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Review

Synaptic signatures of perinatal cannabinoids: A systematic review of rodent hippocampal synaptic plasticity, learning, and memory

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HIGHLIGHTS

- Most studies (24/30) reported memory impairments after perinatal cannabis exposure.
- Two studies found alterations in hippocampal synaptic plasticity.
- Few studies investigated perinatal exposure to cannabidiol or whole cannabis plant.
- Few studies investigated inhaled (smoke/vapour) cannabinoid administration.

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ABSTRACT

The expanding legalization of cannabis raises significant public health concerns about its use during pregnancy, particularly due to the limited understanding of its impact on neurodevelopment. Existing research suggests that perinatal cannabis or cannabinoid exposure may impair learning and memory; however, variations in study design hinder the ability to draw generalizable conclusions. Clinical studies are limited in their observational nature and the lack of insight into neural or cellular mechanisms underlying cognitive changes, underscoring the importance of preclinical studies to explore the effects of perinatal cannabinoids in greater detail. The objective of this systematic review is to consolidate findings from existing preclinical research that investigates the effects of perinatal cannabinoid exposure on learning and memory and the putative mechanism of learning and memory, hippocampal synaptic plasticity, in rodents. This review summarizes studies on hippocampal synaptic plasticity (n = 2), spatial/visual memory (n = 13), working memory (n = 6), recognition memory (n = 12), and associative memory (n = 7). Perinatal cannabinoid-induced impairments were reported in the two synaptic plasticity studies, and in 24 out of 30 studies that examined learning and memory, with spatial memory tasks showing the most consistent deficits. While the existing evidence converges on the notion that perinatal cannabinoid exposure negatively impacts hippocampal physiology and associated memory functions, further research is needed to disentangle the influence of various methodological factors, including offspring sex and age, cannabinoid type, time of gestational exposure, and method of administration.

1. Introduction

Cannabis use during pregnancy has become an increasing public health concern with the expanding legalization and de-stigmatization of its recreational use. In recent years, the prevalence of cannabis use during pregnancy has been reported to range from 2 – 9 % (Volkow et al., 2019; Grywacheski et al., 2021; Young-Wolff et al., 2024).

The developing hippocampus contains a high density of cannabinoid receptors (Wang et al., 2003; Vitalis et al., 2008), and therefore, may be particularly vulnerable to the effects of perinatal cannabinoid exposure, potentially impacting the learning and memory processes governed by this region. Existing research investigating the impact of perinatal cannabinoid exposure on the development of the hippocampus and its related functions are limited. Clinical studies investigating children and

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young adults exposed to cannabis *in utero* have reported some evidence of disruptions to memory and cognition (Fried et al., 1998; Smith et al., 2006; Willford et al., 2021). However, these observational studies are limited in their ability to control for potential confounding factors, such as polysubstance use during pregnancy, offspring postnatal drug use, concurrent medical conditions, socioeconomic status, and other sociological factors.

Preclinical models are needed to elucidate cause-and-effect relationships between perinatal cannabinoid exposure and potential learning/memory deficits. Moreover, preclinical models can allow researchers to explore the neural mechanisms that underly changes to learning and memory, such as synaptic plasticity.

Memory processing and storage is mediated by short-term and long-term changes in the strength of synaptic connections, called synaptic plasticity (Silva et al., 1996; Neves et al., 2008; Takeuchi et al., 2014; Abraham et al., 2019). In the hippocampus, synaptic plasticity can be measured in the perforant or Schaffer collateral pathway using electrophysiological techniques that measure the potentiation of synapses in response to low or high frequency stimulation (Neves et al., 2008). Alterations in synaptic long-term potentiation (LTP) and long-term depression (LTD) within the hippocampus have been associated with changes in memory performance (Malleret et al., 2010; Fontaine et al., 2016; Grafe et al., 2022). Notably, certain forms of hippocampal synaptic plasticity have been shown to depend on cannabinoid receptor type-1 (CB1R) activity (Wang et al., 2016; Peñasco et al., 2019; Fontaine et al., 2020), highlighting these receptors as a potential target of perinatal cannabinoids. While this review will focus on the hippocampus, it is important to consider that CB1R-dependent synaptic plasticity has also been characterized in the nucleus accumbens and prefrontal cortex, regions that are functionally and anatomically connected with the hippocampus (Robbe et al., 2002; Sjöström et al., 2003). Therefore, the cannabinoid-induced effects discussed in this review may arise through interactions with these interconnected brain regions.

Existing preclinical perinatal cannabinoid studies vary in study design, including the type of cannabinoids administered, route of administration, exposure length, the age that offspring are evaluated, and more. This systematic review aims to explore and consolidate the existing findings on the effects of perinatal cannabinoid exposure on hippocampal synaptic plasticity and learning and memory-related behaviours.

2. Methods

2.1. Search strategy

The latest literature search was conducted on February 25th, 2025, in three electronic databases, including 1) PubMed, 2) Web of Science, and 3) Scopus. Searches were limited to titles and abstracts and included the terms: cannabis, marijuana, cannabinoid, tetrahydrocannabinol, cannabidiol, cannabinol, prenatal, perinatal, pregnancy, utero, uterine, learning, memory, hippocamp*, dentate gyrus, cornu ammonis, CA1, CA2, CA3, and CA4. For detailed search strategies, please refer to the Supplementary Appendix.

Study Screening and Eligibility Criteria

In combination, all three databases retrieved 627 results (PubMed: n = 197, Web of Science: n = 205, Scopus: n = 225). Records were imported into the systematic review software, Covidence, (Veritas Health Innovation, 2025) for automatic duplicate removal. This resulted in 271 remaining records for screening. Inclusion criteria included: 1) peer-reviewed study, 2) English full-text available, 3) *in vivo* administration of a cannabinoid agonist during the perinatal period, 4) use of wildtype animals with no transgenic mutations, 5) use of experimental control group, 6) assessment of LTP or LTD in the hippocampus using electrophysiology OR assessment of a hippocampus-related behaviour (see *Data Extraction* for more details on the types of behaviour assessments included). Exclusion criteria included: 1) review paper, 2) conference abstracts, 3) preprints, 4) observational studies (cohort studies, case reports, etc.).

The prenatal or perinatal period was defined as the start of gestation up to postnatal day (PND) 10. In rats and mice, the human gestational trimester equivalents are as follows: trimester 1 (start of gestation to gestational day (GD) 10), trimester 2 (GD 10–20), and trimester 3 (PND 1–10) (Patten et al., 2014). In this review, the start of gestation (i.e., detection of vaginal plug/sperm) will be defined as GD 0. Studies that defined the start gestation to be GD 0.5 or GD 1 were adjusted accordingly, however, many studies did not define the start of gestation. Studies that administered cannabinoids beyond PND 10 and into the lactation period were included if there was also cannabinoid administration during part of a trimester period.

