Pilot Study Investigating The Effect Of Cigarette And E-Cigarette Exposure On Prenatal Facial Movement With Comparison To No Exposure.

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Abstract

Aim: To assess whether prenatal nicotine exposure influences fetal facial movement by comparing cigarette, e-cigarette and non-exposed groups.

Method: 4D ultrasound scans were carried out on pregnant women at 32 weeks and 36 weeks gestational age. The scans of 15 mother-infant pairs were coded using the Fetal Observable Movement System (FOMS). There were three exposure groups: non-smokers, cigarette users and e-cigarette users.

Results: At both 32 and 36 weeks gestational age, no significant difference in relative frequency (RF) of facial movement was found between the three exposure groups. A general increased level of facial movement was observed for those exposed to nicotine compared to no exposure.

Conclusion: High variability in fetal behaviour profiles was observed among the exposed groups, but not within the non-exposed group. Studying 15 pairs is insufficient; a larger cohort is needed to assess the effects of cigarette and e-cigarette exposure on fetal facial movement.

Introduction

Smoking during pregnancy remains a prevalent healthcare foci. In England, 5.6% women smoke at point of delivery (NHS England, 2025) despite well-documented risks. The use of cigarettes increases the risk of fetal growth restriction (FGR) (Sabra et al., 2017), small for gestational age (SGA) (Ko et al., 2014; Tong et al., 2017), low birth weight (LBW) (Bernstein et al., 2005; Ko et al., 2014; Pereira et al., 2017; Hamadneh & Hamadneh, 2021) and sudden infant death syndrome (SIDS) (Mitchell et al., 1993). Impacts persist postnatally, and can be observed through behaviour. A meta-analysis conducted by Froggatt et al. (2020a) identified prenatal cigarette exposure to significantly impact neonatal neurobehavior up to 1 year of age. A Dutch study found that children aged 9 to 11 who were exposed to maternal smoking prenatally had smaller brain volume, surface area, and gyrification (Ekblad, 2022). Smoking cessation during pregnancy is therefore strongly recommended.

Stopping smoking is challenging due to the presence of the highly addictive, carcinogenic substance nicotine (British Lung Foundation, 2016). Healthcare professionals are recommended to provide support to all pregnant women who smoke or have recently quit (World Health Organization, 2013). In the UK this involves referral to stop smoking support and treatment (NICE, 2023). However, evidenced in the United Lincolnshire Hospital NHS Trust (ULHT), only 34.9% of those referred actually access services (Meaton et al., 2023). Those unwilling or unable to engage can be offered Nicotine Replacement Therapy (NRT) (NICE, 2025) as a harm reduction method, delivering nicotine without additional harmful chemical found in cigarettes. Safety of use during pregnancy is contentious (England et al., 2015).

E-cigarettes are a form of NRT, promoted by organisations such as Public Health England, through the UK 'Swap to Stop' scheme (O'Brien, 2023). A meta-analysis of 88 studies identified nicotine-containing e-cigarettes as the most effective smoking cessation method; evidenced across England and Scotland as more effective than NRT patches (Lindson et al., 2025; Hajek et al., 2022). Whilst there is little-to-no effect reported regarding toxic biomarker levels (Smith et al., 2021); a systematic review of 26 studies by Ussher et al. (2024) identified mixed results on the effects of e-cigarette use, deducing the findings as inconclusive. Whilst both McDonnell et al. (2019) and Froggatt et al. (2020b) identified prenatal e-cigarette exposure to have no influence on birth outcomes, Kim & Oancea (2020) reported e-cigarette exposed fetuses more likely to incur adverse effects such as SGA and LBW compared to non-exposed fetuses, similar to those observed in cigarette-exposed fetuses.

Nicotine is a shared chemical in cigarettes and e-cigarettes. It is transferred into the fetal bloodstream across the placenta where it binds to nicotinic acetylcholine receptors (nAChRs) expressed by non-neuronal and neuronal cells in the body, impacting regulation of fetal brain development and maturation (England et al., 2015; Bhardwaj et al., 2025). Nicotine is also metabolised into cotinine, which interferes with formation and distribution of nAChRs. There is a body of preclinical evidence on the impact of prenatal nicotine exposure. Exposure has been identified to delay early motor development in both Wistar rats (Hussain et al., 2022) and long-Evans rats (Torabi et al., 2021). Using postnatal measures, a study on mice found that exposure caused attention deficits and longer-term impairments in behavioural flexibility (Yuki et al., 2016). Sex-specific effects are evident, with nicotine only affecting anxiety-like behaviour in males (Hussain et al., 2022), and accounting for 46% of the impacts of tobacco-smoke extract compared to only 13% in females (Levin & Slotkin, 1998).

