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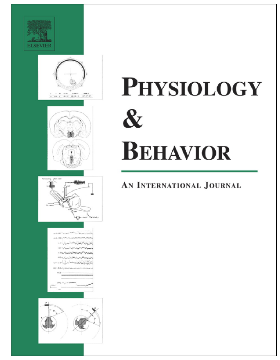

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Associations between Otitis media, taste sensitivity and adiposity: Two studies across childhood

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Abstract

Background: Otitis media (OM), or middle ear infections, are one of the most common diseases during early childhood. OM has been linked to changes in food preferences through potential effects on taste signalling, and thereby, to increased weight. **Objectives:** We investigated the associations between OM, taste sensitivity and adiposity across two studies in early childhood and conducted exploratory post-hoc analyses of sex differences. **Methods:** Study I assessed 101 children between 2 to 3 years old (59.0% boys). Children were weighed and their height was measured to estimate BMI centiles. Waist measurements were taken to calculate Waist-to-Height Ratio (WHtR). Child's taste sensitivity was assessed using Short Sensory Profile questionnaire. Study II included 95 children between 5 to 9 years old (52.9% boys). Children were weighed and their height was measured to calculate their BMI. Children took part in a Sucrose Detection Threshold (SDT) assessment to establish their taste sensitivity. In both studies parents reported child's history of OM. **Results:** In Study I OM was associated with higher WHtR (p=0.047), though this was observed among girls (p=0.011), but not boys (p=0.53). OM was not linked to BMI centiles or taste sensitivity (all p>0.05). In Study II children with OM history had higher BMI centiles (p=0.010), and this effect was stronger in boys (p=0.037) than girls (p=0.17). Multiple OM exposure increased the odds of overweight by 6.2 times (95%CI [1.46, 26.50]). Boys with multiple OM exposure had higher SDT (p=0.022) compared to boys not exposed to OM, akin to lower taste sensitivity. This was not observed in girls (p=0.67). **Conclusions**: OM history was associated with higher BMI among 5-9 year old children and this may be linked to taste impairments. This association was not observed in 2-3 year old children. Potential sex differences in these associations require further investigation.

Keywords: Otitis media; middle ear infection; childhood obesity; overweight; taste sensitivity

Abbreviations

OM	Otitis Media
WHtR	Waist-to-Height Ratio
SDT	Sucrose Detection Threshold
CT	Chorda Tympani
SSP	Short Sensory Profile
BF	Breast Feeding
BMI	Body Mass Index

1.0 Introduction

Otitis media (OM), or middle ear infection, is one of the most common, childhood infections, with high occurrence rates between 6-24 months of age (1). Although prevalence rates differ between the studies, it has been estimated that globally as many as 51% of children will have at least one episode of OM by the age of 5 years (2). This is problematic because OM causes pain, fever and may lead to temporary, or in the most severe cases, permanent hearing impairment (3) and, due to its high incidence, poses a large economic burden on public health (4). As a post-inflammatory response acute OM can progress to OM with effusion and recurrent forms can be treated surgically, with or without tympanostomy tube insertion (3).

Previous research, although limited, has linked OM exposure to increased Body Mass Index (BMI; kg/m^2) among 3-5 year old (5) and 7-10 year old children (6). Clinical evidence shows that 2-7 year olds with a history of OM with effusion had significantly higher BMI compared to children without OM history (7, 8). In a prospective cohort study of 538 infants up to 2 years old, those with recurrent OM treated with tympanostomy tube insertion were more likely to have a weight-for-length measure above ≥95th percentile at 2 years of age (9). Another prospective cohort study showed that 10-11 year old children with obesity were more likely to have experienced OM compared to children with healthy weight (10). However, these associations were not observed in another study of 5-18 year olds (11).

The mechanism through which OM may play a role in an unhealthy weight gain is not well understood. A theoretical model has been proposed, which suggests that OM exposure can lead to changes in taste and somatosensory function due to a damage to the Chorda Tympani (CT) nerve (5, 12). The CT nerve, together with the trigeminal nerve, innervate taste buds in the fungiform papillae on the anterior two thirds of the tongue (13).

The CT is vulnerable to damage as it separates from the lingual nerve and travels through the middle ear, where it may be exposed to pathogens that cause OM (14). Histopathological changes to CT and loss of the nerve function have been reported in a sample of 107 adults with chronic OM (15). Conversely, another study found no differences CT function among 5-18 year olds with a history of OM (11).

Consistent with the CT impairment hypothesis, it has been reported that children with recurrent OM lost the ability to taste quinine on the anterior portion of the tongue and showed enhanced responses to citric acid (16), while adults exposed to OM showed both reduction and enhancement of different tastes, including bitter, salty, sweet and sour (14, 17). In another study patients with chronic OM who were to undergo middle ear surgery showed pre-operative lower taste sensitivity for sour, bitter, salty tastes and sweet taste, and this improved one month post-operatively among those with good intra-operative preservation of CT, while among those with intra-operative CT injury taste function remained reduced (18). Similar taste function impairments were observed among adults with chronic OM mesotympanalis, with the largest changes reported for sweet and salty tastes (19). This model has also been supported in a large sample of healthy women, where history of OM was linked to reduced taste intensity of bitter tastant quinine (20). In the same study, greater central adiposity was associated with history of tonsillectomy and multiple ear infections, and with poorer taste functioning (20). Whilst there is a small literature on the relationships between OM and taste function in adults, taste function among children with OM history requires further investigation.

