 4B, 4D).

Food choice behaviour

There were no significant differences in caloric intake between the groups prior to the start of the 10-day food choice behaviour trial (data not shown). Body weight gain at the end of the 10-day food choice period was significantly increased in MO male offspring compared to all other groups (Fig. 5A). There was an overall effect of maternal taurine supplementation to reduce diet-induced weight gain in males over the trial period ($P < 0.005$) and this was more pronounced in the MO groups as compared to controls (maternal diet × taurine interaction $P < 0.05$). Average daily caloric intakes over the 10-day food choice period were increased in the MO group and reduced with taurine in both CT and MOT male groups compared to CON and MO (Fig. 5C). There was a sexually dimorphic response in the food preference test data. Although there was a significant effect of maternal diet in female offspring on increased weight gain during the trial period ($P < 0.001$), there was no effect of maternal taurine supplementation in females in reducing the propensity for diet-induced weight gain (Fig. 5B). Average daily caloric intakes were increased in MO groups compared to CON and CT, but there was no effect of maternal taurine supplementation (Fig. 5C).

Given that the rats were given a dietary choice (standard chow versus high-fat (HF) diet), we also examined any effects of maternal dietary background on preference for the HF diet in offspring. In males, the MO groups displayed a slight but significant

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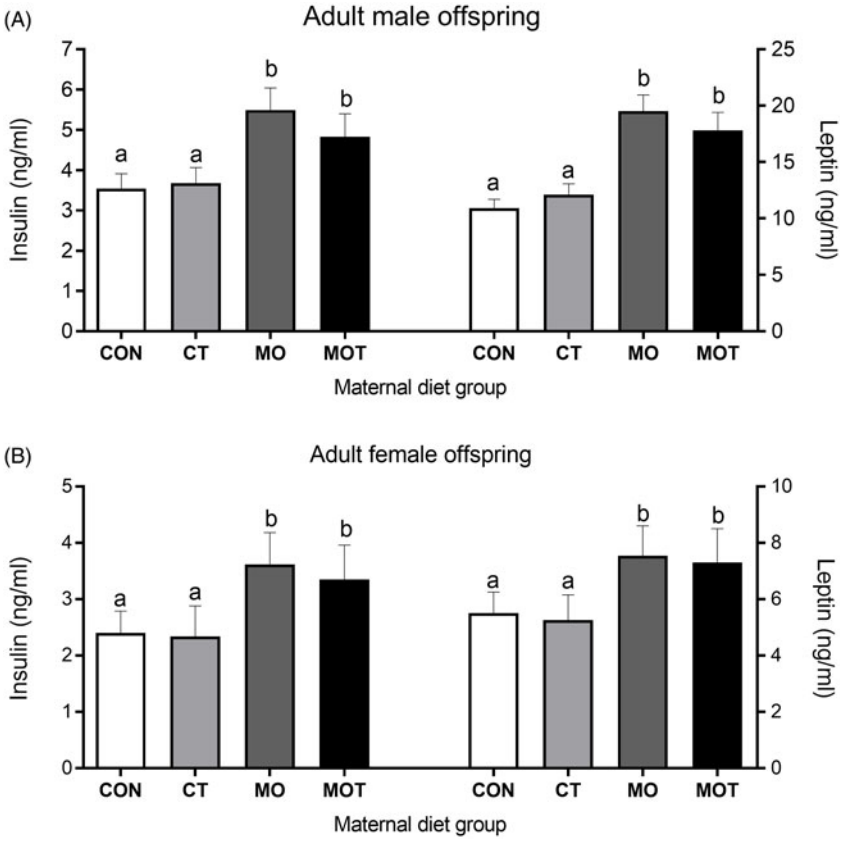

Fig. 3. Fasting plasma insulin and leptin in (A) male and (B) female offspring at day 150. Data are means ± SEM, $n = 7$–9 l represented per group. Letters that are different from each other represent statistically significant differences.