Research on the effects of prenatal nicotine exposure in humans remains limited in comparison. E-cigarette use is sparse within NRT studies (Bowker et al., 2020). Froggatt et al. (2020b) began bridging this gap by comparing the effects of prenatal cigarette exposure, e-cigarette exposure, and no exposure, finding that both cigarette and e-cigarette exposure reduced self-regulation and increased abnormal reflexes postnatally. Further research is needed to better understand the effect of human prenatal exposure.

Brain and central nervous system (CNS) development begins early during the prenatal period. Studying both fetal movement and behaviour can provide an understanding of neurobehavioral development (Antsaklis et al., 2020; Reissland et al., 2012), and can reflect influential maternal and pregnancy-related factors (Einspieler et al., 2021). Using the Fetal Neurobehavioral Assessment System to assess gross body movement, Stroud et al. (2018) found prenatal cigarette exposure to increase fetal activity, particularly isolated movements lacking complexity. These behavioural effects were identified as strongly related to postnatal behaviour, including reduced attention and self-regulation, the latter of which was also reported by Froggatt et al. (2020b). A key neurobehavioral indicator is facial movement, critical for everyday postnatal functioning and communication (Franchak & Adolph, 2024). It is therefore of high importance to assess the effect of exposure on fine-grained fetal movements, such as facial movement.

Fetal facial movement has been analysed using 4D ultrasound. Over gestation, the frequency of facial movements decreases (Reissland et al., 2013; Froggatt et al., 2021), while complexity increases (Reissland et al., 2011, 2013; Hadders-Algra, 2018; Ustun et al., 2022). The Fetal Observable Movement System (FOMS) defines complex, organised facial movements as gestalts, including the "cry-face-gestalt" and "laughter- gestalt", both of which involve the co-occurrence of seven facial movements (Reissland et al., 2016). Between 24 and 35 weeks gestational age, the mean frequency of three or more facial movements comprising these two gestalts increases (Reissland et al., 2011). Between 32 and 36 weeks, a significant increase in the frequency of four or more co-occurring movements has also been observed (Ustun et al., 2022). An increase in facial movement complexity is indicative of CNS maturation and reflects essential preparatory motor coordination for postnatal developmental progression.

Despite growing research into prenatal cigarette and e-cigarette exposure, assessment of the effects in humans remains limited. Existing research is preclinically bound, focusing on postnatal outcomes as opposed to prenatal measures such as fetal facial movement. A deeper understanding of the impact of nicotine on early neurobehavioral development is essential to inform healthcare policy.

Froggatt et al. (2021) explored this, examining the frequency of fetal mouth movements at both 32 and 36 weeks gestational age, comparing cigarette-exposed and e-cigarette-exposed and non-exposed fetuses. No significant differences were identified between groups; however, a significant decline in mouth movement was observed only among the non-exposed fetuses. Further research, involving analysis of a greater facial area was recommended. This pilot study aims to build on this work by investigating the effects of prenatal cigarette and e-cigarette exposure on full facial fetal movement. Given existing research indicating postnatal differences between exposure groups and the identified need for further analysis of facial movements, it is hypothesised that a difference will be observed between exposure groups.

Methodology

This pilot study investigates the influence of nicotine administered via cigarette and e-cigarette smoke on prenatal behaviour, compared to no exposure. It aims to assess whether exposure groups differ in relation to facial movements.

Recruitment:

Participants for this study were selected from the 123 women recruited in the study conducted by Froggatt et al. (2021). See Appendix 1 for the eligibility criteria. The study was noted to women following their 20-week gestational scan, after which eligible individuals could put themselves forward. Scans at both 32 and 36 weeks gestational age were conducted. All 4D ultrasound scans were carried out by the same sonographers at two hospitals within the South Tees Hospitals NHS Foundation Trust: The James Cook University Hospital, Middlesbrough or The

Friarage Hospital, Northallerton. Due to premature birth, participant attrition and poor coding visibility, a pool of 87 mother-infant pairs, with codable scans at both 32 and 36 weeks gestational age, was obtained. Fifteen of these pairs were anonymously selected for inclusion in this study using cluster sampling, drawing five from each of the three exposure groups. Both male and female fetuses were represented in each exposure group (total: 10 females and 5 males). This process was done blind to the primary researcher.