In explaining how OM may be linked to changes in adiposity, effects on taste function may be key. Changes in taste function could potentially translate to changes in dietary preferences and consequently energy intake (21, 22), which would mediate the link between OM exposure and BMI. However, research in this area is limited. An unpublished pilot study showed that US children with history of OM had greater intake of sweet foods and drinks, and decreased intake of vegetables (23). Pre-schoolers with at least three episodes of OM were reported by their parents to have lower liking for fruit and vegetables, and higher liking for high fat sweet foods compared to other pleasurable non-food activities (e.g. playing), suggesting increased reward value of highly palatable energy-dense foods and less healthy dietary preferences (5). However, these differences were more pronounced among boys than girls, pointing to the importance of examining sex differences in these associations. Similarly, among adults it has been shown that OM patients reported increased preference for sweet-fatty foods (14). Two unpublished studies from adult populations cited in Bartoshuk et al. (13) support the findings from Peracchio et al. (5), and suggest that the associations between OM and dietary preferences show slightly different patterns among adult men and women. Adult women with a history of severe OM did not show a typical age-dependent decrease in preference for high-sweet foods, and adult men with history of severe OM had increased preference for high-fat foods, consistent with the hypothesis that OM might affect taste and/or somatosensory function (24, 25).

In summary, previous research suggests that OM history may be linked with increased adiposity and altered taste function. Further research is needed to establish these links in childhood, use alternative measures of adiposity beyond BMI, and examine the potential mechanisms. We have investigated the associations between OM history, measures of adiposity and taste sensitivity across two studies in different age groups, among British children from primarily higher socio-economic status (SES) groups. We defined taste sensitivity as a broad concept that encompasses sensory processing and evaluation in the taste domain. Given a high incidence of OM episodes between 6-24 months (1), in Study I we examined early onset of these associations in a sample of 2-3 year olds. Taste sensitivity was measured using a psychometric measure (26). In Study II, the associations between OM exposure and BMI were examined in a sample of school-age 5-9 year old children. Children took part in sensory testing to establish their detection threshold of sucrose solution, as a proxy of taste sensitivity. We chose to focus on sucrose sensitivity for two reasons; firstly, because higher sucrose detection thresholds (SDT) predict the reinforcing value of foods and thus may be a good indicator of risk of overeating (27) and secondly, from authors' personal experience there is a greater likelihood of compliance of 5-9 year olds with the threshold tasks when asked to taste a series of sweet solutions (rather than bitter, sour, salty or umami tastes), that has also been previously reported (28). In both studies, it was hypothesised that children with history of OM would have higher BMI compared to children without OM exposure, and a higher frequency of OM episodes would be linked to higher BMI. Finally, we hypothesised that children with a history of OM would have poorer taste sensitivity. In both studies we conducted exploratory post-hoc sex effects in these associations.

2.0 Study I

Study I examined early-onset relationships between OM history and measures of adiposity and taste sensitivity among 2-3 year old children.

2.1 Materials and methods

2.1.1 Participants

The participants of this study were 103 children (42 girls and 61 boys; 41% and 59% respectively; four pairs of non-twin siblings) between 2-3 years of age, whose mothers provided information on the child's history of diagnosed OM when they attended the laboratory visit as a part of a larger project on novel fruit introduction. Families were recruited through the University of Birmingham Infant and Child Laboratory register of families interested in taking part in research, as well as the local nurseries. The final sample consisted of 101 children (41 girls and 60 boys; 40.6% and 59.4% respectively), as one child did not assent to being weighed and one child was classified as with underweight which may be indicative of feeding issues not accounted for. The average age of children in the sample was 29.3 months (SEM= 0.47). The mothers were predominantly White British (n= 82; 81.2%), with higher education (n= 72; 71.3%) and with high annual income (n= 76; 75.2%), with the mean age of M= 35.3 (SEM= 0.50) years. Mothers reported child's history of breastfeeding duration. Ethical permission for the study was provided by University of Birmingham Ethics Committee (ERN 12-0465AP1).

2.1.2 Measures and procedures

2.1.2.1 Otitis media

Mothers reported whether their child has ever been diagnosed with an infection of the middle ear (OM) by a medical professional, and to indicate the number of diagnosed episodes. Mothers were given an option to reply that they were not sure.

2.1.2.2 Anthropometrics

Children and their mothers were weighed using Seca 803 weighing scales to the nearest 100g and their height was measured using a Seca Leicester Portable height measure to the nearest 0.1cm in light clothing without shoes during the laboratory visit. Measurements were taken in accordance with the UK-WHO guidance issued by the Royal

College of Paediatrics and Child Health (2009). BMI scores were converted to z-scores and subsequently to BMI centiles corrected for age and sex, based on stature and weight reference curves for the UK, and these were used as an index of full-body adiposity (29-31). BMI centiles were used to classify children as with underweight (≤2nd centile), with healthy weight (>2nd centile, <85th centile), with overweight (≥85th centile, <95th centile), or with obesity (≥95th centile), based on the recommendations from the National Obesity Observatory (32).

