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Vaping and Smoking in Pregnancy—A Meta-Analysis of Neurobehavioural Development in Prenatally Exposed Offspring

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ABSTRACT

Aim: Electronic cigarette usage has become increasingly popular in recent years, advertised as a safe alternative to smoking. However, the long-term impact on prenatal development is not well understood. The aim of this systematic review and meta-analysis is to investigate the impact of prenatal electronic cigarette exposure on self-regulation and motor development in existing human and animal research and to identify the common assessment measures.

Methods: 2116 records from six databases were retrieved, of which 70 (56 human; 14 animal) were retained for review. Random-effects meta-analyses were conducted on eligible studies.

Results: The emerging animal literature provides evidence for the impact of electronic cigarette exposure on offspring development. Meta-analysis results of 42 eligible human studies indicated that prenatal exposure to nicotine or cannabis by combustible or electronic cigarette was associated with deficits in cognitive, emotional, and behavioural self-regulatory domains, as well as motor function and neuromotor development. Only one human study included electronic cigarettes.

Conclusions: The combined findings of human and animal literature suggest overlapping influences of combustible and electronic cigarettes across self-regulation and motor domains. Given the policy implications, there is an urgent need for more research on electronic cigarette use in humans during pregnancy.

1 | Introduction

Combustible cigarette smoking is considered the most prominent modifiable risk factor of adverse outcomes in pregnancy [1]. Tobacco naturally contains nicotine, an addictive compound, which releases harmful byproducts like formaldehyde, tar, and carbon monoxide when smoked in combustible cigarettes [2, 3]. The issue of tobacco smoking is highly prevalent in pregnancy health policy guidelines worldwide [4, 5] due to widely established links between prenatal tobacco smoking and deficits in infant neurobehavioural [6] and motor development [7].

Smoking during pregnancy remains a global concern, with 1%–20% prevalence of nicotine cigarettes [8, 9], particularly among women aged 21–30 [10], and rising cannabis cigarettes use [11]. Combustible cigarette use in pregnancy exposes the

Abbreviations: AChRs, acetylcholine receptor subtypes; BSID, Bayley Scales of Infant and Toddler Development; CBCL, Childhood Behavioural Checklist; IBQ, Infant Behaviour Questionnaire; NBAS, Neonatal Behavioural Assessment Scale.

Summary

- Extensive research links prenatal cigarette exposure to neurodevelopmental deficits in infants, yet human evidence on e-cigarette exposure remains limited, despite concerning findings from animal studies.
- This review highlights the limited research on prenatal e-cigarette exposure and its impact on self-regulatory and motor development, while identifying consistent deficits across both human and animal studies.
- Further research into the long-term neurobehavioural impact of prenatal e-cigarette exposure is crucial to promote public maternal and child health policy.

foetus to harmful byproducts which can impair fetal health and brain development [12, 13]. While smoking during pregnancy has declined over time, its continued global prevalence remains a concern for prenatal and infant development. Alongside this decline, a new consideration has emerged for policy makers and researchers alike—the electronic cigarette.

The electronic cigarette (e-cigarette/vape) has been marketed as a smoking cessation device and a safer alternative to smoking. E-cigarettes deliver high doses of nicotine—derived from tobacco—without some of the harmful byproducts of combustible cigarettes. Instead, nicotine is inhaled via an 'e-liquid', containing propylene glycol and vegetable glycerol among other substances such as aldehydes, metals, and flavourings [14, 15]. One standard 2 mL disposable e-cigarette contains approximately 20 mg/mL of nicotine, equivalent to20–40 combustible cigarettes. The overall appeal of e-cigarettes, namely their diverse range of flavourings, improved inhalation experience, and high levels of nicotine, has led to increased uptake among smokers and non-smokers alike [16–18].

Some healthcare providers recommend e-cigarettes as a potentially less harmful option to combustible cigarettes during pregnancy [19]. While the prevalence of smoking declines significantly in pregnancy, there is little change observed among those using e-cigarettes [20]. Despite their rising popularity, the long-term effects of prenatal e-cigarette usage are largely unexplored [21–23].

Placental health is integral to fetal development, and any disruption to its function poses a significant risk to fetal development [24, 25]. While the foetal brain is somewhat protected against neurotoxins, it is particularly vulnerable to highly concentrated substances such as nicotine or cannabis, which readily cross the placenta [26]. Nicotine mimics acetylcholine and disrupts early brain development by both overstimulating and desensitising neuronal nicotinic acetylcholine receptor subtypes (AChRs), present from the first trimester and playing a vital role in the development of the central nervous system [27]. Similarly, the main psychoactive compound found in cannabis, tetrahydrocannabinol (THC), mimics endocannabinoids but overstimulates cannabinoid receptors in brain regions involved in key neurobehavioural functions [28]. The deleterious effects of these substances can impair neural growth, neurotransmission, and normal brain maturation. Evidence from both human and animal studies suggests that these substances and their related disruptions to fetal brain development and neurotransmission can impact subsequent long-term neurobehavioural development [29–31].