Coding:

The 4D ultrasound scans were coded using Observer XT Version 12 (Figure 1), following the anatomically based Fetal Observable Movement System (FOMS) (Reissland et al., 2016). This coding scheme was developed to assess facial movements of healthy fetuses aged 23 to 37 weeks gestational age at high resolution. It was selected for use to enable comparison with the Froggatt et al. (2021) study. Prior to coding the 30 scans included in this pilot study, the primary researcher completed FOMS training. Reliability testing was subsequently conducted to ensure coding proficiency, with the primary researcher attaining near-perfect agreement ($\kappa = 0.84$).

Both upper and lower facial movements defined by FOMS were coded. Upper facial movements include: inner brow raise (FM1), outer brow raise (FM2), brow lower (FM4) and cheek raiser (FM6). Lower facial movements include: nose wrinkle (FM9), dimpler (FM14), nasolabial crease (FM11) and chin raiser (FM17).

All 4D ultrasound scans lasted approximately 20 minutes in duration and were coded frame-by-frame. For each upper or lower facial movement identified, a start code was added at the first frame of the movement, and stop code was added at the first frame after the movement ended. Similarly, start and stop codes were used to differentiate between sections of the scan where the analysed facial movements could or could not be identified (Figure 2 and 3). During the clips, there were periods when upper and lower facial movements were not identifiable due to several factors, including poor image quality, obstruction by limbs, the placenta or umbilical cord, and fetal, maternal or sonographer movement (Figure 3). Additionally, stop code was used during paused sections when the sonographer allowed for maternal adjustment or to take photographs for the mother. Coding was also stopped during periods when only the 2D scan was visible, which occurred when the sonographer refocused on the face (Figures 3). Ensuring that the code only remains open during codable sections is critical as it influences the relative frequency (RF) of movement calculated during analysis.

All coding was conducted by the primary researcher in order to maintain consistency, which is key for individual study analysis. For analysis, movements coded from the 30 scans included in this study were combined with facial mouth movements previously coded by Dr. Suzanne Froggatt-Gray (Froggatt et al., 2021). Therefore, all codes were peer-reviewed by Froggatt-Gray to ensure consistency between the two studies. At both gestational ages, the RF of facial movements was calculated to assess differences between the three exposure groups. RF was calculated as the total number of movements per minute, divided by the total duration of codable scan time.

Mental health assessment:

Measures of maternal stress, anxiety and depression were obtained at both 32 and 36 weeks gestational age. This was done through the use of a questionnaire completed by the mothers prior to each scan.

Statistical analysis:

Mean RF was used for the analysis of fetal facial movement at both 32 and 36 weeks gestational age. The RF of all facial movements was calculated by dividing the number of movements coded divided by the duration of codable scan time. The RF of singular movements, in which only one movement occurs at a given point in time, was calculated. In addition, the RF of complex movements, defined as instances when three or more movements co-occur or occur within one second of each other, was also calculated. Non-parametric Kruskal-Wallis tests were conducted to determine whether statistically significant differences existed between the three study groups. This test was selected because it allows for comparison between three independent groups, does not assume normal distribution, and is appropriate for temporally distributed data. ANOVA tests were conducted to assess differences in maternal stress, anxiety, and depression between the three exposure groups. The mental health scores used for calculations were taken from the Froggatt et al. (2021) study.

Ethics Statement:

Pregnant women provided informed consent prior to participating in this research. Ethical approval was granted by Durham University Psychology Ethics Committee (PSYCH-2025-7042-6799) and the NHS ethics committee (REC reference 11/NE/0361).