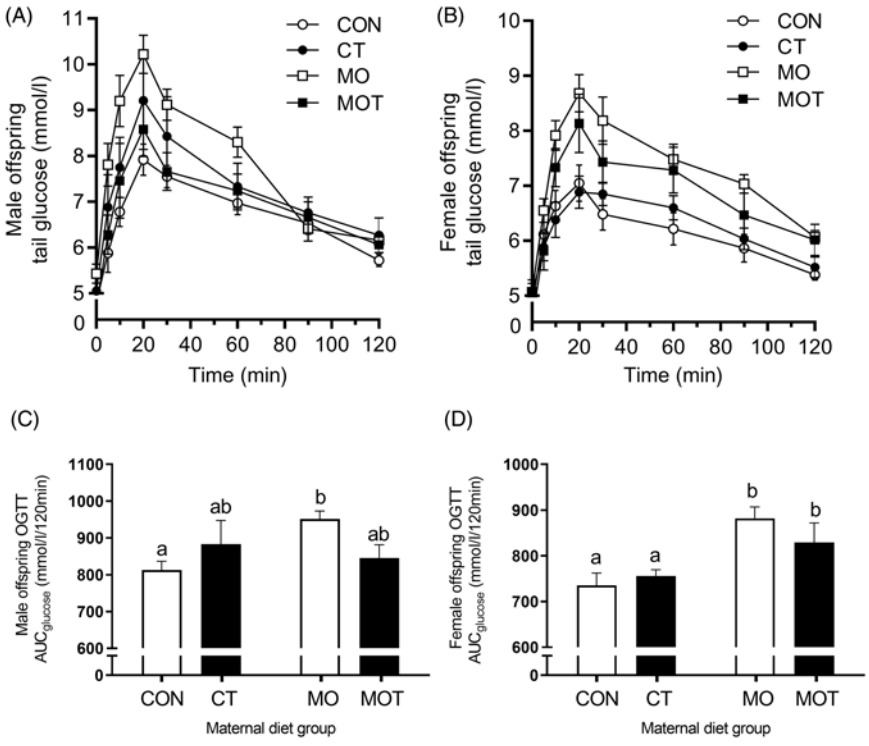

Fig. 4. Response to an oral glucose tolerance test (OGTT) in (A) male and (B) female offspring at day 143 and OGTT area under the curve (AUC) for (C) male and (D) female offspring. Data are means ± SEM, $n = 6$ per group.

preference for the HF diet compared to the CON groups over the 10-day period (CON 84.3 ± 1.6% of total kcals derived from the HF diet, CT 78.9 ± 2.8%, MO 91.1 ± 0.7%, MOT 89.8 ± 1.6%, $P < 0.001$ for effect of maternal diet). A small but significant effect on total caloric intake derived from the HF diet was also observed in females in the MO groups with a significant effect of taurine in

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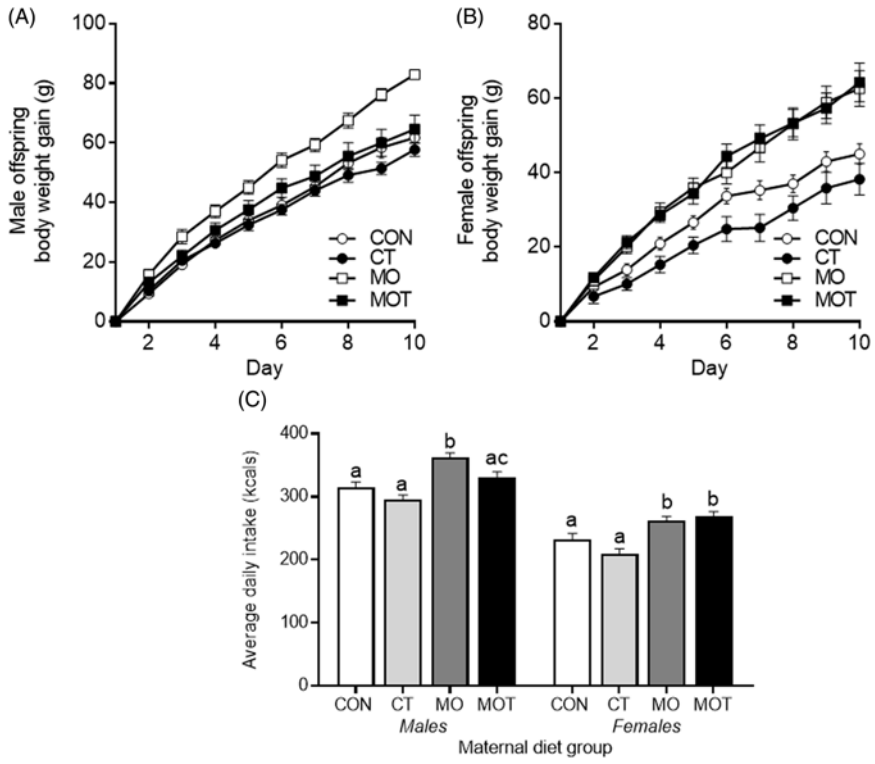