2.2. Data extraction

Two independent reviewers (RP and BJ) extracted data from the included studies using a standardized data extraction form. The form included: title, first author, year published, journal name, animal/strain, sex, cannabinoid type/dose, vehicle solution (if applicable), method of administration, exposure paradigm, age of assessment, sample size, behavioural task, and findings. Sample size information, when available, included the number of dams per treatment group (cannabinoid and control groups) and the number of pups evaluated per litter or treatment group. In cases where this was not specified, the most relevant available details regarding sample size were reported. Some studies included experimental groups that were exposed to a combination of perinatal cannabinoids and an additional non-cannabinoid treatment (e.g., nicotine, ethanol), however, data was exclusively extracted for the cannabinoid-only and control groups. Data pertaining to behavioural tasks with direct relevance to learning and memory were exclusively included. This included assessments of spatial, visual, working, recognition, and associative learning and memory. Although spontaneous behaviour or motor activity tasks (e.g., open field test) can be used to assess habituation to an environment, a form of non-associative learning, such data was not extracted and included in this review. For studies investigating electrophysiological synaptic plasticity, additional records of the recording artificial cerebrospinal fluid recipe, hippocampal pathway, and the LTP or LTD induction protocol were included.

Since this review aimed to provide an exploratory/descriptive synthesis of the existing literature rather than a quantitative meta-analysis, a formal risk of bias assessment of included studies was not conducted. Summarized tables of the extracted data are presented in the text. Impairments or improvements in memory and learning were defined as statistically significant ($p < 0.05$) differences between or within treatment groups. For example, an impairment indicated by a within-group difference could refer to significant learning improvements across trials in the control group that were absent in the cannabinoid group.

3. Synthesis of results

A total of 627 records (356 duplicates) were retrieved from PubMed, Web of Science, and Scopus. Two-hundred and seventy-one (n = 271) titles and abstracts were screened for relevance to the research topic and using the defined inclusion and exclusion criteria (see Fig. 1 for study selection flowchart). Forty-nine records (n = 49) were sought for full-text retrieval. Three records (n = 3) did not have full English text availability and were not retrieved. A subset of the remaining studies was excluded for having no outcomes of interest (n = 14) or no perinatal cannabinoid exposure (n = 2). Thirty studies (n = 30) were included for data extraction.

All 30 studies included a hippocampus-related behavioural task and only two studies included assessments of hippocampal synaptic plasticity. Most experiments were conducted on rats, except for four studies that examined mice (de Salas-Quiroga et al., 2020; Wanner et al., 2021; Compagno et al., 2025; Ritchie et al., 2025). Most studies administered

perinatal tetrahydrocannabinol (THC; n = 17; Abel et al., 1990; O'Shea and Mallet, 2005; Silva et al., 2012; Drazanova et al., 2019; Brancato et al., 2020; de Salas-Quiroga et al., 2020; Beggiato et al., 2020; Lallai et al., 2022; Castelli et al., 2023b, 2023a, 2024; Lei et al., 2023; Sarikahya et al., 2023; DeVuono et al., 2024; Penman et al., 2024; Black et al., 2025; Ritchie et al., 2025). Other studies administered cannabidiol (CBD; n = 6; Wanner et al., 2021; DeVuono et al., 2024; Wadhwa et al., 2024; Black et al., 2025; Compagno et al., 2025; Ritchie et al., 2025), cannabis resin (n = 2; Gianutsos and Abbatiello, 1972; Kawash et al., 1980), cannabis flower (n = 2; Sandini et al., 2023; Black et al., 2025), or synthetic cannabinoids, WIN-55,212–2 (WIN; n = 5; Mereu et al., 2003; Antonelli et al., 2005; Shabani et al., 2012; Manduca et al., 2020; Pinky et al., 2023), or CP-55,940 (CP; n = 2; O'Shea et al., 2006; Breit et al., 2019). Injections were the most common method cannabinoid administration, including subcutaneous (s.q.; n = 11; Gianutsos and Abbatiello, 1972; Mereu et al., 2003; O'Shea and Mallet, 2005; Antonelli et al., 2005; O'Shea et al., 2006; Shabani et al., 2012; Brancato et al., 2020; Manduca et al., 2020; Castelli et al., 2023b, 2023a, 2024) and intraperitoneal routes (i.p.; n = 7; Kawash et al., 1980; Breit et al., 2019; de Salas-Quiroga et al., 2020; Sarikahya et al., 2023; DeVuono et al., 2024; Wadhwa et al., 2024; Black et al., 2025). Two studies (n = 2) administered cannabinoids by infusion via a s.q. minipump or intravenous catheter (Silva et al., 2012; Pinky et al., 2023). The remaining studies administered cannabinoids orally (n = 7; Abel et al., 1990; Drazanova et al., 2019; Beggiato et al., 2020; Wanner et al., 2021; Lallai et al., 2022; Compagno et al., 2025; Ritchie et al., 2025) or via smoke or vapour inhalation (n = 4; Lei et al., 2023; Sandini et al., 2023; Penman et al., 2024; Black et al., 2025).