In addition to measuring BMI we also collected a measure of child's waist circumference as an estimate of central adiposity, which has been shown to be a good predictor of cardio-metabolic risk (33, 34) and a better index of child adiposity than BMI, albeit in older age groups (35). Each child's waist circumference was measured to the closest 0.1 cm, in duplicate following standard WHO guidelines (36) and the average was used to calculate child's Waist-to-Height Ratio (WHtR), with higher ratio indicating larger central adiposity. The WHtR data were obtained from 95 children, as 8 children (2 boys) showed distress over having their waists measured. All measures of anthropometry were collected by two trained and experienced researchers.

2.1.2.3 Taste sensitivity

Empirical assessment of taste sensitivity was deemed not viable due to children's young age. To assess children's taste sensitivity, mothers completed the Short Sensory Profile (SSP) questionnaire (26). This measure was validated on children from 3 years old and has been shown to discriminate well (>95%) between children with and without sensory dysfunction. SSP contains 38 items completed by the parent, which evaluate sensitivity in 7 domains: tactile sensitivity, taste/smell sensitivity, movement sensitivity, underresponsive/seeks sensation, auditory filtering, low energy/weak and visual/auditory sensitivity (26). For the purpose of this study only taste/smell sensitivity was examined and hereafter referred to as taste sensitivity. This scale contains 4 items (My child: *Will only eat certain tastes; Avoids certain tastes or food smells that are typically part of children's diets; Limits self to particular food textures/temperatures; is a picky eater, especially regarding food textures*). The responses range from Always to Never on a 5 point Likert scale (1-20 points). The scores in the taste domain were cumulated and used to classify children to typical (15-20 points) or atypical behaviour group (4-14 points) following guidelines by Dunn. This measure has been previously used in studies examining children's eating behaviours (37). Sensory Profile and SSP are the most widely used measures of sensory processing in children from clinical populations (38).

2.2 Statistical analyses

The assumptions for parametric tests were broadly met, although BMI centile data distribution slightly departed from normality. Nevertheless, ANCOVA models were considered to be sufficiently robust (39). As the sample size was relatively small and groups were unbalanced, all analyses were supplemented with bootstrapped 95% bias-corrected accelerated CIs, with simple sampling procedure to reduce error variance. OM exposure was treated as a categorical binomial (No history of OM vs History of OM) and polynomial (No history of OM, Single vs Multiple exposure to OM) variable in separate tests. Measures of anthropometry were treated as continuous outcomes in the ANCOVA models and as categorical outcomes (weight status) in the logistic regression models.

Child's sex, child's age, breastfeeding status, SES and mother's BMI were selected as potential confounders and were controlled for in all analyses. Child's taste sensitivity was also identified as a potential confounder in the models examining the associations between OM history and measures of adiposity, and was considered as an additional covariate.

To test the hypothesis that children with history of OM would have higher adiposity than children without the OM history, two adjusted ANCOVA models were computed. The first model examined group differences between children not exposed to OM vs those with OM history. This analysis was repeated after stratifying by child's sex to examine exploratory post-hoc sex differences. The second model examined group differences when three OM exposure groups were considered. Sex differences were not examined here due to the small sample size of girls with a single OM episode (n=2). Additional logistic regression adjusted for covariates was conducted to compare the odds for being classified as with overweight among children who differ in OM history. To test the hypothesis that children with OM history would have higher odds of atypical taste sensitivity, adjusted logistic regression was conducted. Sex differences were not examined in the logistic regression models as the sample sizes of children with overweight and with atypical sensitivity, when also split by gender, were too small to yield reliable findings. All analyses were performed in SPSS 21.0 and alpha level of 0.05 was considered statistically significant.

2. 3 Results

2.3.1 Study Sample

Table 1 summarises sample characteristics in indices of adiposity, frequencies of children within different weight categories and taste sensitivity, as well as sex differences in these outcomes. The proportions of children with BMI indicative of overweight (n= 16; 16%) or obesity (n= 10; 10%) were small, so these two groups were merged together and were referred to as with overweight throughout. Among children with OM history, 5 had overweight (22%) and 7 were categorised as having atypical sensitivity (30%). There were no sex differences in BMI centiles, WHtR, weight category or taste sensitivity (all $p>0.05$).

Based on maternal reports 23 children in the sample were diagnosed with OM (22%). In the OM group the range of episodes varied between 1 and 10. A single episode of OM was reported by 12 mothers (12%), and multiple episodes were reported by the remaining 11 mothers (11%). Table 2 summarises the characteristics of the study sample across the OM exposure groups. There were no significant differences in age, breastfeeding duration, maternal age or BMI, annual family income or mother's education level between children with no OM history and those with single vs multiple reported episodes of OM (all $p> 0.05$).

2.3.2 OM and adiposity

The mean values per group supplemented with bootstrapped 95% CI are presented in Table 3. Children with OM history did not differ from children without OM history in BMI centiles ($F(1, 79)= 1.39$, $p= 0.24$, ${}_p\eta^2= 0.02$). Additional stratification by sex supported these findings and showed no group differences in BMI centiles among girls ($F(1,30)= 1.28$, $p= 0.27$, ${}_p\eta^2= 0.04$) or boys ($F(1, 43)= 0.25$, $p= 0.62$, ${}_p\eta^2= 0.01$). When three groups of OM exposure were examined BMI centiles did not vary by the OM exposure status ($F(2, 29)= 1.15$, $p= 0.33$, ${}_p\eta^2= 0.01$). The adjusted odds of being classified as with overweight did not vary by OM exposure ($\chi^2= 4.30$, $p= 0.74$; OR: 1.04 95%CI [0.31, 3.50], $p= 0.95$, Nagelkerke's $R^2= 0.07$).