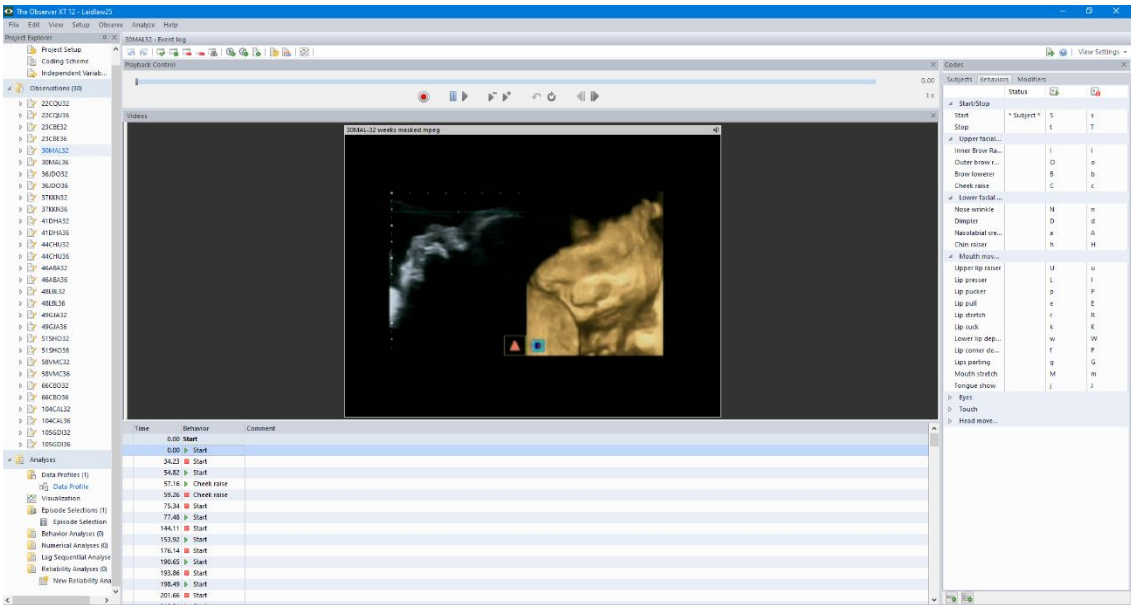

Figure 1: Screenshot of the Observer XT version 12 platform used for coding.

Figure 2: Screenshots exemplifying sections of 4D ultrasound acceptable for coding.

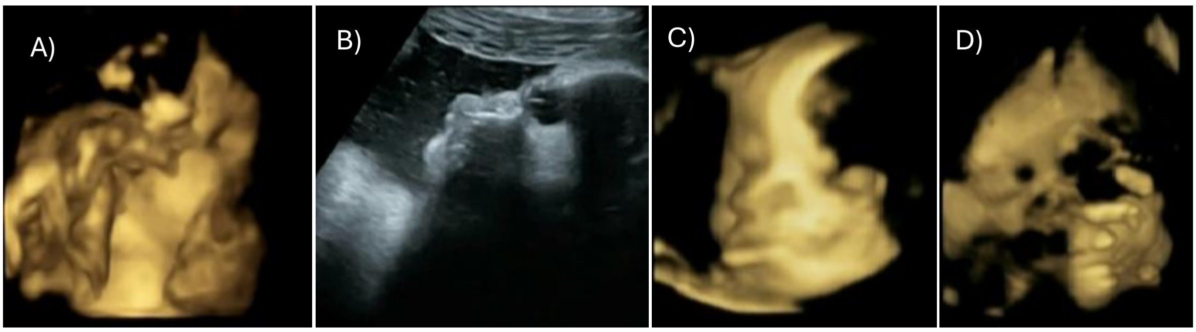

Figure 3: Screenshots exemplifying sections of 4D ultrasound unacceptable for coding. A) Placental obstruction. B) Section of 2D-ultrasound to re-focus on the face. C) Poor image quality due to blurring. D) Poor image quality due to shadowing.

Results

Single movements:

There appears to be an increased level of movement for e-cigarette exposed fetuses compared to those with no nicotine exposure at both 32 and 36 weeks gestational age (Figure 4). The level of movement also appears to be increased for cigarette exposed fetuses compared to no nicotine exposed, but only at 36 weeks gestational age. At both 32 and 36 weeks gestational age, the non-parametric Kruskal-Wallis test shows no significant difference between the groups ($X^2(2, N=15) = 4.020$, $p= .134$.) and ($X^2(2, N=15) = 1.580$, $p= .454$.) respectively.