3.1. *Synaptic plasticity*

Two studies (4 reports) were identified that investigated the effects

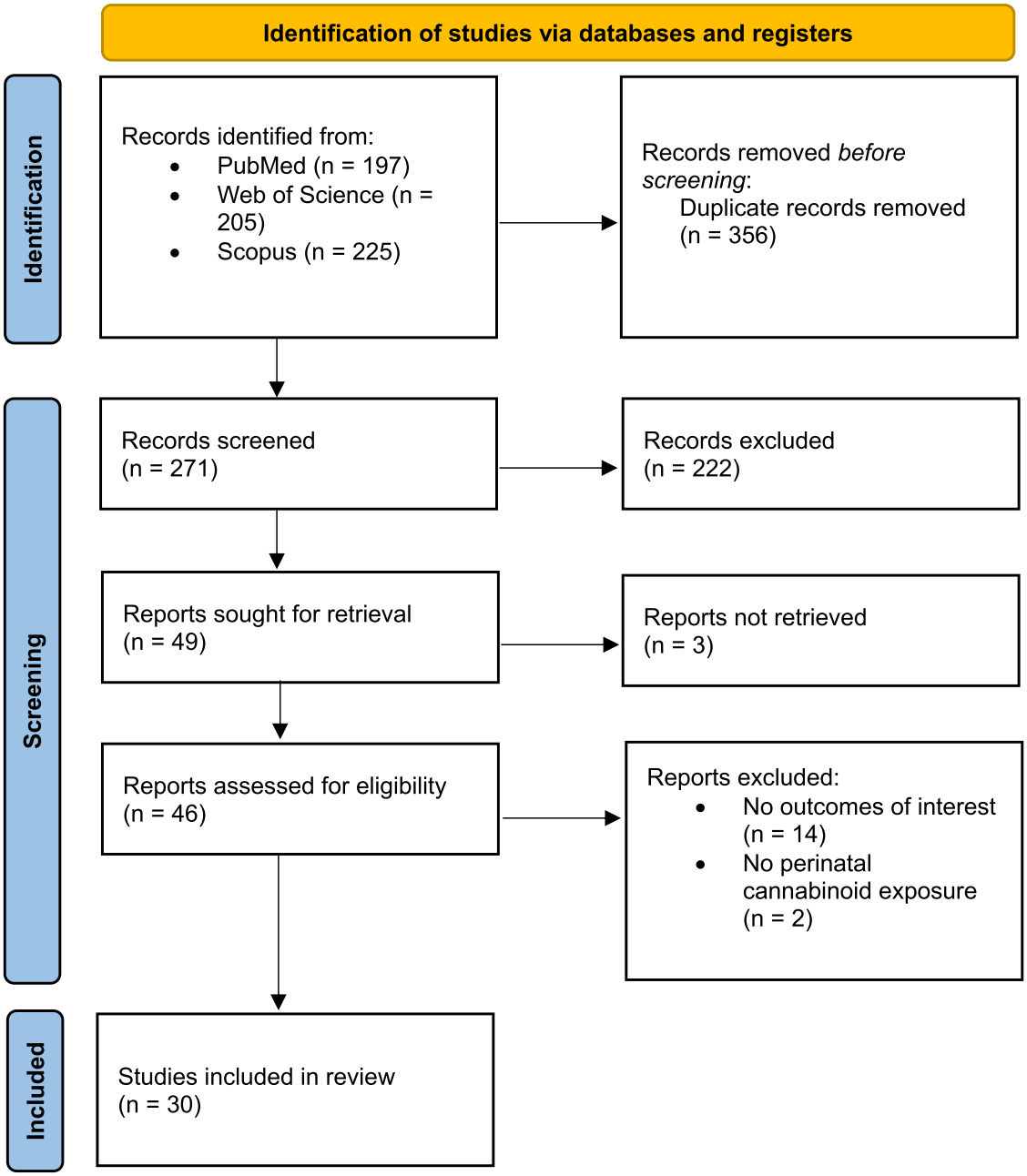

Fig. 1. PRISMA study selection & eligibility flow diagram detailing the database searches, duplicate removal, records screened, and the final included studies.

Table 1
Summary of Studies Investigating Perinatal Cannabinoid Exposure & Synaptic Plasticity.

Study	Animal	Sex	Cannabinoid	Exposure Paradigm	Age	Sample Size	Pathway	Induction Protocol	Short-Term Plasticity^{+}	Long-Term Plasticity
Mereu et al. (2003)	Wistar rat	Male	WIN−55,212–2	0.5 mg/kg (s.q.) daily GD5–20	PND40	n = 9–10 dams/ group n = 1 pup/ litter n = 21–22 slices/group	Schaffer collateral (CA3→CA1)	LTP: 2x trains of 100 Hz for 1 s w/ 25 s interval	No effect	↓ LTP*
Pinky et al. (2023)	Sprague-Dawley rat	Male	WIN−55,212–2	2 mg/kg (osmotic minipump, s.q.) daily GD3-PND2	PND58–62	n = 6–10 pups/group	Schaffer collateral (CA3→CA1)	LTP: 5x TBS sweeps w/ 20 s inter-TBS interval LTD: 2 × 900 pulses @ 1 Hz w/ 10 min interval	Not reported	↓ LTP** ↑ LTD**

+ = change in the EPSP slope at 5–20 min post-induction (compared to baseline)
* = change in the EPSP slope at 20–180 min post-induction (compared to baseline)
** = change in the EPSP slope at 50–60 min post-induction (compared to baseline)
Abbreviations: Subcutaneous (s.q.); gestational day (GD); postnatal day (PND); cornu ammonis (CA), long-term potentiation (LTP); long-term depression (LTD); theta burst stimulation (TBS); excitatory post-synaptic potential (EPSP)

perinatal cannabinoid exposure on synaptic plasticity in the Schaffer collateral pathway of the hippocampus (Table 1). Both studies found alterations in long-term synaptic plasticity (Mereu et al., 2003; Pinky et al., 2023).

Studies investigating synaptic plasticity following perinatal cannabinoid exposure have exclusively used the synthetic cannabinoid, WIN. Mereu et al. (2003) injected WIN (0.5 mg/kg; s.q.) daily throughout the first and second trimesters (GD 5–20) and found reduced LTP with no effect on short-term potentiation in male offspring. Similarly, Pinky et al. (2023) administered a higher dose of WIN (2 mg/kg; s.q. via infusion) from GD 3 to PND 2 and found reduced LTP and increased LTD in male offspring. Although these studies differed in their LTP induction protocols (Mereu et al.: 2 ×100 Hz trains; Pinky et al.: 5x theta burst stimulation (TBS) sweeps) and age that offspring were tested (Mereu et al.: PND 40; Pinky et al.: PND 58–62), both groups of researchers described consistent synaptic plasticity disruptions with associated memory deficits. Reductions in brain-derived neurotrophic factor (BDNF) could be a contributing factor to this synaptic plasticity dysfunction, as BDNF facilitates the induction and maintenance of LTP through pre- and post-synaptic mechanisms (Lin et al., 2018). Moreover, previous reports have found reductions in hippocampal BDNF expression following perinatal WIN exposure (Maj et al., 2007), further supporting this mechanistic hypothesis.

There is a clear absence of research investigating how synaptic strength and communication is modulated by perinatal cannabinoid exposure. Existing literature is limited to male offspring, synthetic cannabinoids, and injection methods of administration. Readers should consider the possibility of a publication bias, wherein findings that align with public health interests (i.e., perinatal cannabinoids being harmful) are more likely to get published. By overrepresenting the studies that demonstrate synaptic impairments, the true impact of perinatal cannabinoid exposure may be obscured. Although synaptic plasticity is hypothesized to be a major cellular mechanism of learning and memory (Neves et al., 2008; Takeuchi et al., 2014), it is possible that these activity-related changes may not consistently be associated with behavioural impairments. Neural changes could be mild enough such that they don't produce a behavioural deficit, or such changes could be accompanied by functional adaptations in neighbouring pathways to help maintain memory function (Sharma et al., 2016). Moreover, synaptic plasticity in different neural pathways, are likely associated with different behavioural functions. The following review of studies assessing the behavioural impact of perinatal cannabinoid exposure warrants further research on understanding the underlying neural mechanisms for the reported cognitive effects.

3.2. *Spatial/visual memory*

Thirteen studies (26 reports) assessed the impact of perinatal cannabinoid exposure on spatial/visual learning and memory (Table 2). Spatial/visual memory enables individual to recognize, remember, and navigate through environments. It is primarily coordinated by hippocampal pyramidal place cells that encode specific locations based on input from grid cells in the entorhinal cortex (Hafting et al., 2005; Park et al., 2011). Nine studies reported a spatial/visual memory impairment, and one study reported a spatial/visual memory improvement. Most studies investigated spatial learning and memory using maze navigation tasks, including the Barnes maze (n = 4), water maze (n = 5), Lashley III maze (n = 1), and the Y-maze (n = 1). Two studies investigated spatial and visual learning using the Can test, a reinforcement-motivated spatial and visual discrimination task (see Castelli et al. 2023b for more details). One study assessed visual learning using touchscreen-based pairwise discrimination task (n = 1). One study assessed spatial learning through automated IntelliCage behaviour tracking where rodents were tasked to learn the location of a water reward in social home cage setting (n = 1).