Although mostly limited in human research, emerging animal research has highlighted the hypoxic–ischemic effects of e-cigarette aerosol exposure [32]. Human research is limited by the lack of true controls, making it difficult to attribute teratogenicity to nicotine or cannabis independent of the additional substances contained in a combustible cigarette. In this context, animal models provide key insight into how different delivery methods, combustible smoke or electronic vapour, impact fetal development. While studies on prenatal e-cigarette exposure are limited, early findings, both in human and animal models, suggest similar deficits in self-regulation and motor development to those seen with combustible cigarette exposure, even among otherwise typically developing offspring [22, 33, 34].

Froggatt, Reissland et al. [23] found that prenatal exposure to both combustible and electronic cigarettes is linked to developmental delays in self-regulatory and motor domains. These abilities typically develop progressively from infancy through early childhood [35, 36] and are early indicators of long-term outcomes such as academic performance, cognitive ability, physical activity, and social engagement in later childhood and adolescence [37–39].

This review and meta-analysis aims to explore the influence of prenatal e-cigarette exposure on the development of self-regulation and motor skills by integrating meta-analytical evidence from human studies and evidence from relevant preclinical animal studies [40] to identify potential overlaps and key areas for further exploration.

2 | Methods

This systematic review and meta-analysis was conducted and updated according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The protocol for this review was pre-registered with the International Prospective Register of Systematic Reviews (PROSPERO) and can be accessed using CRD42024557121.

2.1 | Definitions of Main Variables of Interest

Electronic cigarettes refer to any electronic device through which nicotine, flavourings, or other substances are inhaled through an aerosolised solution.

Self-regulation is a multi-faceted concept involving the ability to manage and direct cognitive processes, emotions, and behaviours to achieve a specific goal [41], which will be divided into cognitive, emotional, and behavioural self-regulation as outlined by Roebers [42]. Cognitive self-regulation refers to higher-order cognitive processes such as executive functioning, emotional self-regulation involves the management and understanding of one's emotions, and behavioural self-regulation refers to the ability to control one's actions and impulses to adhere to social expectations.

Motor skills refer to the development of physical movement and coordination abilities across the lifespan. These will be

TABLE 1 | Search strategy used to search electronic databases. A PECO framework was utilised to develop the search strategy, divided into population (human/animal offspring), exposure (prenatal exposure), comparator (cigarette/e-cigarette, nicotine/cannabis), and outcome (neurobehavioural development).

#1	Infan* OR child* OR preschool OR animal* OR rodent* OR "child development" [MeSH] OR "models, animal" [MeSH]
#2	"Prenatal smoking exposure" OR "prenatal tobacco exposure" OR "prenatal ENDS exposure" OR "prenatal electronic cigarette exposure" OR "prenatal marijuana exposure" OR "prenatal cannabis exposure" OR "prenatal exposure delayed effects" [MeSH]
#3	Cigarette* OR tobacco OR nicotine OR e-cigarette* OR marijuana OR cannabis OR "cigarette smoking" [MeSH] OR "electronic nicotine delivery systems" [MeSH] OR vaping [MeSH] OR "marijuana smoking" [MeSH]
#4	Cogniti* OR self-regulation OR regulat* OR "executive function*" OR behavio* OR neurodevelopment* OR neurocogniti* OR neurobehavior* OR "neural development*" OR "neuropsychology*" OR inhibit* OR "motor skill*" OR "motor development" OR cognition [MeSH] OR "executive function" [MeSH] OR "motor skills" [MeSH] OR "child behaviour" [MeSH] OR "behaviour, animal" [MeSH]
#5	#1 AND #2 AND #3 AND #4

divided into motor function [43], including gross and fine motor skills, and neuromotor development [44], including reflexes, involuntary physical responses to stimuli, tremors, and muscle tone.

2.2 | Literature Search

Six databases were searched from June to September 2024. Articles were also identified through hand searching of reference lists of key papers, which were then further screened for eligibility and inclusion.

Key terms and the search strategy were developed following an initial search of the literature and consultation with a UCD librarian with expertise in the area of systematic reviews. Relevant search options, including Boolean operators, MeSH terms, and truncation operators, were used to construct and combine searches across each database. Results were uploaded as RIS files to EndNote to identify and track duplicates. Files were then uploaded to COVIDENCE systematic review software (Veritas Health Innovation, Melbourne, Australia. Available at www.covidence.org) for screening. The search string and search strategy are reported in Table 1.

2.3 | Eligibility Criteria

Inclusion criteria were developed in line with an existing, relevant systematic review including humans [45], expanded to include animal literature and older children [46, 47]. Details of the eligibility criteria can be found in Table S1.

2.4 | Data Collection and Analysis

2.4.1 | Study Selection

Once duplicates were removed, two reviewers (AOC and RR) performed an abstract screening, full text review, and data extraction for articles meeting the inclusion criteria. Inclusion agreement between both reviewers was required to proceed to the next stage of screening. Conflicts were resolved through discussion or consultation with a third independent reviewer (MD) (Figure 1).