Children with OM history had higher WHtR compared to children without OM history ($F(1, 75)=4.07$, $p= 0.047$; ${}_p\eta^2= 0.05$). These differences were observed among girls ($F(1, 26)= 7.54$, $p= 0.011$; ${}_p\eta^2= 0.23$), but not boys ($F(1, 43)=0.40$, $p= 0.53$; ${}_p\eta^2= 0.01$). When the three OM exposure groups were compared, the differences in WHtR were not statistically different ($F(2, 74)= 2.00$, $p= 0.14$, ${}_{p}\eta^2= 0.05$). Additionally controlling for BMI did not change these findings (unreported).

2.3.3. OM and taste sensitivity

The adjusted odds of atypical sensitivity were similar between children with and without OM history ($\chi^2= 2.46$, $p= 0.87$; OR: 1.09 $p= 0.78$, 95% CI [0.35, 3.37], Nagelkerke's $R^2= 0.04$). Similarly, no differences in the adjusted odds for atypical taste sensitivity were detected when three OM groups were considered ($\chi^2= 2.59$, $p= 0.86$; OR: 1.18-1.19, $p= 0.98$, Nagelkerke's $R^2= 0.04$).

2.4 Conclusions

Among 2-3-year-old children, OM history was not linked to child BMI. However, children with OM history, specifically the girls, had significantly higher WHtR compared to children without OM history, indicating higher central adiposity. This was not observed among boys. Children with OM did not differ from children without OM history in parent-reported measure of taste sensitivity.

3.0 Study II

Study II examined the associations between OM history, BMI and taste sensitivity among 5-9 year old children.

3.1 Materials and methods

3.1.1 Participants

The participants were 99 children (50 boys and 49 girls; 50.5% and 49.5% respectively; two pairs of non-twin siblings) aged between 5 to 9 years old, recruited from four primary schools in Birmingham (UK), as part of a broader study on children's eating. Information sheets, consent forms and questionnaires were distributed to parents by the schools. Once information was returned, children took part in SDT assessment and were weighed and measured in the school by the researcher. Two parents did not provide information on OM history and three children did not consent to being weighed (including one child with missing OM data), so data of 95 children were used in the analyses (48 boys and 47 girls; 50.5 % and 49.5 % respectively). The mean age of children in the sample was M= 7.20 (SEM= 0.13) years and mean parental age was M= 38.91 (SEM= 1.00) years. The majority of responders were mothers (n= 84; 88.4%) who identified themselves as White British (n= 87; 91.6%) and the remaining as South Asian.

For ethical reasons, information on other demographic characteristics was not collected to minimise identifying information as the questionnaires were not anonymous, and were not returned directly to us but were initially handed to the teachers. Nevertheless, index of Multiple Deprivation Rank (2010) indicated that all four schools were located in the top 5% of the most affluent areas in the UK. The variables not collected in Study II were not linked to OM exposure in Study I. Ethical permission was provided by the University of Birmingham Ethics committee (ERN 10-0010).

3.1.2 Measures and procedures

3.1.2.1 Otitis media

Parents were requested to report child's OM history using the same questionnaire as described in Study I (2.1.2.1).

3.1.2.2 Anthropometrics

Children were weighed and their height was measured to calculate BMI centiles and classify them into weight categories using the same procedure and equipment as described in Study I (2.1.2.1). We did not measure child's waist circumference in this study for ethical reasons, as there was no chaperone or caregiver in the room where the assessments took place and accurate measurement of waist circumference cannot be taken over clothing.

3.1.2.3 Taste sensitivity

Taste sensitivity was established using two proxies i.e. the taste/smell dimension of the SSP (26) questionnaire as described in Study I (2.1.2.3), and the SDT. One child was excluded from the SSP (Dunn, 1999) assessment due to a large number of missing answers.

Sucrose solutions were prepared from commercially available castor sugar and distilled water. The concentration of sugar in the solution was then confirmed with the use of a refractometer (Mettler Quick-Brix 60 Meter) on two occasions. The solutions were served at room temperature (22 °C) in white opaque paper cups (10 ml per serving), in the following weight-to-volume concentrations: 0%, 0.2%, 0.4%, 0.6%, 0.8%, 1.0%, 1.2%, 1.4% and 1.6%. Those concentrations were chosen after an initial pilot study that showed that these concentrations could differentiate between children with various SDT.

The 'sip and spit' triangle method for establishing the SDT was adapted after Zhang et al. (40) and is described in detail elsewhere (41). Children did not eat or drink anything other than water for at least 1 hour before testing and were tested in the morning, before lunch. Children were presented with three liquids during each round, which contained one sucrose solution (S) and two water solutions (W), presented in randomised order

(WWS,WSW, SWW) in increasing concentrations. The cups had random numbers written on them, to aid children's memory. Children were asked to indicate which one of the three liquids was different from the other two. The inter-trial interval was approximately 60 seconds and each trial was followed by double mouth rinsing. The test was stopped when the child identified the correct solution on three consecutive trials and the SDT was established as the middle correctly identified solution, or as the highest possible when the child correctly identified only the last solution presented. For reliability, the middle correctly identified solution was used as a SDT to control for the first correctly identified solution occurring by chance.