The effects of perinatal cannabinoid exposure on spatial learning and memory appears dependent on the trimester that offspring are exposed and the method of cannabinoid administration. Most studies found spatial memory deficits following THC or cannabis resin injections throughout the first and/or second trimesters (Gianutsos and Abbatiello, 1972; Kawash et al., 1980; Castelli et al., 2023b, 2023a, 2024; Lei et al., 2023; Pinky et al., 2023). Two studies that found no such effects had exposed offspring to THC or CP injections during the third trimester (O'Shea and Mallet, 2005; Breit et al., 2019). However, one study that investigated CBD injections during the third trimester found a female-specific deficit (Wadhwa et al., 2024), suggesting that the type of cannabinoid is also an important consideration along with the trimester of exposure.

The two studies that investigated the effects of perinatal THC vapour exposure on maze learning have described conflicting results. Whereas Penman et al. (2024) found no spatial learning deficits in offspring, Lei et al. (2023) found a female-specific deficit. Both studies exposed offspring during the first and second trimesters and assessed similar aged offspring (i.e., late adolescence) in the same behavioural task (i.e., Morris Water Maze), so it is unclear why they found discrepant results. The singly identified spatial learning study in mice also described a female-specific impairment following THC oral gavage during the

Table 2
Summary of Studies Investigating Perinatal Cannabinoid Exposure & Spatial/Visual Memory.

Study	Animal	Sex	Cannabinoid	Exposure Paradigm	Age	Sample Size	Task	Finding
Gianutsos and Abbatiello (1972)	Wistar rats	Male	Cannabis sativa resin	GD7-GD10 250 mg/kg (s.q.) daily	PND65	n = 13–21 dams/group n = 10–15 pups/sex/group	Lashley III Maze	Impairment
	-	Female	-	-	-	-	Lashley III Maze	No effect
Kawash et al. (1980)	Wistar rats	Unspecified	Cannabis resin (55 % THC, 19 % CBD, 14 % CBN)	GD2-GD6 4.2 mg/kg (i.p.) daily	PND22	n = 8 dams/group n = 5 pups/litter	Water maze	Impairment
O'Shea and Mallet (2005)	Wistar rats	Male	THC	PND4–14 5 mg/kg (s.q.) daily	PND56	n = 5–7 pups/group	Y-maze (Spatial discrimination)	No effect
Breit et al. (2019)	Sprague-Dawley rats	Male + Female	CP−55,940	PND4–9 0.4 mg/kg (i.p.) daily	PND40–46	n = 13–15 dams/group n = 1 pup/sex/litter	Morris Water Maze	No effect
Lei et al. (2023)	Sprague-Dawley rats	Male	THC	GD5–20 100 mg/mL (vapour) daily	PND40–45	n = 12–14 dams/group n = 1 pup/sex/litter	Morris Water Maze	No effect
	-	Female	-	-	-	-	Morris Water Maze	Impairment
Pinky et al. (2023)	Sprague-Dawley rats	Male	WIN−55,212–2	GD3-PND2 2 mg/kg (s.q.; osmotic minipump) daily	PND46–47	n = 12–13 pups/group	Morris Water Maze	Impairment
Castelli et al. (2023a)	Wistar rats	Male	THC	GD5–20 2 mg/kg (s.q.) daily	PND35–42	n = 10 pups/group	Can test (spatial)	Impairment
	-	-	-	-	-	-	Can test (visual)	Impairment
	-	-	-	-	-	n = 12 pups/group	Barnes Maze (+reversal learning)	Impairment
Castelli et al. (2023b)	Wistar rats	Male	THC	GD5–20 2 mg/kg (s.q.) daily	PND35–46	n = 1–2 pups/litter n = 9–10 pups/group	Can test (spatial)	Impairment
	-	-	-	-	-	-	Can test (visual)	Impairment
	-	-	-	-	-	n = 1–2 pups/litter n = 12 pups/group	Barnes Maze (+reversal learning)	Impairment
Castelli et al. (2024)	Sprague-Dawley rats	Male	THC	GD5–20 2 mg/kg (s.q.) daily	PND35–46	n = 1–2 pups/sex/litter n = 13–15 pups/group	Barnes Maze (+reversal learning)	Impairment
	-	Female	-	-	-	-	Barnes Maze (+reversal learning)	Impairment No effect on reversal learning
Penman et al. (2024)	Sprague-Dawley rats	Male + Female	THC	GD2-GD22 40 mg (vapour) daily	PND28–30	n = 5–8 dams/group n = 16 pups/sex/group	Morris Water Maze	No effect
	-	-	-	-	PND49–51	-	Morris Water Maze	No effect
	-	-	-	10 mg (vapour) daily	PND28–30	-	Morris Water Maze	No effect
	-	-	-	-	PND49–51	-	Morris Water Maze	No effect
Sandini et al. (2023)	Sprague-Dawley rats	Male + Female	Cannabis (19.51 % THC, <0.07 % CBD)	GD6-GD20 200 mg (smoke) daily	PND90	n = 10–12 dams/group n = 7–11 pups/sex/group	Visual pairwise discrimination (+reversal learning)	Improvement
Wadhwa et al. (2024)	Sprague-Dawley rats	Male	CBD	PND1,3,5 50 mg/kg (i.p.)	PND42	n = 17–24 pups/sex/group	Barnes Maze	No effect
	-	Female	-	-	-	-	Barnes Maze	Impairment
Ritchie et al. (2025)	C57BL/6 mice	Male	THC oil	GD6–11 20 mg/kg (p.o.; gavage) daily	PND56–77	n = 2–5 dams/group n = 3–13 pups/sex/group	IntelliCage Spatial Learning (+reversal learning)	No data*
-	-	Female	-	-	PND77–98	-	IntelliCage Spatial Learning (+reversal learning)	Impairment

(*continued on next page*)

Table 2 (*continued*)

Study	Animal	Sex	Cannabinoid	Exposure Paradigm	Age	Sample Size	Task	Finding
-	-	Male	CBD oil	GD6–11 20 mg/kg (p.o.; gavage) daily	PND56–77	-	IntelliCage Spatial Learning (+reversal learning)	No effect
-	-	Female	-	-	PND77–98	-	IntelliCage Spatial Learning (+reversal learning)	No effect

* = no data due to cage-mate aggression hindering completion of assessment
Abbreviations: Subcutaneous (s.q.); intraperitoneal (i.p.); gestational day (GD); postnatal day (PND); tetrahydrocannabinol (THC); cannabidiol (CBD); cannabinol (CBN)

second half of the first trimester (Ritchie et al., 2025). No effects were found in male mice. Although both Lei et al. (2023) and Ritchie et al. (2025) described female-specific spatial learning deficits following perinatal THC exposure via vapour inhalation and oral gavage, respectively, other studies describe male-specific deficits from perinatal THC injections. Injections of a high dose of cannabis resin (250 mg/kg; s.q.) in the first trimester induced maze learning deficits that were specific to male rats (Gianutsos and Abbatiello, 1972). Injections of THC (2 mg/kg; s.q.) in the first and second trimesters also induced performance deficits in the Barnes maze reversal trial that was specific to male rats (Castelli et al., 2024). These studies highlight the potential interaction between sex and method of administration.