2.4.2 | Data Extraction

Human and animal studies were reviewed separately. The following information was extracted for each included human study: year, country, sample size, offspring age, substance and method of prenatal exposure, outcome measure, outcome domain, and confounding factors. Means and standard deviations for standardised developmental assessments were also extracted for meta-analysis. Adjusted scores were extracted when provided. Scores were only extracted from articles where individual scores were provided for either nicotine or cannabis exposure, in order to limit confounding. The following information was extracted for each included animal study: year, country, sample size, offspring age at assessment, species, substance type and delivery method, outcome measure, outcome domain, and confounders.

2.4.3 | Risk of Bias Assessments

Two reviewers (AOC and RR) independently assessed the methodological quality of the selected studies using the ROBINS-I [48] for human studies and the Systematic Review Centre for Laboratory animal Experimentation (SYRCLE) risk of bias tools for animal studies [49]. Reviewers followed the procedure of the ROBINS-I detailed guide [50].

2.5 | Meta-Analysis

42 human studies were retained for quantitative meta-analysis. Extracted information included main outcome measure, participant characteristics, exposure type and measurement, results. Cohen's *D* was used to measure effect size as it is robust when dealing with samples of varying sizes and provided reliable estimates. Where effect size was not reported, it was calculated from the published data using the Campbell Collaboration effect size

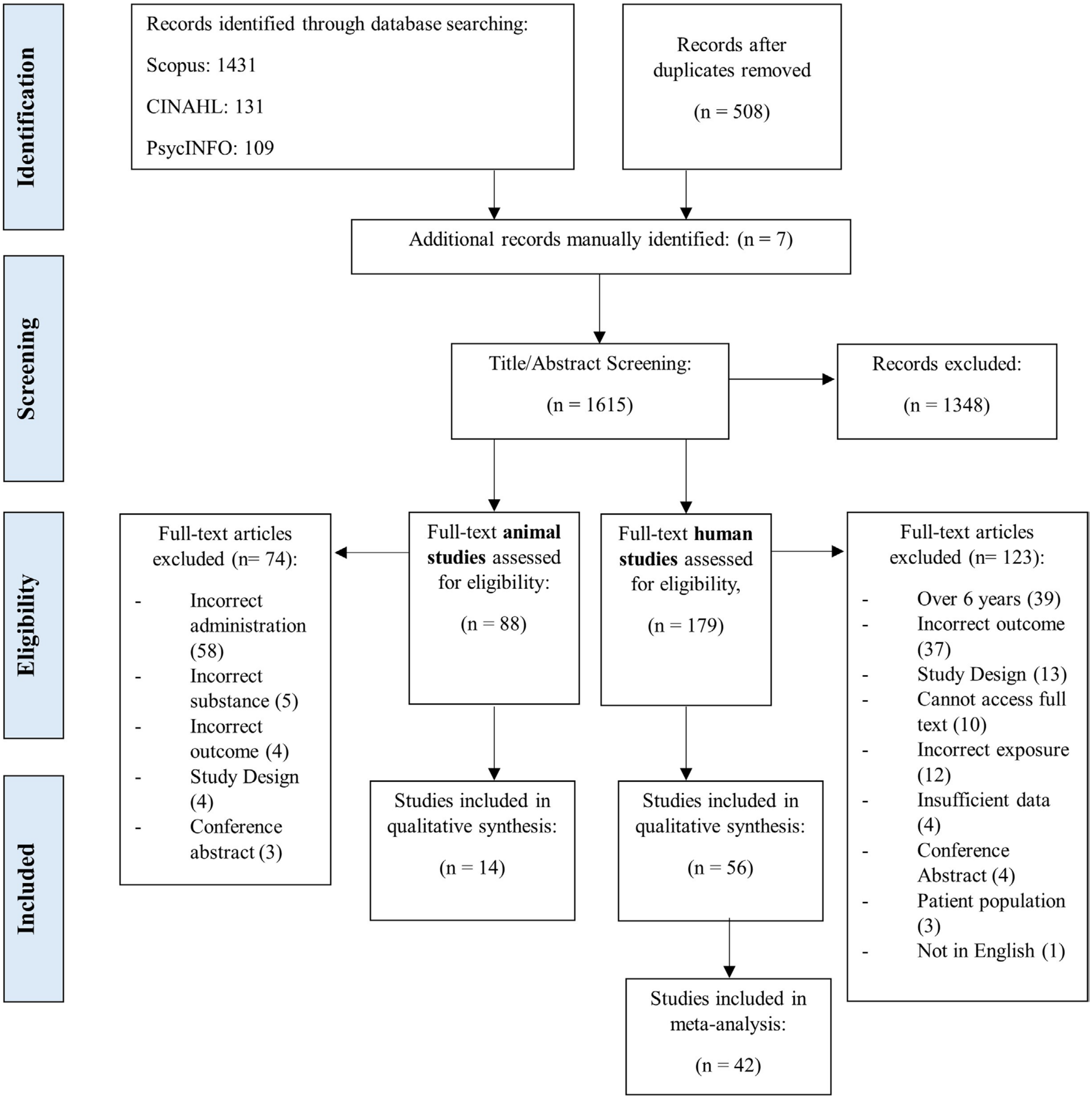

FIGURE 1 | PRISMA diagram of included studies in systematic review and meta-analysis.

calculator online. Where possible, effect sizes were based on analyses in which the most prominent potential confounding variables (preterm birth, maternal demographics, gestational age at birth, etc.) were considered. Mixed-effect model meta-regressions were conducted using the 'metareg' package in R to examine the effects of prenatal exposure to combustible or electronic cigarettes on self-regulation or motor skills.