Fig. 5. Body weight gain in males (A) and females (B) and average daily caloric intake (C) during a 10-day high-fat dietary preference test at day 130. Data are means ± SEM, $n = 7$–9 l represented per group.

reducing HF-derived intake (CON 95.3 ± 0.7% of total kcals derived from the HF diet, CT 91.4 ± 1.5%, MO 96.7 ± 0.4%, MOT 95.2 ± 0.7%, $P < 0.001$ for the effect of maternal diet and taurine supplementation). There was also a sex-specific effect with total calories derived from the HF diet higher overall in females compared to males ($P < 0.001$).

Discussion

The current study provides evidence for long-term beneficial effects of maternal taurine supplementation in the setting of a MO diet on offspring outcomes. Importantly, these effects were seen to be sex-specific in nature and directionally dependent upon the maternal dietary background. As previously reported by us and others, a MO diet resulted in increased absolute body weights in offspring in adulthood concomitant with increased adiposity and increased circulating insulin and leptin concentrations.[19,20,21,22] Interestingly, maternal taurine supplementation had a lasting effect on reducing adult fat mass in offspring exposed to an *in utero* obesogenic diet. Although the mechanisms underlying the anti-obesity action of taurine remain to be defined, taurine has been suggested to ameliorate obesity through stimulation of energy expenditure, modulation of lipid metabolism and anti-inflammatory and antioxidative effects.[23] Recent work by Wen *et al.* has highlighted the role of taurine in energy metabolism in muscle, adipose tissue and liver.[24] In the non-pregnant state, taurine supplementation results in a reduction in white adipose tissue and was related to upregulation of peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α) expression, suggesting that taurine stimulates energy expenditure.[23,24] Our previous work in this model has shown that the MO neonates display a pro-inflammatory hepatic profile which is partially rescued in MOT offspring[17] and these effects may have persisting beneficial effects into adulthood, albeit in a sex-specific manner.

To date, there only a few reports to date where sex-specific effects in offspring following maternal taurine supplementation have been examined. In a model of uterine artery ligation, perinatal taurine exposure was shown to alter arterial pressure control in adult rats in a sex-specific manner.[25] These effects were proposed to be mediated via taurine exposure resulting in changes in sex hormone status in early life which impacted upon longer term tissue function. Maternal taurine supplementation in the late pregnant rat also has been shown to lead to sex-specific effects with the adult phenotype more pronounced in female offspring.[26] It has also been suggested that, in male offspring, taurine is mainly improving β-cell function, whereas in females, the predominant effect of taurine is in peripheral insulin-sensitive tissues.[15] In female rats, it has been suggested that changes in maternal taurine status alters the interplay of the renin–angiotensin system and estrogen on glucose–insulin regulation.[27] Similarly, taurine has been shown to normalise steroidogenesis in diabetic male rats via amelioration of inflammation and oxidative stress and attenuation of hyperglycemia,[28] but no data on maternal taurine supplementation on male offspring hormone status are currently available.

Maternal taurine supplementation resulted in a lasting effect on reducing plasma HcY concentrations in adult male and female offspring. We have previously reported that an obesogenic diet results in hyperhomocysteinemia in mothers during pregnancy.[17] However, the association between maternal HcY status and relative hypohomocysteinemia in offspring in the present study is unclear. It is possible that altered regulation of maternal hepatic methionine metabolism as a result of taurine intake impacts on in utero methionine exposure and could result in fetal hepatic adaptations that result in changes in postnatal HcY metabolism.

We have previously shown that a MO diet leads to early onset of puberty in male and female offspring that is associated with increased weight at weaning, hyperleptinemia and increased fat mass in the immediate pre-pubertal period.[29–32] In the current

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study, a maternal high-fat:high-fructose diet resulted in an overall early onset of puberty in males with no overall effect of maternal taurine supplementation. However, there was a maternal diet × taurine interaction whereby pubertal onset was earlier in CT versus CON animals, but no effect of taurine observed in MO groups. In females, there was no main effect of maternal diet but post hoc testing showed that pubertal onset was earlier in MO offspring compared to CON. As in male offspring, maternal taurine reduced pubertal onset in CON animals but had no further impact on MO offspring. The signalling pathways that elicit changes in pubertal onset are unclear, but it is possible that taurine exposure during vulnerable windows of hypothalamic–pituitary–gonadal development changes neuronal connections and gonadotrophic regulators.[33] Further, the effects of taurine supplementation on pubertal onset may be driven by changes in leptin, a permissive factor in the initiation of puberty, in the early post-weaning period but this was not investigated in the present study. The sex-specific differences observed in the current study may reflect different dietary compositions on offspring outcomes; previous work has utilised a single source HF diet,[29,30] whereas the current study has utilised a high-fat:high-fructose diet. Nonetheless, these observations further highlight the effect of the maternal nutritional environment as a mediator of pubertal outcomes in offspring.