Full facial movements:

For all facial movements, use of the non-parametric Kruskal-Wallis test identified no significant difference in mean RF between the three exposure groups. At 32 weeks $X^2(2, N=15) = 2.720$, $p= .257$. At 36 weeks $X^2(2, N=15) = .666$, $p= .717$. At both 32 and 36 weeks gestational age there appears to be an increased level of full facial movement among fetuses in both nicotine exposure groups compared to those with no exposure (Figure 5). Both the cigarette and e-cigarette exposure groups attained higher mean RF values (Table 1).

Complexity:

There is no statistically significant difference in the RF of complex facial movements between the three exposure groups at either gestational age. At 32 weeks gestational age, the non-parametric Kruskal-Wallis result was $X^2(2, N=15) = 2.660$, $p= .264$. At 36 weeks gestational age, the non-parametric Kruskal-Wallis result was $X^2(2, N=15) = 1.040$, $p= .595$. There appears to be an elevated level of complex facial movements for both cigarette and e-cigarette exposed fetuses compared to those with no exposure (Figure 6)(Table 1).

Participant mental health:

No significant variation in mental state of the 15 women from the included mother-infant pairs has been indicated. There is no significant difference in level of stress ($F(2,14).684$, $P=.523$), anxiety ($F(2,14).874$, $P=.442$) or depression ($F(2,14)1.175$, $P=.342$) between exposure groups.

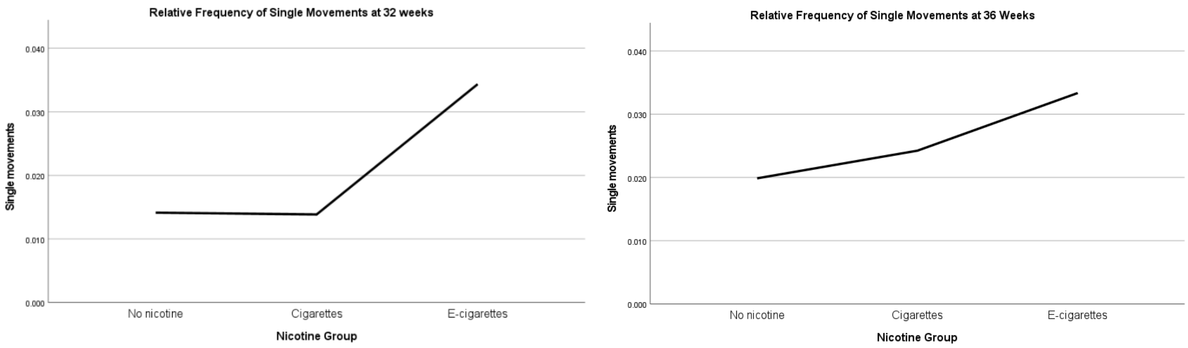

Figure 4: Graph showing the mean RF of single facial movements at 32 and 36 weeks gestational age for fetuses with prenatal cigarette exposure, e-cigarette exposure and no nicotine exposure.

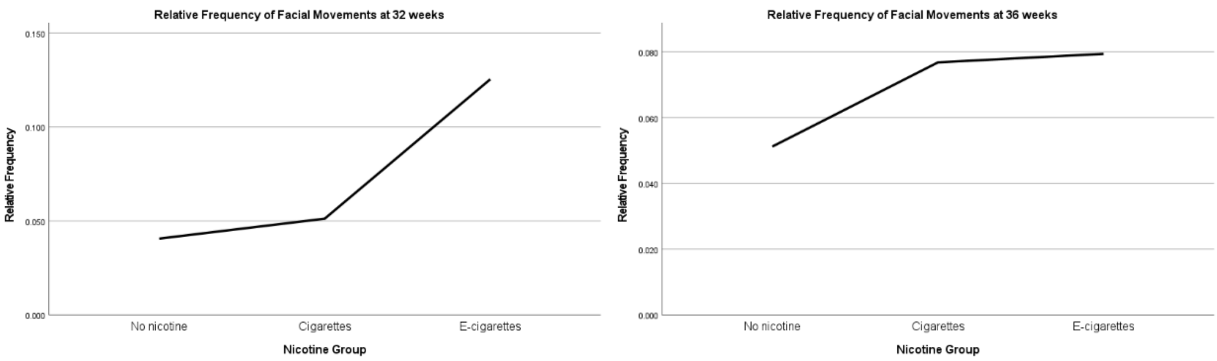

Figure 5: Graph showing the mean RF of full facial movements at 32 and 36 weeks gestational age for fetuses with prenatal cigarette exposure, e-cigarette exposure and no nicotine exposure.