Animal studies were not included in the meta-analysis as the purpose of their inclusion was to identify overlaps with the human literature rather than providing quantitative comparison. A similar approach was taken in Otten et al. [40].

3 | Results

3.1 | Selection of Studies

In total, 2116 articles were retrieved from the database search, with an additional seven by reference screening. Following the removal of duplicates, the abstracts of 1615 papers were then screened to assess eligibility, of which 1348 were removed. The full-text versions of the 267 remaining reports were screened and those meeting the inclusion criteria were included. 70 papers were retained for data extraction (56 human studies, 14 animal studies).

3.2 | Animal Studies Characteristics

14 animal studies were included in the final review (10 from North American, two from Oceania, one from Europe, and one from South America). Further details on the included animal studies and bias assessments can be found in Tables S2 and S3, respectively.

Prenatal exposure to nicotine and cannabis, via combustible or electronic cigarettes, was associated with self-regulatory and motor impairments in offspring. Combustible cigarette exposure was found to negatively impact spatial memory [51], behavioural flexibility [52, 53], fine motor skills, and neurological reflexes [52, 54].

E-cigarette exposure was found to impair cognitive self-regulatory domains attention [55], short-term memory, and object discrimination [56], in addition to motor coordination [57–59] and reflexes [60]. Cannabis or co-use with nicotine via e-cigarette was found to further hinder sensorimotor development and play [33, 55, 59].

Emotional self-regulation outcomes, namely anxiety and reactivity, were inconsistent. Three studies found increased emotional reactivity and anxiety behaviours in e-cigarette exposed groups [55, 60, 61], this was not observed in others [57, 62]. Reduced anxiety behaviours were found in combustible cigarette [51] and e-cigarette [63] exposure.

3.3 | Human Studies Charactersitics

56 human studies were included in the final review (38 from North America, 12 from Europe, four from Oceania, one from South Africa, and one from South America) (Table S4). Offspring age at assessment ranged from 2 days to 6 years. Based on ROBINS-I, 36 studies were classed as low risk and 20 were classed as moderate risk (Table S5). Summary of findings can be found in Table 2. Further analysis of human studies was conducted to identify research gaps. Studies were divided by their exposure type and neurobehavioural domain (Figure 2). The most commonly used assessment measures are reported in Table S6.

3.4 | Meta-Analysis

42 of the 57 (73%) human studies were included in the meta-analysis. Studies were excluded due to insufficient or non-extractable data. Self-regulation subdomain analysis can be found in the supplementary document (Figures S1–S3, for cognitive, emotional, and behavioural subdomains respectively).

3.4.1 | Cognitive Self-Regulation

A total of 14,672 infants and children (3080 exposed, 17 752 non-exposed) ranging from 1 week to 6 years across 26 studies were included for cognitive self-regulation. The range of effect sizes across individual studies was between –1.516 and –0.009. Due to heterogeneity (Q = 139.411, p < 0.0001, I^2 = 74.41%), the random effects size model is reported. The combined effect size for cognitive self-regulation was significant (d = −0.35; 95% CI = [−0.44, −0.26]; z = −7.57, p < 0.0001). Based on the results of 26 studies, one of which included data from e-cigarette exposure, offspring prenatally exposed to combustible and electronic cigarettes demonstrated significantly poorer cognitive self-regulation ability.

3.4.2 | Emotional Self-Regulation

A total of 99,396 infants and children (10 697 exposed, 88 699 non-exposed) ranging from 1 day to 6 years across 19 studies were included for emotional self-regulation. The range of effect sizes across individual studies was between −1.392 and −0.038. Due to the heterogeneity (Q = 146.25, p < 0.0001, I^2 = 96.58%), the random-effects model is reported. The combined effect size was significant (d = −0.36; 95% CI = [−0.49, −0.22]; z = −5.08, p < 0.0001). Based on the results of 19 studies, one of which included data from e-cigarette exposure, offspring prenatally exposed to combustible and electronic cigarettes demonstrated significantly poorer emotional self-regulation ability.

3.4.3 | Behavioural Self-Regulation

A total of 12,619 infants and children (3067 exposed, 9552 non-exposed) ranging from 1 month to 6 years across 11 studies were included for behavioural self-regulation. The range of effect sizes across individual studies was between −1.83 and −0.012. Due to the heterogeneity (Q = 113.25, p < 0.001, I^2 = 91.94%), the random-effects model is reported. The combined effect size was significant (d = −0.49; 95% CI = [−0.65, −0.32]; z = −5.71, p < 0.001). Based on the results of 11 studies, offspring prenatally exposed to combustible cigarettes demonstrated significantly poorer emotional self-regulation ability. No study included in this analysis assessed the impact of prenatal e-cigarette exposure (see Figure 3).