The few existing visual-focused assessments (i.e., visual learning tasks that do not rely on navigation memory) have shown conflicting results, likely explained by the study design differences. In the reinforcement-motivated visual Can test, where rodents are tasked on their ability to visually discriminate a reward can independent of location, first and second trimester THC injections impaired male rat memory (Castelli et al., 2023b, 2023a). A similar finding was described for the spatial navigation component of this task where the reward can was in a fixed position among identical cans. In a study using a touch-screen visual discrimination task, THC-dominant cannabis smoke exposure during the first and second trimesters improved performance in both male and female offspring (Sandini et al., 2023). This finding was from one of the two reported studies that identified any learning and memory improvement following perinatal cannabinoid exposure.

While most studies indicate that perinatal cannabinoid exposure can induce deficits in spatial/visual learning and memory, the effects appear to depend on sex, trimester of exposure, and method of administration. More studies are needed evaluate the effects of inhalation (vapour/smoke) methods of administration, in addition to third trimester cannabinoid exposure. It is also important to highlight that performance on the spatial/visual memory tasks described above are often dependent on working memory and recognition memory. Therefore, these findings should be interpreted in the context of performance on other memory assessments.

3.3. *Working memory*

Six studies (10 reports) assessed the impact of perinatal cannabinoid exposure on working memory (Table 3). Working memory refers to the temporary storage and manipulation of information that is critical for reasoning, decision-making, and goal-directed behaviour (Repovš and Baddeley, 2006). Its proper functioning relies on communication

Table 3
Summary of Studies Investigating Perinatal Cannabinoid Exposure & Working Memory.

Study	Animal	Sex	Cannabinoid	Exposure Paradigm	Age	Sample Size	Task	Finding
Abel et al. (1990)	Long Evans rats	Male + Female	THC	GD6-birth 10 mg/kg (p.o.; gavage)	PND16	n = 1–2 pups/sex/litter n = 11–20 pups/sex/group	T-maze (Spontaneous alternation)	No effect
	-	-	-	25 mg/kg	-	-	T-maze (Spontaneous alternation)	No effect
O'Shea and Mallet (2005)	Wistar rat	Male	THC	PND4–14 5 mg/kg (s.q.) daily	PND56	n = 5–7 pups/group	Y-maze (Spontaneous alternation)	Impairment
Beggiato et al. (2020)	Wistar rats	Male	THC	GD5–20 5 mg/kg (p.o.; gavage) daily	PND65–90	n = 7 dams/group n = 1 pup/litter	Y-maze (Spontaneous alternation)	Impairment
Wanner et al. (2021)	Agouti viable yellow mice (C57BL/6)	Male	CBD	14-d prior to pairing – lactation 20 mg/kg (p.o.; gavage) daily	PND84	n = 7–9 dams/group n = 16–17 pups/group	Y-maze (Spontaneous alternation)	No effect
	-	Female	-	-	-	-	Y-maze (Spontaneous alternation)	Improvement
Lei et al. (2023)	Sprague-Dawley rats	Male	THC	GD5–20 100 mg/mL (vapour) daily	PND55–60	n = 12–14 dams/group n = 1 pup/sex/litter	Modified Morris Water Maze	No effect
		Female	-	-	-	-	Modified Morris Water Maze	No effect
Sarikahya et al. (2023)	Wistar rats	Male	THC	GD7–22 3 mg/kg (i.p.) daily	PND70–100	n = 12–13 dams/group n = 17–20 pups/sex/group	Spontaneous alternation	Impairment
	-	Female	-	-	-	-	-	Impairment

Abbreviations: Oral (p.o.); subcutaneous (s.q.); intraperitoneal (i.p.); gestational day (GD); postnatal day (PND); tetrahydrocannabinol (THC); cannabidiol (CBD)

between the prefrontal cortex and hippocampus, where the hippocampus plays a particularly important role in spatial working memory (Duda and Węsierska, 2021). Three studies reported a working memory impairment, and one study reported a working memory improvement. Working memory was most assessed via measures of spontaneous alternation in a T- or Y-maze apparatus (n = 4). One study assessed working memory in a modified Morris Water Maze (n = 1). One study did not describe the apparatus used for their assessment of spontaneous alternation (n = 1; Sarikahya et al., 2023).

Age of offspring testing and the method of administration appear to be key factors in establishing whether perinatal THC affects working memory performance. Abel et al. (1990) and Beggiato et al. (2020) conducted studies administering THC via oral gavage during the first and second trimesters, yielding distinct results on working memory performance. The former group administered daily doses of 10 or 25 mg/kg THC and found no effects on working memory, whereas the latter group administered a lower daily dose of 5 mg/kg THC and observed a working memory deficit. This discrepancy could potentially be explained by the age that offspring were tested. Abel et al. assessed offspring at an infantile age (PND 16), whereas Beggiato et al. assessed offspring in adulthood (PND 65–90). As working memory has been shown to develop into late adolescence in rodents (Kirschmann et al., 2018), it is possible that deficits would have been observed in the former study (Abel et al., 1990) at a later age of testing.

Different findings result from different methods of administration. Vapour inhalation of THC during the first and second trimesters had no effect on working memory at PND 55–60 in male or female rats (Lei et al., 2023). Injections of THC (3 mg/kg; i.p.) during the first and second trimesters resulted in working memory deficits in both male and female rats at PND 70–100 (Sarikahya et al., 2023). Injections of THC (5 mg/kg; s.q.) during the third trimester resulted in working memory deficits in male rats at PND 56 (O'Shea and Mallet, 2005).

Sex differences in working memory in response to perinatal cannabinoid exposure was only described for CBD. Wanner et al. (2021) investigated the effects of a prolonged oral CBD exposure that began 14 days prior to pairing and throughout lactation (20 mg/kg daily) in mice. The researchers found no effect on working memory in males tested at PND 84, in contrast to the improvement found in females.

Together, these studies suggest that perinatal THC exposure may impair working memory, whereas perinatal CBD exposure may improve working memory in females. However, when cannabinoids are administered via vapour inhalation or when offspring are tested too early in development (< PND 22), the impact on working memory appears minimal.

3.4. Recognition memory

Twelve studies (52 reports) assessed the impact of perinatal cannabinoid exposure on recognition memory (Table 4). Recognition memory consists of two parts: 1) familiarity and recency discrimination and 2) recollection of previously encountered stimuli. The standard model of recognition memory proposes that the perirhinal cortex and hippocampus separately process familiarity and recollection, respectively (Brown and Aggleton, 2001). Other models suggest that both brain regions are involved in processing familiarity and recollection, and instead differ in regional activation based on the details of the stimuli (Squire et al., 2007). Nine studies reported a recognition memory impairment, and no studies reported a recognition memory improvement. This included assessments of novel object recognition (NOR; n = 8), temporal order object recognition (n = 3), social recognition (n = 2), object location recognition (n = 1), emotional object recognition (n = 1), and odour recognition (n = 1).