3.2 Statistical analysis

Analytical procedure was similar to Study I and is described in detail in section 2.2. Child's age and sex were adjusted in all analyses. Child's taste sensitivity as well as SDT were additional covariates in analyses that examined the associations between OM exposure and BMI. We conducted ANCOVA analyses with bootstrapped post-hoc pairwise comparisons to compare OM exposure groups in BMI and SDT, and logistic regressions to examine the odds of being classified as with overweight or with atypical taste sensitivity among children with OM history. Similarly to Study I due to the small number of children classified as with overweight and a small number of children with OM history it was not viable to conduct exploratory post-hoc sex differences in logistic regression models. However, as child sex was more balanced in this study compared to Study I, it was possible to test sex differences in the analyses that included three OM groups.

3.3 Results

3.3.1 Sample description

Among children included in the study 25 (27.4 %) had a reported history of OM, with the frequency of lifetime occurrence between 1 and 12 times. Of these, 11 children were reported to have experienced a single OM episode, and 13 children had multiple OM exposure. One parent who reported OM history did not specify the number of episodes and this child was not considered in the analyses focused on single and multiple reported episodes.

Table 1 summarises anthropometric outcomes, weight category classification, frequencies of typical and atypical taste sensitivity and SDT, as well as sex differences in these outcomes. There were 10 (11%) children who were classed as with overweight and 10 with obesity (11%) and the two groups were merged to a single group referred to as with overweight throughout. Among children with OM history 9 were classified as with overweight (36%) and 7 (29.2%) were categorised as atypical sensitivity. The median SDT in the sample was 1.00% (Range 0.4- 1.6%). There were no sex differences in any of the measures (all $p > 0.05$).

Table 2 summarises group characteristics across children with and without OM history. Children exposed to OM did not differ from those not exposed in age, maternal age or sex (all $p>0.05$).

3.3.2. Otitis media and BMI

The mean values per group supplemented with bootstrapped 95% CI are presented in Table 3. Children with reported OM history had significantly higher BMI centiles compared to children with no OM history ($F(1,88)= 6.88$, $p= 0.01$, ${}_p\eta^2= 0.07$). Stratification by sex revealed that these differences were larger among boys ($F(1,42)= 4.62$, $p= 0.037$, ${}_p\eta^2= 0.10$) compared to girls ($F(1,42)= 1.99$, $p= 0.17$, ${}_p\eta^2= 0.05$). These results were consistent when three OM exposure groups were compared ($F(1,87)= 4.61$, $p= 0.013$, ${}_{p}\eta^2= 0.10$). Children with multiple reported episodes had significantly higher BMI centiles compared to children with no OM (Δ= 26.2, p= 0.001, 95% CI [9.0, 41.2]). There were no significant differences in BMI between children with a single OM episode and those not exposed to OM (Δ= 8.9, p= 0.31, 95% CI [-7.8, 28.1]) or those with multiple reported episodes (Δ= -17.2, p= 0.099, 95% CI [-5.0, 35.5]). There was a non-significant trend for these differences to be marginally stronger among boys ($F(2,41)= 2.52$, $p= 0.093$, ${}_{p}\eta^2= 0.11$) than girls ($F(1,41)= 2.07$, $p= 0.14$, ${}_{p}\eta^2= 0.09$).

Children exposed to OM had 3.2 times higher odds to be classified as with overweight ($\chi^2= 12.25$, p= 0.032; OR: 3.24, p= 0.050, 95% CI [1.01, 10.46], Nagelkerke's $R^2= 0.19$), and children with multiple OM history had 6.2 times higher adjusted odds for overweight compared to children with no OM history ($\chi^2= 14.63$, p= 0.023; OR: 6.23, p= 0.013, 95% CI [1.46, 26.50], Nagelkerke's $R^2= 0.23$). Children with a single reported OM episode (B= 0.29, p= 0.75, OR: 1.33, 95% CI [0.23, 7.72]) and those with no OM history (B= 0.29, p= 0.75, OR: 1.33, 95% CI [0.23, 7.72]) had similar adjusted odds of overweight.

3.3.3. Otitis media and taste sensitivity

The adjusted odds of atypical taste sensitivity did not vary by OM exposure ($\chi^2= 8.53$, p= 0.074; OR:1.60, p= 0.41, 95% CI [0.52, 4.88], Nagelkerke's $R^2= 0.13$) or among those with a single and multiple reported episodes ($\chi^2= 8.08$, p= 0.089; OR: 1.00-2.20, p= 0.51, Nagelkerke's $R^2= 0.14$).