3.4.4 | Motor Function Development

A total of 4797 infants and children (920 exposed, 3877 non-exposed) ranging from 6 months to 4 years across nine studies were included for motor function development. The range of effect sizes across individual studies was between −0.738 and 0.391. Due to the heterogeneity (Q = 47.57, p < 0.001, I^2 = 67.01%), the random-effects model is reported. The combined effect size was significant (d = −0.20; 95% CI = [−0.34, −0.06]; z = −2.93, p < 0.001). Based on the results of nine studies, offspring prenatally exposed to combustible cigarettes demonstrated significantly poorer motor function development. No study included in this analysis assessed the impact of prenatal e-cigarette exposure (see Figure 4).

3.4.5 | Neuromotor Development

A total of 524 infants (190 exposed, 334 non-exposed) ranging from 1 week to 9 months across five studies were included for neuromotor development. The range of effect sizes across individual studies was between −1.857 and −0.087. Due to the heterogeneity (Q = 32.97, p < 0.001, I^2 = 69%), the random-effects model is reported. The combined effect size was significant (d = −0.663; 95% CI = [−0.93, −0.39]; z = −4.78, p < 0.001). Based

TABLE 2 | Summary of findings from human studies.

Domain	# Studies	Main Finding
Cognitive Self-Regulation	37	• 36 studies found overall cognitive and cognitive subdomain (attention, executive function, language) scores were lower in cigarette and e-cigarette exposed offspring [6, 7, 23, 46, 64–95]. • One study found no difference in executive functioning between cigarette and control exposure groups [96].
Emotional Self-Regulation	25	• 19 studies found emotional reactivity, internalising behaviour problems (anxiety, depression) were higher in cigarette exposed groups [6, 65, 68–71, 82, 93, 97–107]. These skills have not yet been assessed in e-cigarette exposed groups. • Seven studies found emotional regulation skills, self-soothing, and emotional enjoyment were lower in cigarette and e-cigarette exposed groups [23, 82, 93, 105–108]. • Two studies found no difference in emotion self-regulation between cigarette and control exposure groups [81, 91].
Behavioural Self-Regulation	18	• 15 studies found externalising behaviour problems, impulsivity, social withdrawals, hyperactivity, and sleep problems were higher in cigarette exposed groups [64, 65, 68, 69, 71, 74, 75, 82, 96–99, 101, 109, 110]. • One study found adaptive behaviour scores were lower in cigarette exposed groups [111]. • Two studies found no difference in behavioural self-regulation between cigarette and control exposure groups [112, 113]. • These skills have not yet been assessed in e-cigarette exposed groups.
Motor Function	18	• 13 studies found gross and fine motor skills, and motor maturity were lower in cigarette and e-cigarette exposed groups [7, 23, 46, 67, 74, 79, 83, 86, 89, 90, 92, 93, 106]. • Three studies found gross and fine motor skills were higher in cigarette exposed groups compared to controls [71, 76, 94]. • Two studies found no difference in motor function between cigarette and control exposure groups [84, 87].
Neuromotor Development	8	• Eight studies found abnormal reflexes, tremors, startles, and lethargy were higher in cigarette and e-cigarette exposed groups [23, 73, 78, 93, 95, 106, 114, 115].

on the results of five studies, one of which included data from e-cigarette exposure, offspring prenatally exposed to combustible and electronic cigarettes demonstrated significantly poorer neuromotor development (see Figure 5).

4 | Discussion

This review had four specific aims: (1) to investigate how exposure to nicotine or cannabis through electronic cigarettes influences the development of self-regulation and motor skills as compared to combustible cigarettes, (2) to identify the overlaps in human and animal literature, (3) to identify current gaps in the human literature, and (4) to identify what measures have been used in human literature, and what has not been measured. The results of this review will be discussed in relation to these aims.

4.1 | Self-Regulation and Motor Skill Development Following Prenatal Exposure to Electronic vs. Combustible Cigarettes

Animal literature identifies differences between combustible and electronic exposure, particularly in cognitive self-regulation and motor activity, suggesting that substance has long-term effects on offspring development regardless of its method of delivery. Notably, working memory deficits were identified in offspring exposed to sham e-cigarette vapour (without substance), suggesting long-term effects specific to electronic vapour.

While the literature on e-cigarette exposure in humans was limited (one study), results highlighted the potentially harmful long-term self-regulatory and motor impact of prenatal exposure, regardless of its means of delivery. Cognitive and emotional self-regulation was found to be impaired in cannabis and nicotine cigarette and nicotine e-cigarette exposed infants. Abnormal reflexes and tremors were observed in both cigarette and e-cigarette exposed infants.