Both studies that administered THC to rats via oral gavage (5 mg/kg daily) found deficits in the NOR task, where rodents are assessed on their preference for a familiar versus novel object (Drazanova et al., 2019; Lallai et al., 2022). Deficits were apparent regardless of exposure paradigm (trimester 1–2 vs. trimester 2–3) and age that offspring were tested (PND 35 vs. PND 180). However, a study that administered a higher THC dose (20 mg/kg) during the second half of the first trimester found no NOR deficits in young adult mice (PND 63–77) (Ritchie et al., 2025). It's possible that the absence of the effect, despite a higher dose, could be result of inter-species differences or the shorter duration of THC exposure.

No evidence of effects on NOR were found in response to first and/or second trimester THC injections (Brancato et al., 2020; de Salas-Quiroga et al., 2020) or vapour inhalation (Penman et al., 2024). Although Brancato and colleagues did not find any effect on recognition of a neutral novel object, when an object was paired with an aversive shock, THC-exposed animals show a recognition impairment of the shock-associated object (Brancato et al., 2020). Similarly, although de Salas-Quiroga et al. (2020) found no THC-induced effects on the standard NOR task, there was an impairment found in object displacement recognition. No studies were identified that investigated the impact of THC exposure during the third trimester and/or lactation period on NOR performance. However, O'Shea et al. (2006) found that injections of the synthetic cannabinoid, CP, during the third trimester and lactation period induced NOR impairments in male late adolescent rats (PND 53).

In contrast to the NOR findings, sex differences have been described for temporal order recognition (TOR) memory. To assess TOR, rodents are first exposed to a pair of identical objects, followed by a delay. They are then presented with a novel pair of identical objects, followed by another delay, and are then evaluated based on their preference for the older or more recently presented objects (see DeVuono et al. 2024 for more details). Injections of THC (3 mg/kg daily; i.p.) during trimesters 1 and 2 induced a TOR impairment in male and female adult rats (PND 70–100) and male adolescent rats (PND 35–45), but not female adolescent rats (Sarikahya et al., 2023; DeVuono et al., 2024). A similar sex-specific pattern was described for social recognition memory, where impairments (i.e., more time spent with familiar vs novel conspecifics) were only evident in adult males and females, and adolescent males only. These results are suggestive of an age-dependent effect of perinatal THC on TOR and social recognition memory in females. In contrast to findings with the phytocannabinoid, THC, injections of the synthetic cannabinoid, WIN, did not induce TOR deficits in male or female rats during adolescence or young adulthood (Manduca et al., 2020). When interpreting results on TOR and social recognition memory tasks, it is important to consider the potential deficits in basic recognition memory that may confound performance and obscure task-specific deficits.

Only two studies that investigated perinatal cannabinoid effects on recognition memory utilized a vapour or smoke inhalation paradigm (Penman et al., 2024; Black et al., 2025). Following perinatal vapour exposure to THC, Black et al. (2025) found recognition memory deficits in adolescent (PND 30–40) rat offspring, whereas Penman et al. (2024) found no recognition memory deficits in early (PND 25) and late adolescent (PND 46) rat offspring. These contrasting results could possibly be due to the different inhalation products (Penman *et al.*: THC vs. Black *et al.*: high THC cannabis flower) or different types of recognition memory assessed (Penman *et al.*: NOR; Black *et al.*: odour recognition). Black and colleagues also investigated smoke exposure to high CBD cannabis and found odour recognition deficits in male and female, adolescent and adult rats.

Other methods of perinatal CBD administration describe varying results. When mice were administered CBD orally (100 mg/kg daily) throughout gestation and lactation, only adult males experienced NOR deficits (Compagno et al., 2025). Female and male offspring did not acquire NOR deficits following the various other exposure paradigms tested, including oral administration during gestation only (GD 0–22) or during the third trimester and lactation (PND 0–24). A separate mice study that administered a lower dose of CBD (20 mg/kg) via oral gavage from GD 6–11 also found no effects on NOR in both male and female offspring (Ritchie et al., 2025). Perinatal CBD injections during the first and second trimester have been shown to induce recognition

Table 4
Summary of Studies Investigating Perinatal Cannabinoid Exposure & Recognition Memory.

Study	Animal	Sex	Cannabinoid	Exposure Paradigm	Age	Sample Size	Task	Finding
O'Shea et al. (2006)	Wistar rats	Male	CP−55,940	PND4–25 0.15–0.3 mg/kg titration (s.q.) daily	PND53	n = 12 pups/group	Novel object recognition	Impairment
Drazanova et al. (2019)	Sprague-Dawley rats	Male	THC	GD15-PND9 5 mg/kg (p.o.; gavage) daily	PND180	n = 3–4 dams/group n = 10 pups/group	Novel object recognition	Impairment
de Salas-Quiroga - et al. (2020)	C57BL/6 mice	Male	THC	GD10.5–17.5 3 mg/kg (i.p.) daily	PND60	n = 3–7 pups/sex/group	Novel object recognition	No effect
	-	Female	-	-	-	-	Novel object recognition	No effect
	-	Male	-	-	-	-	Object location task	Impairment
	-	Female	-	-	-	-	Object location task	Impairment
Brancato et al. (2020)	Wistar rats	Male	THC	GD5–20 2 mg/kg (s.q.) daily	PND25–30	n = 12 pups/group	Novel object recognition	No effect
	-	-	-	-	-	-	Emotional object recognition	Impairment
Manduca et al. (2020)	Wistar rats	Male	WIN−55,212–2	GD5–20 0.5 mg/kg (s.q.) daily	PND28–35	n = 8–12 dams/group n = 1 pup/sex/litter	Temporal order object recognition	No effect
	-	Male	-	-	PND50–60	-	Temporal order object recognition	No effect
	-	Female	-	-	PND28–35	-	Temporal order object recognition	No effect
	-	Female	-	-	PND50–60	-	Temporal order object recognition	No effect
Lallai et al. (2022)	Wistar rats	Male	THC	5-d prior to pairing – GD20 5 mg/kg (p.o.; gavage) daily	PND35	n = 7–16 pups/sex/group	Novel object recognition	Impairment
	-	Female	-	-	-	-	Novel object recognition	Impairment
Sarikahya et al. (2023)	Wistar rats	Male	THC	GD7–22 3 mg/kg (i.p.) daily	PND70–100	n = 12–13 dams/group n = 17–20 pups/sex/group	Social interaction test (memory)	Impairment
	-	Female	-	-	-	-	Social interaction test (memory)	Impairment
	-	Male	-	-	-	-	Temporal order object recognition	Impairment
	-	Female	-	-	-	-	Temporal order object recognition	Impairment
DeVuono et al. (2024)	Wistar rats	Male	THC	GD7–22 3 mg/kg (i.p.) daily	PND35–45	n = 8–13 dams/group n = 6–13 pups/sex/group	Social interaction test (memory)	Impairment
	-	Female	-	-	-	-	Social interaction test (memory)	No effect
	-	Male	CBD	30 mg/kg (i.p.) daily	-	-	Social interaction test (memory)	No effect
	-	Female	-	-	-	-	Social interaction test (memory)	Impairment
	-	Male	THC+CBD	THC (3 mg/kg; i.p.) + CBD (30 mg/kg; i.p.) daily	-	-	Social interaction test (memory)	No effect
	-	Female	-	-	-	-	Social interaction test (memory)	Impairment
	-	Male	THC	3 mg/kg (i.p.) daily	-	n = 8–13 dams/group n = 7–11 pups/sex/group	Temporal order object recognition	Impairment
	-	Female	-	-	-	-		No effect
	-	Male	CBD	30 mg/kg (i.p.) daily	-	-	Temporal order object recognition	No effect
	-	Female	-	-	-	-	Temporal order object recognition	Impairment
	-	Male	THC+CBD	THC (3 mg/kg; i.p.) + CBD (30 mg/kg; i.p.) daily	-	-	Temporal order object recognition	Impairment
	-	Female	-	-	-	-	Temporal order object recognition	No effect