The mean values per group supplemented with bootstrapped 95% CI are presented in Table 3. There were no SDT differences between children with a reported history of OM and those not exposed ($F(1,91)= 1.24$, $p= 0.27$, ${}_{p}\eta^2= 0.01$). Consistent with the observed differences in BMI, stratification by sex showed a non-significant trend for a higher SDT among boys with OM history compared to boys with no OM history ($F(1,45)=3.03$, $p= 0.089$, ${}_{p}\eta^2= 0.06$). This trend was not observed among girls ($F(1,44)= 0.01$, $p= 0.98$, ${}_{p}\eta^2< 0.01$). When three OM exposure categories were examined, there was a non-significant trend ($F(2, 91)= 2.57$, $p= 0.082$, ${}_{p}\eta^2= 0.05$) for higher SDT among children with multiple OM exposure compared to children with a single (Δ= 0.29%, p= 0.092, 95% CI [-0.05, 0.62]) or no OM exposure (Δ= 0.23%, p= 0.087, 95% CI [-0.02, 0.50]). Analysis stratified by sex confirmed that these differences were observed among boys ($F(2, 44)= 4.17$, $p= 0.022$ ${}_{p}\eta^2= 0.16$), but not girls ($F(2, 43)= 0.42$, $p= 0.67$, ${}_{p}\eta^2= 0.02$), albeit small sample and effect sizes. Boys with multiple exposure to OM had significantly higher SDT compared to boys with a single (Δ= 0.50, p= 0.024, 95% CI [0.03, 0.90]) or no OM exposure (Δ= 0.50, p= 0.001, 95% CI [0.26, 0.74]). Among girls, all post-hoc comparisons were non-significant ($p>0.3$).

3.4 Conclusions

Among 5-9 year old children OM exposure is linked to higher BMI and higher odds of being classified as with overweight. Children with multiple exposure to OM had the highest BMI, while a single reported OM episode was associated with a similar risk for higher BMI as no exposure. Boys with multiple OM exposure tended to have higher SDT compared to boys with single or no OM history. Among girls, OM exposure was not associated with SDT.

4.0 Discussion

The results of these studies showed that OM exposure was associated with increased BMI among 5-9 year old children particularly among those with multiple OM episodes. Importantly, by the age of 5-9 years children with OM history were over 6 times more likely to be classed as with overweight. Exploratory post-hoc analysis of sex differences showed that these differences were stronger among boys than girls. Boys with multiple OM exposure also had higher SDT compared to boys with a single reported exposure or unexposed. In contrast, among 2-3 year olds OM was not linked to taste sensitivity or BMI, although children with reported OM history tended to have higher central adiposity, especially if female.

There is increasing interest in developmental cascade models of paediatric obesity, which attempt to capture the cumulative, downstream effects and consequences of early life risk factors, amplifying their effects on adiposity across time (42). Our findings would fit with such a model, with 5 to 9 year olds having had greater temporal opportunity for effects of OM to interact with other environmental factors to influence adiposity. In contrast, in the 2-3 year old group, effects of OM on BMI might not have yet manifested, though other early measures of adiposity show trends which may suggest the beginning of such a developmental cascade. Furthermore, it is possible that the slightly higher number of OM episodes in the 5 to 9 year old children (up to 12 vs up to 10 in the 2 to 3 year old group), may have resulted in more substantial impairments to their physiology. This is in line with previous research, which demonstrated increased BMI among 3 to 5 year olds with the highest OM exposure in the US sample (5).

There were some sex differences in the reported relationships. It is unclear why among 5 to 9 year old children boys seemed to be more susceptible to the effects of OM on BMI, independent of their exposure category. Among 2 to 3 year old children, the associations between OM and WHtR were primarily observed among girls. Although not significant, in the 2-3 year old sample more girls than boys had multiple OM history, so it is possible that the apparent sex effect on adiposity here is actually an effect of greater OM exposure. Further longitudinal studies with larger samples should examine whether the sex effects seen in these studies are spurious, are manifestations of other effects (such as OM exposure or exposure to other risk factors) or whether sex truly moderates the effects of OM exposure on adiposity outcomes. Nonetheless, together, these results suggest that children with the highest risk of increased BMI are those with recurrent OM episodes, and that these associations emerge during early childhood and are observable during school-age.

It has been previously suggested that OM may impair taste and somatosensory signalling, causing changes to taste perception and food preferences, which would then manifest in more unhealthy eating behaviours (13, 14). OM has been previously linked to reduced sensitivity to the bitter tastant quinine and increased sensitivity to the sour taste of citric acid in children (17), and to reduced taste sensitivity to sour, bitter, salty tastes and sweet taste in adults (16, 17). Furthermore, Shin et al., (8) demonstrated significantly higher taste thresholds for sweet and salty tastes in 3 to 7 year old Korean children with chronic OM with effusion in comparison to children with no OM history. The results of the current study are consistent with these findings, demonstrating that in the UK, 5-9 year old children with multiple OM exposure tended to have higher detection thresholds for sucrose, suggesting poorer sensitivity to sweet taste. Previous research linked damage to CT nerve to increased preferences for sweet foods and increased preference for fats in adults (13). Studies which directly measured the associations between OM exposure and food intake showed that the more severe history of OM was linked to increased intake of sweet foods and decreased intake of vegetables in US children (23), as well as increased liking for sweet/fat foods and decreased liking of fruits and vegetables in 3 to 5 year old children in the US (5). The results of the current study suggest that recurrent OM may be linked to decreased sensitivity to sweet taste, and further research is needed to examine OM's effects on dietary preferences and intake. That we did not find effects of OM on parent report of taste sensitivity in 2 to 3 year olds may be due to the choice of measure. The items that index taste sensitivity in the SSP (26) do not differentiate between specific tastes and include measures of smell reactivity as well as reactions to food textures. Whilst we chose this measure because very young children are unable to comply with the methods required for threshold detection tests, further research with measures better suited to examination of taste perception in young children is necessary.