4.2 | Overlaps in Human and Animal Literature

Several overlaps emerged across the human and animal literature, revealing consistent patterns of developmental impairment across self-regulatory and motor domains regardless of mode of delivery or substance. Both human and animal studies indicate that combustible cigarette exposure, particularly nicotine, leads to significant deficits in cognitive self-regulation, with impairments in both memory and attention. Similar effects are observed in emotional self-regulatory development, where prenatal nicotine exposure is linked to elevated emotional reactivity, internalising behaviour problems, and anxiety in both human infants and animal offspring. Evidence of both motor function

Age (Months)/ Domain	0-12	12-24	24-36	36-48	48-60	60-72
Combustible Cigarette - Nicotine						
Cognitive	9	5	4	4	6	4
Emotional	10	5	4	4	5	4
Behavioural	0	5	4	4	4	3
Motor Function	5	4	5	0	4	3
Neuromotor	5	6	5	4	0	0
Combustible Cigarette - Cannabis						
Cognitive	1	0	0	3	1	0
Emotional	1	0	1	1	1	0
Behavioural	0	1	0	2	1	0
Motor Function	2	1	2	0	0	0
Neuromotor	0	0	0	0	0	0
Electronic Cigarette - Nicotine						
Cognitive	1	0	0	0	0	0
Emotional	1	0	0	0	0	0
Behavioural	0	0	0	0	0	0
Motor Function	0	0	0	0	0	0
Neuromotor	1	0	0	0	0	0

FIGURE 2 | Heat maps representing the number of studies included in this review, across age, exposure type, and domain. Darker colours indicate a higher number of studies, while lighter colours indicate fewer studies.

and neuromotor developmental deficits is outlined throughout human and animal literature, across both nicotine and cannabis cigarette exposure.

Of significant note, prenatal exposure to electronic cigarettes mirrors these findings, with both human and animal studies demonstrating negative influence on cognitive, emotional, and motor outcomes. These converging results highlight the consistent impact of prenatal exposure to substances through combustible and electronic cigarette smoking across species. However, further research is needed to understand the long-term neurobehavioural effects of prenatal exposure to electronic cigarettes, as evidence in this area remains limited in human populations.

4.3 | Current Gaps in the Human Literature

There is a significant lack of human research on prenatal e-cigarette exposure, with only one rigorous study to date, which was limited by a small sample size, a single assessment measure (NBAS), and omission of key covariates. Despite these limitations, emerging findings from this study and animal models consistently indicate neurobehavioural deficits following prenatal exposure to nicotine via combustible or electronic cigarettes, particularly in self-regulatory and motor domains.

Based on a number of studies included in this review, nicotine dosage appears to influence neurobehavioural outcomes, with evidence suggesting e-cigarettes deliver levels comparable to combustible cigarettes [14, 23]. However, it remains unclear whether these observed effects are based entirely on nicotine itself or the influence of additional substances specific to the delivery method.

4.4 | Assessment Measures Currently Used in Human Literature

A range of assessment measures was utilised across age groups, examining neurobehavioural functioning, internal and external behavioural problems, and general child development, which are outlined in Table S6.

This review highlights several underexplored neurobehavioural domains affected by prenatal e-cigarette exposure. While self-regulation and motor development display consistent negative effects, subdomain meta-analyses (Figures S1–S3) also reveal specific deficits in attention, language, and emotional regulation. Key developmental areas such as executive functioning and behavioural regulation are less researched, despite established links between self-regulatory and motor skill development and children's long-term well-being, educational achievement, and health through to adolescence [116–119]. Further application of common measures such as the BSID, IBQ, and CBCL, alongside domain-specific measures, may improve understanding of the long-term impact of prenatal e-cigarette exposure.

4.5 | Limitations

There is a significant lack of research on the neurobehavioural impact of e-cigarette exposure, particularly when considering the components beyond nicotine or cannabis, such as the chemical additives found in the e-liquid. Similar to combustible cigarette research, it is difficult to distinguish specific effects of nicotine or cannabis alone. Developmental differences across self-regulatory or motor domains may be partially attributed to the additional components found in either a combustible or electronic cigarette.

The only human study investigating the impact of e-cigarette exposure is limited by a small sample size of exposed infants, the use of only one early developmental measure, and the early age of testing. Since developmental delay often emerges between 3 and 24 months [120, 121], a broader, longitudinal approach using diverse assessment tools is needed to accurately detect long-term deficits [122]. The findings of prenatal e-cigarette exposure would be strengthened with a larger sample, comprehensive developmental assessments, and a follow-up into early childhood, based on the early findings in human newborns and the emerging results from the animal literature.

4.6 | Future Research

E-cigarettes continue to be promoted as a smoking cessation device, with major health providers such as the NHS [19] suggesting e-cigarettes as a safer nicotine replacement. However, this perception of safety is misleading. While e-cigarettes lack certain harmful substances found in combustible cigarettes, animal studies reveal that prenatal e-cigarette exposure can lead to cognitive, emotional, and motor deficits comparable to those caused