(*continued on next page*)

Table 4 (*continued*)

Study	Animal	Sex	Cannabinoid	Exposure Paradigm	Age	Sample Size	Task	Finding
Penman et al. (2024)	Sprague-Dawley rats	Male + Female	THC	GD2–22 40 mg (vapour) daily	PND25	n = 5–8 dams/group n = 16 pups/sex/group	Novel object recognition	No effect
	-	-	-	-	PND46	-	Novel object recognition	No effect
	-	-	-	10 mg (vapour) daily	PND25	-	Novel object recognition	No effect
	-	-	-	-	PND46	-	Novel object recognition	No effect
Black et al. (2025)	Sprague-Dawley rats	Male + Female	Cannabis (17.98 % THC, 0.1 % CBD)	GD6–20 300 mg (smoke) daily	PND30–40	n = 13–17 dams/group n = 1–2 pups/litter	Odour recognition	Impairment
	-	-	-	-	PND56–90	-	Odour recognition	Impairment
	-	-	Cannabis (12.83 % CBD, 0.68 % THC)	-	PND30–40	-	Odour recognition	Impairment
	-	-	-	-	PND56–90	-	Odour recognition	Impairment
	-	-	THC	3 mg/kg (i.p.) daily	PND30–40	-	Odour recognition	Impairment
	-	-	-	-	PND56–90	-	Odour recognition	Impairment
	-	-	CBD	10 mg/kg (i.p.) daily	PND30–40	-	Odour recognition	Impairment
	-	-	-	-	PND56–90	-	Odour recognition	Impairment
Compagno et al. (2025)	C57BL/6 J	Male	CBD	GD0-PND24 100 mg/kg (p.o.) daily	PND109–116	n = 49 dams n = 95 pups	Novel object recognition	Impairment
	-	Female	-	-	-	-	Novel object recognition	No effect
	-	Male	-	GD0–22	-	-	Novel object recognition	No effect
	-	Female	-	-	-	-	Novel object recognition	No effect
	-	Male	-	PND0–24	-	-	Novel object recognition	No effect
	-	Female	-	-	-	-	Novel object recognition	No effect
Ritchie et al. (2025)	C57BL/6 mice	Male	CBD oil	GD6–11 20 mg/kg (p.o.) daily	PND77	n = 2–5 dams/group n = 4–13 pups/sex/group	Novel object recognition	No effect
	-	Female	-	-	PND63	-	Novel object recognition	No effect
	-	Male	THC oil	-	PND77	-	Novel object recognition	No effect
	-	Female	-	-	PND63	-	Novel object recognition	No effect

impairments in two studies (DeVuono et al., 2024; Black et al., 2025). DeVuono et al. (2024) described a female-specific effect of perinatal CBD injections (30 mg/kg; i.p.; GD 7–22), where only female adolescent rats showed TOR and social recognition deficits. Black et al. (2025) found an odour recognition deficit that was not sex-specific following a lower dose CBD injection paradigm (10 mg/kg; i.p.; GD 6–20). The differing impact of sex in these CBD injection studies are likely due to the different types of recognition memory that were assessed (odour vs. temporal order & social). DeVuono and colleagues also showed that when CBD was administered in combination with THC (3 mg/kg; i.p.), a TOR deficit was induced in the male but not the female rats (DeVuono et al., 2024). Interestingly, there was an opposite effect of sex in the social recognition test, where a deficit was only found in the female rats following the combination exposure.

The findings of studies investigating recognition memory are mixed and depend on a multitude of factors, including the type of cannabinoid, method of administration, exposure paradigm, age of testing, and sex. Thus, the evidence presented is not sufficient to form conclusions about the effects of perinatal cannabinoid exposure on recognition memory.

3.5. Associative memory

Seven studies (12 reports) investigated the impact of perinatal cannabinoid exposure on associative learning and memory (Table 5). Associative learning involves forming associations between unrelated stimuli to influence behaviour (i.e., classical and operant conditioning). In preclinical models, associative learning is often assessed in fear-related paradigms where an aversive shock stimulus is paired with a context that rodents learn to escape (active avoidance) or avoid (passive avoidance; Branchi and Ricceri, 2013). Previous research has demonstrated that bi-directional communication between the ventral hippocampus and amygdala mediates the encoding and extinction of these fear-based memories (Kim and Cho, 2020; Nguyen et al., 2023). Six studies reported an associative learning impairment, and no studies reported an associative learning improvement. Associative learning was measured by assessments of passive avoidance (n = 4), active avoidance (n = 2), contextual fear conditioning (n = 1), emotional object recognition (n = 1), and operant instrumental learning (n = 1).

Impairments in passive avoidance learning have been described following perinatal THC or WIN injections throughout the first and second trimesters (Mereu et al., 2003; Shabani et al., 2012; Silva et al., 2012). In contrast, Abel et al. (1990) found no evidence of passive avoidance impairment when THC was administered in the same gestational period via oral gavage. In addition to the methodological difference in the route of cannabinoid administration, Abel and colleagues had also tested offspring on PND 17, an age where memory is still under development and may not be subject to detectable deficits. A similar result was described for this research group's working memory task where they found no THC-induced effects, contrary to findings from an oral gavage study that assessed older offspring (discussed in 3.3 –

Table 5
Summary of Studies Investigating Perinatal Cannabinoid Exposure & Associative Memory.