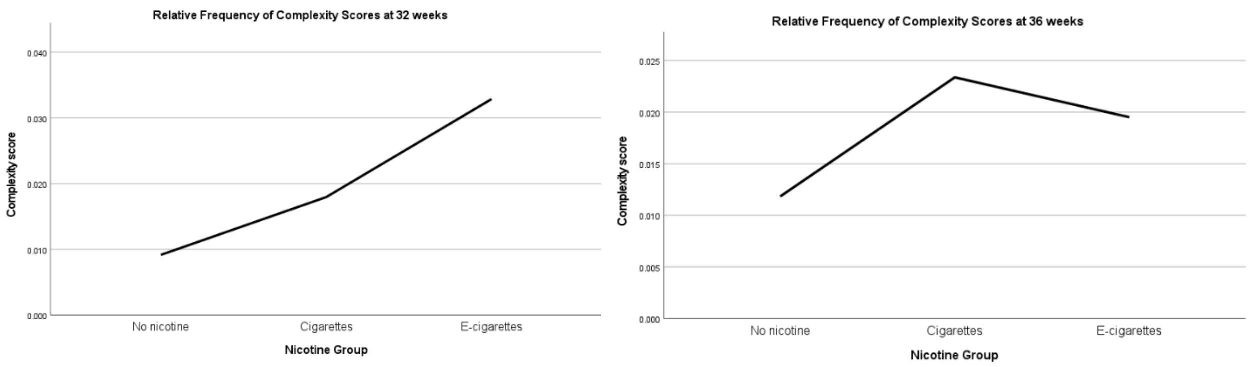

Figure 6: Graph showing the mean RF of complex facial movements at 32 and 36 weeks gestational age for fetuses with prenatal cigarette exposure, e-cigarette exposure and no nicotine exposure.

Single Movements		
	Mean Relative Frequency (3sf)	
	32 Weeks	36 Weeks
No Nicotine	0.0141	0.0199
Cigarette	0.0139	0.0242
E-cigarette	0.0344	0.0334

Full Facial Movements		
	Mean Relative Frequency (3sf)	
	32 Weeks	36 Weeks
No Nicotine	0.0406	0.0512
Cigarette	0.0512	0.0768
E-cigarette	0.125	0.0794

Complex Facial Movements		
	Mean Relative Frequency (3sf)	
	32 Weeks	36 Weeks
No Nicotine	0.00916	0.0118
Cigarette	0.0180	0.0234
E-cigarette	0.0329	0.0195

Table 1: Table showing the mean RF values (3sf) for each of the three exposure groups at both 32 and 36 weeks gestational age. Values shown analyse single facial movements, full facial movements and complex facial movements.

Discussion

This pilot study aimed to extend the research of Froggatt et al. (2021) by analysing full facial movement. It was hypothesised that prenatal nicotine exposure would result in a significant difference in fetal facial movement compared to no exposure. However, no statistically significant differences were identified between the three exposure groups.

To ensure completion within the timeframe of this research, only 15 mother-infant pairs were included. Although participants were evenly distributed across the three exposure groups, this remains a small sample size and is a likely contributing factor to the results obtained. This represents a large limitation of the study. There was low variability within the non-exposed group; however, both the cigarette and e-cigarette exposed groups exhibited high variability in RF of fetal movement between individuals, making it challenging to obtain a representative average. This variability must be considered when interpreting the findings. Thus, it is recommended that further research is carried out using a larger cohort, preferentially including all applicable 87 mother-infant pairs from the Froggatt et al. (2021) study. Such course would account for independent fetal variability and provide a more reliable mean value.

A contributing factor to the high variability in the RF of movement among fetuses within the cigarette and e-cigarette exposure groups may be the actual amount of nicotine each fetus was exposed to. Dose-responsive effects of maternal cigarette smoking have been observed in postnatal outcomes such as SGA infants (Tong et al., 2017). In this study, the daily number of cigarettes smoked by mothers in the cigarette-exposed group fell into two categories: fewer than 10 per day and 11–20 per day, indicating varying levels of prenatal nicotine exposure between fetuses. This variation should be accounted for when interpreting the findings. In the e-cigarette exposed group, both the nicotine content of e-cigarettes and typical daily use was self-reported. Dowd et al., (2023) identified a significant discrepancy between self-reporting and observed e-cigarette use behaviour, with self-reports tending to overestimate usage. This suggests that the reliance on self-reported data in the present study may limit the accuracy of estimated fetal nicotine exposure. Further research should aim to objectively quantify nicotine intake within the e-cigarette exposure group. Given the variation in reported usage across participants, individual differences in prenatal nicotine exposure within the e-cigarette exposure group must also be considered during analysis.