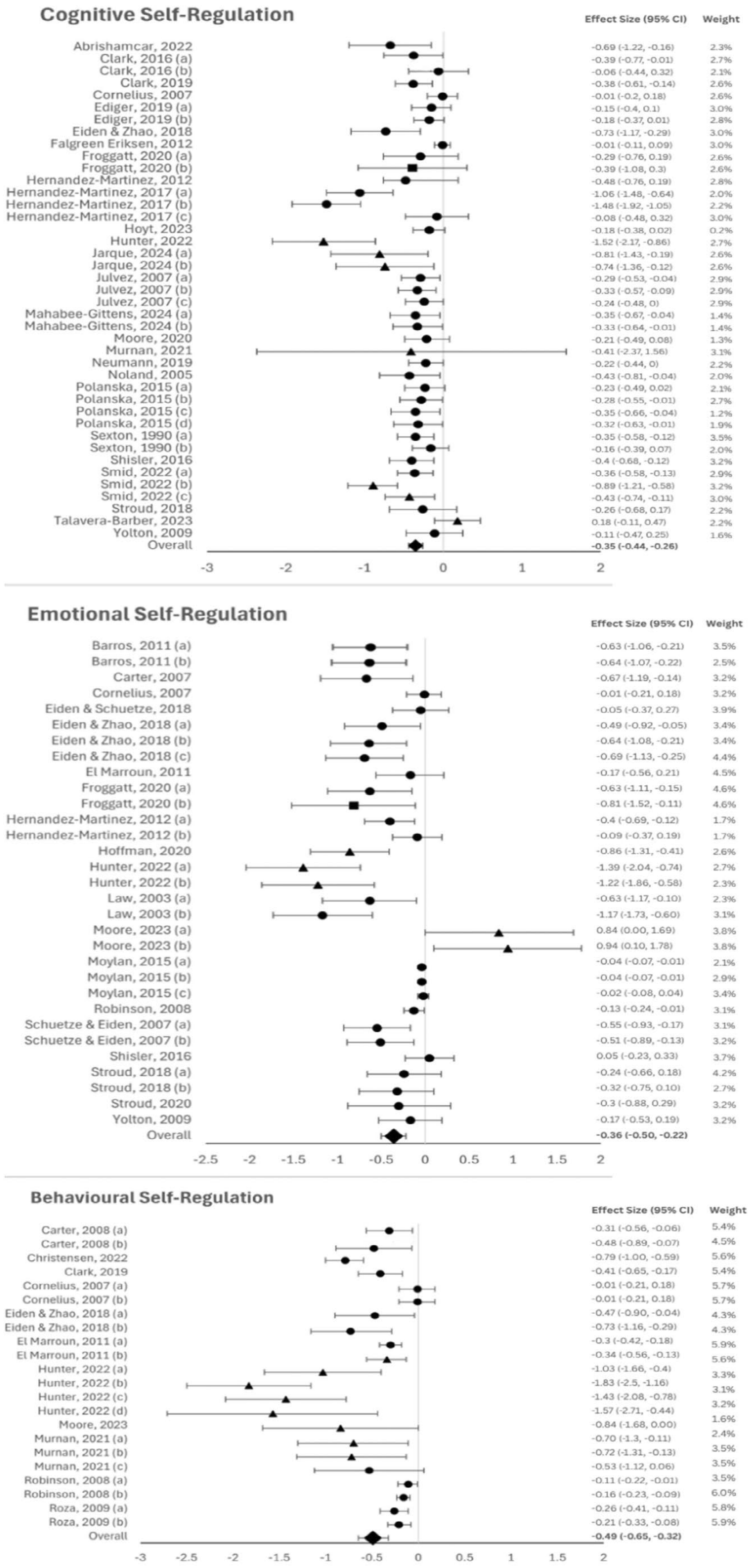

FIGURE 3 | Forest plots of self-regulation studies. Combustible nicotine studies are depicted with a circle; combustible cannabis studies are depicted with a triangle; and electronic nicotine cigarettes are depicted with a square.