The effects of maternal taurine supplementation on improving glucose metabolism (β-cell function and insulin sensitivity) have been well characterised across a range of programming models. A MO diet resulted in an overall impaired glucose intolerance in male and female MO offspring compared to offspring of control-fed mothers. We observed an effect of maternal taurine supplementation in ameliorating impaired glucose tolerance in male MO but not female MO offspring. Of note, the effect of taurine supplementation in response to the OGTT in males was directionally dependent upon prior maternal nutritional status with overall beneficial effects seen in the MOT group only with supplementation in control males worsening glucose responsiveness to the OGTT. Such directionally dependent programming effects have been reported by our group previously[34] and suggest that maternal supplementation in the setting of replete systems may actually lead to aberrant longer term regulation of key systems, including glucose homeostasis. This fits with the observations of Merezak *et al*. whereby taurine supplementation protected pancreatic islets in offspring from low-protein mothers, but unnecessary supplementation of taurine to control animals had detrimental effects including increased islet sensitivity.[14] Maternal taurine supplementation has been shown in other models of altered maternal nutrition to exert positive effects on both hepatic and pancreatic function in offspring,[13–15] possibly via protection from cytokine toxicity, so the protective effects of taurine observed in the MO groups in the present study, though not unsurprising, are the first reports in a MO model.

A striking observation in the present study was the effect of a dietary preference test on weight gain in offspring of mothers fed the obesogenic diet. Males and female MO and MOT groups both exhibited increased body weight gain compared to CON groups paralleled by increased total caloric intake over the test period. Offspring exposed to an obesogenic environment prior to birth appear to have established a preference for the HF diet regardless of their postnatal environment, which made them susceptible to obesity. Maternal taurine supplementation resulted in a protective effect in males, whereby weight gain was significantly reduced in MOT males compared to MO males. In addition to absolute changes in caloric intake, these effects may also be mediated in part due to programmed differences in energy utilisation and energy expenditure across the different dietary groups. Whether maternal taurine supplementation had direct and persisting effects on central brain regions controlling appetite regulation and energy expenditure in offspring has to be studied further.

In contrast to the present data, taurine supplementation in late gestation has been reported to result in accelerated postnatal growth and adult obesity and insulin resistance in both intrauterine growth restriction (IUGR) and control offspring.[26] However, this was a model of uterine artery ligation-induced growth restriction and not a dietary model and, moreover, only 12% of IUGR pups survived until adult age thus representing a survivor analysis. However, such studies do serve to reinforce that fetal taurine status is an important determinant for postnatal growth, insulin sensitivity and fat accumulation. Taurine has also recently been shown to have protective effects in the setting of maternal alcohol consumption[16] and perinatal taurine exposure affects adult arterial pressure control.[35] Recent work has also suggested that whereas perinatal taurine supplementation appears to have only minor effects on adult physiology, perinatal taurine depletion is associated with multiple adverse health effects, especially in animals exposed postnatally to other insults including a HF diet.[36]

In summary, the present study has highlighted the long-term effects of a MO diet on metabolic and pubertal outcomes in male and female offspring and partial amelioration as a result of maternal taurine supplementation. Importantly, in the context of the present study, some programming effects were only unmasked in the presence of a dietary preference test or a glucose tolerance test. The present study also further highlights the importance for the examination of sex-specific effects in these models[37] given that many of the observations were sexually dimorphic in nature. These data add further evidence for a supportive role of early-life taurine in protecting against aberrant early-life metabolic programming, although the mechanistic basis of these observations remains to be fully defined.

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Conflicts of interest. None.

Ethical standards. The authors assert that all animal procedures were performed in accordance with the New Zealand Animal Welfare Act 1999 and were approved by the Animal Ethics Committee of the University of Auckland, New Zealand.

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