The findings indicate high variability in frequency of movement between exposure groups. Maternal mental health has been identified as influencing prenatal behaviour profiles. Maternal depression and anxiety have been found to cause differing effects on fetal eye-blinks (Reissland et al., 2018). Although the mental health status of the mothers in this study varied, no significant difference in stress, anxiety or depression was identified between exposure groups and therefore not attributable to the differences observed.

Moreover, fetal sex should also be considered when analysing the results. Rodent studies using postnatal measures, have identified sex-specific effects, with males presenting at a greater risk to the effects of prenatal nicotine exposure (Levin & Slotkin, 1998; Hussain et al., 2022). Both male and female fetuses are included in this pilot study making this a potential source of variability in the results. However, not only are both sexes distributed across the three exposure groups, variability resides between fetuses of the same sex within exposure groups. Furthermore, fetal sex has been identified as insignificant for producing the differences found within this study.

Although no significant differences were identified, an apparent increase was observed in the mean RF of fetal facial movement, at both 32 and 36 weeks gestational age, amongst those with prenatal nicotine exposure compared to the non-exposed group. This is suggestive of a different behavioural profile. It aligns with previous studies examining the effect of prenatal nicotine exposure on postnatal measures. Preclinical research has shown prenatal nicotine exposure to increase the frequency of repetitive, non-locomotive head turns during the early postnatal period (Torabi et al., 2021). Clinically, both cigarette and e-cigarette exposure have been found to significantly increase abnormal reflexes, as well as reduce self-regulation and motor maturity (Froggatt et al., 2020b). Findings both clinically and preclinically are indicative of potential neurobehavioral consequences from prenatal nicotine exposure. The development of proficient facial movement is critical for postnatal functioning (Franchak & Adolph, 2024). Therefore, the apparent increase in fetal facial movement among nicotine exposed fetuses warrants further exploration. Given the potential implications for public health policy regarding the use of all forms of nicotine administration during pregnancy, including cigarettes and e-cigarettes, a more comprehensive understanding is needed.

Considering this study holistically, it is important to acknowledge that, despite having a specific eligibility criteria for participant inclusion, such as the exclusion of medicated or recreational drug use, there remains numerous unmeasured sources of potential variance. These include both maternal caffeine and dietary intake. Prenatal caffeine exposure has been identified to alter fetal brain structure (Zhang et al., 2021) and cause deficits in neurobehavioral development (Santana et al., 2024), suggesting it could be a source of variability in the results obtained. Future research should therefore assess the potential influence of these additional prenatal exposures on the findings to improve interpretability of results.

Finally, the FOMS was used for analysis within this study; however, no significant difference was identified between exposure groups. As suggested by Froggatt et al. (2021) the conjunctive use of alternative assessment measures could be considered. Such course for this present study is unlikely to have a great effect due to the small sample size and large variability between fetuses.

Conclusion

Human study into the effect of prenatal nicotine exposure remains limited. This pilot study concludes no significant difference in fetal facial movement between those exposed to maternal cigarette use, e-cigarette use and no exposure, paralleling the findings of Froggatt et al. (2021) in their assessment of fetal mouth movement. An apparent increase in fetal facial movement was identified for both nicotine exposure groups compared to non-exposed fetuses. Due to the alignment with findings from postnatal studies, further exploration is needed. The primary recommendation is to extend this pilot study by analysing a larger number of participants in order to sufficiently assess the effect of prenatal nicotine exposure of fetal neurobehavioral development. Further understanding is needed to best guide healthcare policy regarding the use of nicotine-administering products during pregnancy.

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Appendix 1

Eligibility criteria used for study participation:

- Maternal age between 18-40 years old.
- Pre-pregnancy BMI between 18-25.
- Not under the care of a consultant for pregnancy complications and a low-risk pregnancy.
- Not currently taking any medication.
- Not diagnosed with medical or mental health condition that would affect the fetus.
- Not taking any recreational drugs or drinking alcohol.

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