OM is one of the most common childhood diseases (1, 2), that has been linked to increased BMI and obesity risk (5-10), which poses an important public health challenge (4).The results of the current study showed that 5 to 9 year old children with OM history were over 6 times more likely to be classed as with overweight, highlighting the need to develop appropriate interventions targeting at-risk children. Public health campaigns should focus on the promotion of factors that are established to reduce risk of OM such as breastfeeding and reducing passive smoking (43, 44). Vaccination may help to reduce acute OM and reduce the use of antibiotics (45). In addition, the findings of this study suggest that clinicians who work with children with chronic OM should consider making referrals for, or delivering, support to families with regards to dietary changes or feeding behaviours that may be necessary to reduce obesity risk. This may include advice about the use of repeated exposure to facilitate preference for less palatable, lower energy density foods (46).

These studies had several limitations worth noting. Child's OM exposure was a retrospective parental report not verified against child's medical records, which limits its reliability. Nevertheless, parental report of child's OM history has been shown to be reliable when validated against the medical records (47). In both studies we had no detailed information about the severity of OM and the associated treatment with tympanostomy tubes or antibiotics, or information on other potential confounders such as air pollutants or smoking status that may explain the associations between OM and adiposity (48, 49, 50). Additionally in Study II we did not collect information on maternal BMI, household income or breastfeeding history, and although they were not significantly related to outcomes in Study 1, they may still be important confounders (51 , 52-54). As we recruited our samples from affluent populations, the proportion of children with OM history was low and the samples were likely to have relatively few of the risk factors for chronic or repeated OM. Further work with higher risk samples is therefore warranted. Small number of children with OM history precluded any further exploration of the interactions with the potential confounders and for this reason any reported sex differences should be interpreted with caution.

This work has been based on the assumption that OM may cause taste impairments which could subsequently lead to greater adiposity. However, it is possible that metabolic disturbances associated with obesity lead to changes in taste sensitivity (55), although the causal pathways linking obesity to taste responsiveness are not yet clear (56). Longitudinal studies examining the development of these relationships are needed. Furthermore, we acknowledge that the adiposity measures that we used have limitations i.e. WHtR measurement in European pre-schoolers has been demonstrated to be less reliable than measurement of height and weight (57), and BMI has been suggested to lack appropriate sensitivity to be a marker of adiposity in comparison to more intensive measurements such as body composition techniques (58). Finally, the sensory evaluation in the 2 to 3 year old group was conducted using a questionnaire that was originally validated for older children (from 3 years of age) and the taste/smell sensitivity subscale of this questionnaire does not allow us to differentiate taste from olfactory sensitivity. Further research is needed using an age-appropriate empirical measure of child's taste sensitivity for 2-3 year olds.

Conclusions

The results of this study support earlier research in this area and highlight associations between OM, BMI and taste sensitivity, as well potential sex-specific effects. Among 2 to 3 year old children OM exposure was not associated with BMI or reported measure of taste sensitivity, although girls with OM history had higher WHtR. Intriguingly, these sex differences showed opposite links with BMI in 5 to 9 year old children. Among 5 to 9 year olds, children with multiple OM episodes had over six times higher odds of being classified as with overweight compared to children with no OM history, and these differences were primarily observed among boys. Although there were no overall differences in SDT, consistent with differences in BMI, boys with multiple OM history had significantly higher SDT compared to boys with a single or no OM episodes, suggesting that multiple exposure to OM infection may be particularly detrimental to taste function. Future studies should systematically examine these sex differences and potential influence on children's food preferences and dietary intake.

Authors declare no conflict of interest

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Author contributions

AF and JB conceived the studies, analysed and interpreted data. Both authors were involved in writing and finalising the manuscript. Both authors had full access to the data and final responsibility for the decision to submit for publication.

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Table 1. Sample characteristics in BMI centiles, WHtR (Mean ± SEM), weight category and taste sensitivity classification as well as sex differences in these variables.

	Total	Boys	Girls	p-value[1]
Study I				
BMI centiles	61.9 ± 2.67	59.89 ± 3.42	64.72 ± 4.28	0.38
WHtR	0.57 ± 0.004	0.57 ± 0.004	0.57 ± 0.005	0.88
Weight category				0.46
Healthy weight	75 (74%)	46 (77%)	29 (71%)	
Overweight or obesity	26 (26%)	14 (23%)	12 (29%)	
Taste sensitivity				0.54
Typical	73 (72%)	42 (70%)	31 (76%)	
Atypical	28 (28%)	18 (30%)	10 (24%)	
Study II				
BMI centiles	54.7 ± 3.0	58.0 ± 4.11	51.3 ± 4.34	0.26
Weight category				0.96
Healthy weight	75 (79%)	38 (79%)	37 (78.7%)	
Overweight	20 (21%)	10 (21%)	10 (21.3%)	
Taste sensitivity				0.16
Typical	70 (75%)	32 (68%)	38 (81%)	
Atypical	24 (25%)	15 (32%)	9 (19%)	
SDT (%)	0.89 ± 0.04	0.90 ± 0.06	0.88 ± 0.05	0.77

BMI- Body Mass Index; WHtR- Waist-to-Height Ratio; SDT- Sucrose Detection Threshold; [1]p-value for T-tests reported for BMI centiles and WHtR; p-value for Chi-squared reported for Weight category and taste sensitivity classification.