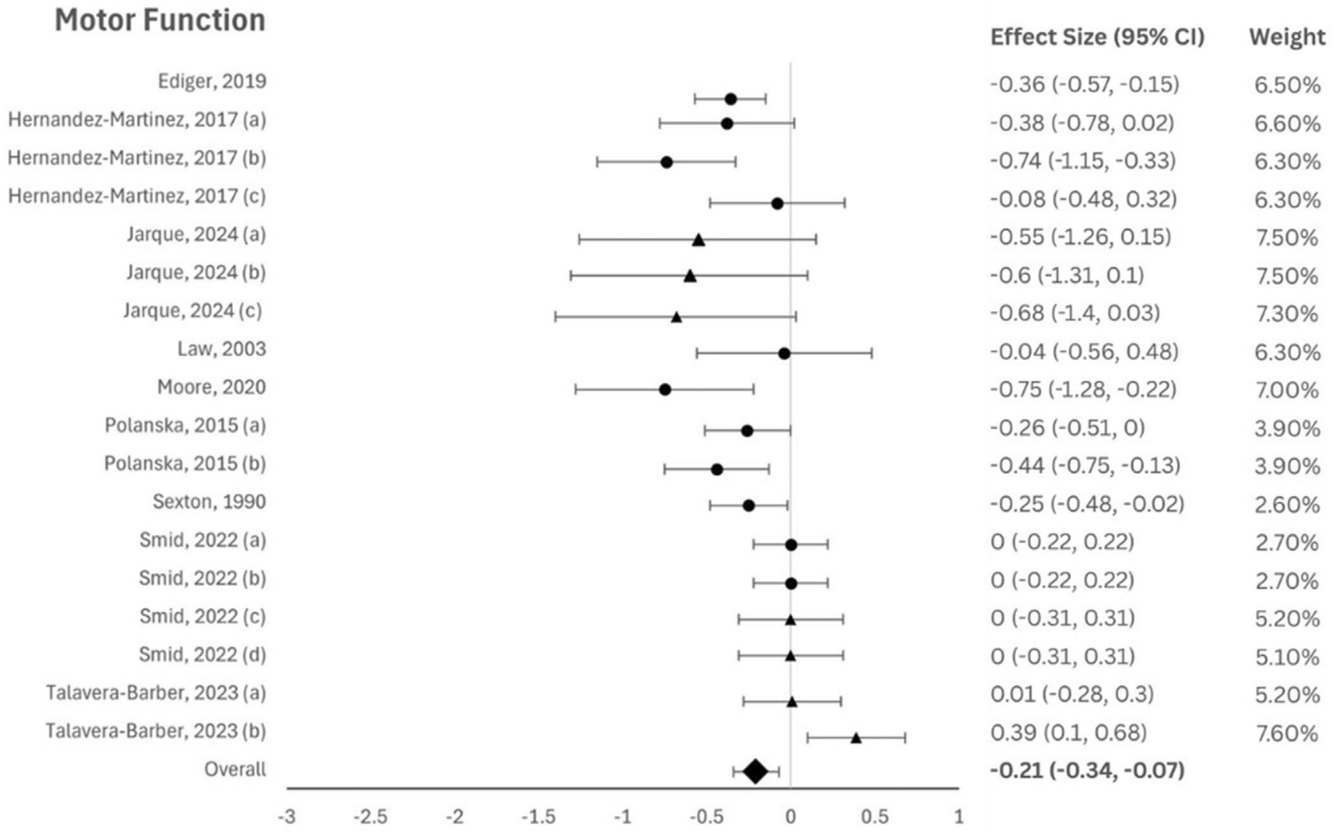

FIGURE 4 | Forest plot of motor-function studies. Combustible nicotine studies are depicted with a circle; combustible cannabis studies are depicted with a triangle. No study investigated electronic nicotine exposure.

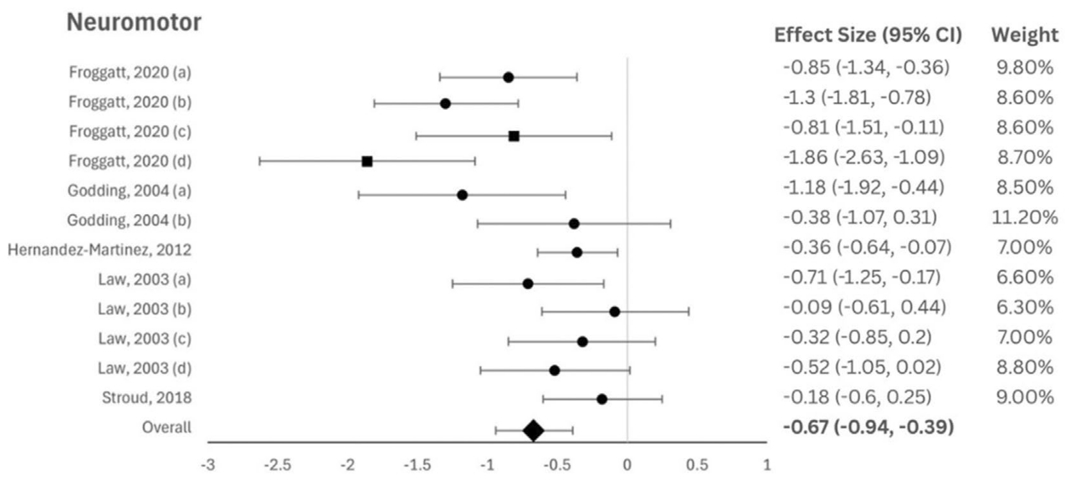

FIGURE 5 | Forest plot of neuromotor studies. Combustible nicotine studies are depicted with a circle; electronic nicotine cigarettes are depicted with a square. No study investigated combustible cannabis exposure.

by combustible cigarettes. The lack of long-term human data may falsely imply harmlessness [123]. Based on the findings of this review and emerging evidence from animal studies, it is strongly recommended that expecting mothers receive adequate support to completely quit both combustible and electronic cigarette use during pregnancy. One ongoing Irish longitudinal study, entitled the Impact of E-cigarettes on Childhood Health Outcomes (ECHO), aims to provide critical insight into the impact of prenatal e-cigarette usage [124].

5 | Conclusions

This systematic review and meta-analysis provide an integrated approach to understanding the influence of combustible and electronic cigarette exposure on offspring neurobehavioural development. This analysis highlights specific self-regulatory and motor developmental deficits across both human and animal populations. This review also stresses the lack of studies on prenatal e-cigarette exposure in humans, emphasising the need for further research in line with the current global prevalence of vaping, particularly among young women. Our findings call for more research to ensure accurate and substantiated evidence to support pregnancy health guidelines.

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Ethics Statement

No ethical approval was required for this review.

Conflicts of Interest

The authors declared no conflicts of interest.

Data Availability Statement

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Data S1:** apa70285-sup-0001-Supinfo.docx.