Study	Animal	Sex	Cannabinoid	Exposure Paradigm	Age	Sample Size	Task	Finding
Abel et al. (1990)	Long Evans rat	Male + Female	THC	GD6-birth 10 mg/kg (p.o.; gavage) daily	PND17	n = 1–2 pups/sex/litter n = 11–20 pups/sex/group	Passive avoidance	No effect
	-	-	-	25 mg/kg	-	-	Passive avoidance	No effect
Mereu et al. (2003)	Wistar rat	Male	WIN−55,212–2	GD5–20 0.5 mg/kg (s.q.) daily	PND40	n = 8 dams/group n = 1 pup/litter	Passive avoidance	Impairment
	-	-	-	-	PND80	n = 8 dams/group n = 1 pup/litter	Passive avoidance	Impairment
Antonelli et al. (2005)	Wistar rat	Male	WIN−55,212–2	GD5–20 0.5 mg/kg (s.q.) daily	PND80	n = 10 dams/group n = 1 pup/litter	Active avoidance	Impairment
Shabani et al. (2012)	Wistar rat	Male	WIN−55,212–2	GD5–20 0.5 mg/kg (s.q.) daily	PND49	n = 8 pups/group	Passive avoidance	Impairment
Silva et al. (2012)	Sprague-Dawley rats	Male + Female	THC	GD0–20 0.15 mg/kg (i.v.; catheter) daily	PND22	n = 9–12 dams/group n = 16–24 pups/sex/group	Passive avoidance	Impairment
	-	Male	-	-	PND45	n = 9–11 dams/group n = 8–11 pups/sex/group	Active avoidance (+reversal trial)	No effect Impairment (reversal trial)
	-	Female	-	-	-	-	Active avoidance (+reversal trial)	No effect
Brancato et al. (2020)	Wistar rats	Male	THC	GD5–20 2 mg/kg (s.q.) daily	PND25–30	n = 12 pups/group	Emotional object recognition	Impairment
	-	-	-	-	-	unspecified	Instrumental learning (operant)	Impairment
Pinky et al. (2023)	Sprague-Dawley rats	Male	WIN−55,212–2	GD3-PND2 2 mg/kg (s.q.; osmotic minipump) daily	PND46–47	n = 12–13 pups/group	Contextual Fear Conditioning	Impairment

Abbreviations: Oral (p.o.); subcutaneous (s.q.); intravenous (i.v.); gestational day (GD); postnatal day (PND); tetrahydrocannabinol (THC)

Working Memory; Beggiato et al., 2020). However, Silva et al. (2012) found a passive avoidance deficit in THC-exposed offspring at as early as PND 22, suggesting that age is likely not the dominant factor in this case.

The few studies that investigated active avoidance have shown mixed results. Perinatal WIN exposure (0.5 mg/kg; s.q.) has been shown to reduce conditioned aversion response in male adult rats, with no reported evaluation in reversal learning trials (Antonelli et al., 2005). In contrast, perinatal THC exposure (0.15 mg/kg; i.v.) has been shown to have no effect on active avoidance in male or female adolescent rats, except for a male-specific deficit in the reversal trials of this task (Silva et al., 2012). The limited findings from these two studies with differing study design do not allow any conclusions to be drawn regarding active avoidance learning.

Associative learning impairments were also found in the contextual fear conditioning task (Pinky et al., 2023), emotional object recognition task and operant instrumental learning of a lever press task (Brancato et al., 2020). Collectively, these studies provide some evidence of perinatal cannabinoid-induced associative learning deficits. However, more studies exploring different associative learning tasks, methods of cannabinoid administration, and trimester exposure periods are needed to elucidate the generalizability of these findings.

4. Synthetic cannabinoids vs. phytocannabinoids vs. cannabis flower

The two existing studies that investigated hippocampal synaptic plasticity used the synthetic cannabinoid, WIN (Mereu et al., 2003; Pinky et al., 2023). WIN is a full agonist at the cannabinoid type-1 receptor, in contrast to THC's partial agonist activity (Paronis et al., 2012). In addition to their differing receptor interactions, these cannabinoids have been shown to differ in their effects on hippocampus-related functions (Acheson et al., 2011). Synthetic cannabinoids can still provide valuable information on how modulation to cannabinoid receptor activity affects development, however, it is important that future studies continue investigating phytocannabinoids, such as THC or CBD, that are found in cannabis to ensure the clinical relevance of findings.

Most of the existing research on perinatal cannabinoid exposure and learning and memory investigates the phytocannabinoid, THC (n = 17; Abel et al., 1990; O'Shea and Mallet, 2005; Silva et al., 2012; Drazanova et al., 2019; Brancato et al., 2020; de Salas-Quiroga et al., 2020; Beggiato et al., 2020; Lallai et al., 2022; Castelli et al., 2023b, 2023a, 2024; Lei et al., 2023; Sarikahya et al., 2023; DeVuono et al., 2024; Penman et al., 2024; Black et al., 2025; Ritchie et al., 2025), with few studies investigating CBD (n = 6; Wanner et al., 2021; DeVuono et al., 2024; Wadhwa et al., 2024; Black et al., 2025; Compagno et al., 2025; Ritchie et al., 2025). As cannabis plants continue to be bred to contain increasing THC concentrations (Freeman et al., 2021), it remains of great value to understand how perinatal THC exposure impacts development. However, with the consideration of the limited available studies investigating CBD, it is also clear that more research is needed to understand how this non-psychoactive cannabinoid affects development, including how it might interact with THC to affect development.

An additional important consideration is the scarcity of studies investigating the effects of perinatal cannabis flower exposure (Sandini et al., 2023; Black et al., 2025). Whole cannabis flower contains phytocannabinoids, terpenes, and flavonoids, that are likely to have their individual and combinatorial effects on the brain and body (Ferber et al., 2020; Zagzoog et al., 2022; Al-Khazaleh et al., 2024). Although it remains of value to explore how the phytocannabinoid constituents of cannabis flower impact neurodevelopment, future research should also work towards understanding the effects of whole cannabis flower for clinical relevance.

5. Vapour/smoke exposure method of administration

Smoking is the most common method of consumption amongst cannabis users, including cannabis users who are pregnant (Subbaraman and Kerr, 2021; Young-Wolff et al., 2024), yet only four studies were identified that utilized a cannabinoid inhalation model in this review (Lei et al., 2023; Sandini et al., 2023; Penman et al., 2024; Black et al., 2025). These studies investigated spatial and visual memory, working memory, and recognition memory, with no assessments for synaptic plasticity or associative memory. Although smoking and vaping are not identical methods of administration with the latter requiring lower temperatures than combustion, both methods involve the inhalation of the combusted or vapourized product and follow similar pharmacokinetic profiles. Most of the studies presented in this review utilized injection methods for cannabinoid administration, underscoring concerns for translatability to clinically relevant modes of cannabis use. In fact, recent preclinical work has shown that injected THC produces higher concentrations of psychoactive THC metabolites in the brain compared to inhaled THC (Baglot et al., 2021; Black et al., 2023), and these differences in pharmacokinetics may correspond with the differing magnitudes of behavioural effects observed between these two methods of administration (Moore et al., 2021).

6. Conclusion

The existing literature on perinatal cannabinoid exposure is limited by the variety of methodological factors that differ between studies and make it challenging to compare findings. While the current findings appear to converge towards perinatal cannabinoid-induced deficits in synaptic plasticity and memory, more research using clinically translatable methods of cannabinoid exposure is necessary before making any firm conclusions. Future research in this field will be critical for elucidating the neurodevelopmental impacts of cannabis use during pregnancy and guiding evidence-based public health recommendations. Furthermore, investigating the circuit- and cellular-level changes in the rodent hippocampus, using electrophysiology, will provide deeper insights into the mechanisms through which perinatal cannabinoid exposure may disrupt learning and memory.

CRediT authorship contribution statement

Rebecca Przy: Writing – original draft, Project administration, Writing – review & editing, Visualization, Methodology, Investigation, Conceptualization. **Christie Brian Ross:** Supervision, Conceptualization, Writing – review & editing, Funding acquisition. **Ben Jacoby:** Investigation, Writing – review & editing.

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Declaration of Competing Interest

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