Table 2. Group differences (Counts or Mean ± SEM) across various sample characteristics[1] between children exposed and not exposed to Otitis Media in Study I and Study II.

	Otitis media history			
	No OM (n= 78)	OM (n= 23)	Single (n= 12)	Multiple (n= 11)
Study I[2]				
Child's sex				
Boys	46 (59%)	14 (61%)	10 (83%)	4 (36%)
Girls	32 (41%)	9 (39%)	2 (17%)	7 (64%)
Child's age (mths.)	29.1 ± 0.54	30.0 ± 0.92	28.9 ± 1.3	31.2 ± 1.2
Child BF (mths.)	4.9 ± 0.4	4.7 ± 0.5	4.9 ± 0.7	4.4 ± 0.7
Household Income (£)				
Below 30k	22 (28%)	3 (13%)	1 (8%)	2 (18%)
Above 30k	56 (72%)	20 (87%)	11 (92%)	9 (82%)
Mother with higher education				
Yes	53 (68%)	20 (87%)	11 (92%)	9 (82%)
No	25 (32%)	3 (13%)	1 (8%)	2 (18%)
Mother's age (yrs.)	34.7 ± 0.6	37.2 ± 0.9	37.0 ± 1.0	37.6 ± 1.6

Mother's BMI (kg/m^2)	26.0 ± 0.7	24.3 ± 0.8	23.6 ± 1.0	25.0 ± 1.22
Study II[3]	**No OM (n= 70)**	**OM (n= 25)**	**Single (n= 11)**	**Multiple (n= 13)**
Child's sex				
Boys	37 (53%)	11 (44%)	5 (46%)	5 (38%)
Girls	33 (47%)	14 (56%)	6 (54%)	8 (62%)
Child's age (yrs.)	7.2 ± 0.16	7.0 ± 0.27	7.1 ± 0.40	7.0 ± 0.40
Mother's age (yrs.)	39.6 ± 1.19	37.0 ± 1.85	38.8 ± 1.01	38.6 ± 1.63

BF: Breastfeeding ; **BMI**: Body Mass Index; **Mths.:** months; **Yrs**.: years; **OM**: Otitis media; [1] Chi-squared tests used to examine the differences in sex and education; t-tests used to examine the differences where two Otitis media groups were considered and ANOVA where three groups were compared; [2] All group differences were non-significant; Some information was missing as 8 parents did not report child's history of breastfeeding, 2 mothers did not report their age and 3 mothers did not consent to being weighed. [3] All group differences were non-significant *Note* In Study I

Table 3. Group differences (mean and bootstrapped 95% CIs) in the main study outcomes among children with different history of OM exposure.

	Otitis media history			
	OM	No OM	Single	Multiple
Study I[2]				
BMI centiles	69.7 [58.6, 78.8]	63.3 [56.5, 69.7]	67.2 [44.3, 87.3]	71.7 [59.9, 83.0]
Boys	66.0 [48.6, 82.3]	62.6 [54.5, 70.5]	-	-
Girls	74.1 [60.2, 86.8]	64.2 [53.9, 73.5]	-	-
WHtR	0.58 [0.56, 0.60][a]	0.57 [0.55, 0.58][a]	0.59 [0.54, 0.62]	0.58 [0.56, 0.61]
Boys	0.57 [0.54, 0.60]	0.57 [0.55, 0.59]	-	-
Girls	0.60 [0.57, 0.62][a]	0.56 [0.55, 0.58][a]	-	-
Study II[3]	**OM**	**No OM**	**Single**	**Multiple**
BMI centiles	65.8 [54.2, 76.4][a]	50.2 [43.3, 57.0][a,b]	56.0 [39.8, 73.5]	75.7 [61.0, 88.4][b]
Boys	73.2 [59.3, 85.7][a]	52.8 [43.4, 62.4][a,#]	65.9 [45.2, 88.3]	71.3 [6.41, 11.03][#]
Girls	60.6 [42.8, 77.7]	47.3 [37.1, 57.2]	46.1 [21.2, 70.3]	71.4 [52.3, 90.0]
SDT (%)	0.97 [0.79, 1.15]	0.87 [0.78, 0.95][#]	0.82 [0.63, 1.04][#]	1.11 [0.84, 1.37][#]
Boys	1.09 [0.82, 1.37][#]	0.85 [0.75, 0.96][a]	0.87 [0.53, 1.20][b]	1.36 [1.13, 1.60][a,b]
Girls	0.87 [0.68, 1.07]	0.88 [0.76, 1.04]	0.77 [0.60, 0.92]	0.95 [0.60, 1.31]

BMI- Body Mass Index; WHtR: Waist-to-Height Ratio; OM: Otitis media; SDT: Sucrose Detection Threshold; *Note* The same suprascript (a, b) indicates significant differences between annotated groups with $p<0.05$; # indicates non-significant trend with $p< 1.0$;

Highlights

- In 2-3 year olds, OM was not associated with BMI or taste sensitivity
- 2-3 year old girls with OM history had higher waist to height ratio.
- In 5-9 year olds, children with OM history had significantly higher BMI.
- Multiple OM exposure significantly increased risk of overweight in 5-9 year olds.
- 5-9 year old boys with multiple OM exposure had higher sucrose detection threshold.