1-1-2022

THE NEGATIVE EFFECTS OF CANNABIS ON MEMORY PROCESSES

Kiera Wingo

THE NEGATIVE EFFECTS OF CANNABIS ON MEMORY PROCESSES

by

KIERA WINGO

Presented to the Faculty of the Honors College of

The University of Texas at Arlington in Partial Fulfillment

of the Requirements

for the Degree of

HONORS BACHELOR OF SCIENCE IN PSYCHOLOGY

THE UNIVERSITY OF TEXAS AT ARLINGTON

May 2023

ACKNOWLEDGMENTS

There are many people who have supported me throughout this process, but firstly I would like to thank my research mentor Dr. Robison for his diligence and time committed to this project. I would also like to thank Dr. Rebekah Chojnacki for her advising over the honors research process and everything it entails. In addition, I would like to thank my friends and family for their continued support and understanding throughout my academic career.

November 18, 2022

ABSTRACT

THE NEGATIVE EFFECTS OF

CANNABIS ON MEMORY

PROCESSES

Kiera Wingo, B.S. Psychology

The University of Texas at Arlington, 2023

Faculty Mentor: Matthew Robison

The purpose of this review is to determine if there is a negative effect of cannabis on memory processes. Specifically, the negative effects of cannabis on short-term, working, and episodic memory were examined within acute or chronic users. Several formal databases and Google Scholar were used to find relevant literature, where key words provided search parameters and narrowed results. A final total of 29 relevant studies were used in the results. The resulting literature employed numerous study methods including N-back, Sternberg, verbal recall measures, and neuroimaging techniques. The results confirmed a negative relationship between cannabis and memory when participants were acutely intoxicated but showed either adaptation or no effect in chronic users who were not intoxicated during testing. These results confirmed the hypothesis and established a negative association between cannabis use and disruptions to normal memory processing.

TABLE OF CONTENTS

LIST OF ILLUSTRATIONS

LIST OF TABLES

CHAPTER 1

INTRODUCTION

The perception of cannabis as an illicit drug is changing rapidly. With drastic increases in recreational legality, reductions in criminality, and high ease of access, it is imperative to understand the full effect of cannabis on cognitive processes (Terry-McElrath et al., 2017). According to annual data from the Substance Abuse and Mental Health Services Administration, cannabis remains the most widely used psychoactive drug with upwards of 18% of the American population using cannabis at least once annually (Substance Abuse and Mental Health Services Administration, 2021). Widespread acceptance of cannabis as a casual drug has led to increasing concerns over its efficacy, such as being a useful substitute for opioids, or its detriments, such as prevalent use amongst adolescent populations and potential side effects (Howard et al., 2020; Wilkinson et al., 2016). While there is information and research about cannabis, there is also a lack of depth on the cognitive effects of the drug, namely its effects on memory. The founding reason for this review is then to discern if a negative relationship exists between cannabis use and memory processes.

Cannabis, extracted from the plant *Cannabis sativa*, contains over 400 chemicals of which only two are widely known. Both of those chemicals, Δ-9-tetrahydrocannabinol (THC) and cannabinoid (CBD), are psychoactive compounds acting on the brain in opposing ways (Atakan, 2012). Where THC is known for the euphoric feelings of being ‘high,’ CBD is known for its calming and medicinal benefits, and both compounds are found in most forms of ingestible cannabis (Morgan et al., 2010). Beneficial uses of cannabis include its support of anorexia, Crohn's disease, muscle spasticity, anti-epileptic effects, pain modulation, post-traumatic stress disorder (PTSD), and as an analgesic or anxiolytic agent. Many of these effects are the direct result of CBD's modulating effects on the endocannabinoid system (Carlini, 2004; Wilkinson et al., 2016; Morales & Regio, 2019). Adverse side effects of cannabis stem from THC and include symptoms such as distortions to time and spatial perception, subjective anxiogenesis, panic reactions, delusions and hallucinations, and reductions in-memory processing capabilities (Carlini, 2004). The benefit to harm ratio of cannabis is highly dependent on the balance of CBD to THC, as noted by a British study by Morgan et al., 2010, which determined that cannabis strains high in THC and low in CBD produce the most significant adverse side effects whereas strains low in THC and high in CBD produce the least severe cognitive deficits and the most medicinal benefits (Morgan et al., 2010).

As THC and CBD are not naturally occurring in humans, both act as antagonists in the body's natural endocannabinoid system. The endocannabinoid system is comprised of two G protein inhibitory receptors CB_1 and CB_2, where CB_1 is prominent throughout the central nervous system and brain regions such as the hippocampus, amygdala, prefrontal cortex, and cerebellum (Lu & Mackie, 2021; Batalla et al., 2014). CB_1 receptors specifically operate as inhibitory receptors modulating neurotransmitter release from the presynaptic neuron. The endocannabinoid system naturally produces anandamide, which acts on the CB_1 receptor (Meyer & Quenzer, 2019). CBD functions on this system differently by acting on the post-synaptic cell to increase the production of anandamide by reducing the natural enzymatic breakdown of the chemical before it can leave the cell. THC mimics the actual mechanism of action of anandamide by inhibiting CB_1 receptors on the presynaptic terminal foot (Meyer & Quenzer, 2019). The hippocampus, known for memory encoding and consolidation, is a focal point of the endocannabinoid system and acts as a key region for the mechanism of action by cannabis (Meyer & Quenzer, 2019; Adams & Martin, 1996). More specifically, THC binds to calcium channels in the terminal foot, thus blocking the releases of neurotransmitters and stopping an action potential from occurring in the post synaptic (Hampson & Deadwyler, 1998). Over time the action by THC reduces the excitability of hippocampal neurons and interferes with long-term potentiation, essentially reducing the signaling between two neurons and causing apoptosis, functionally reducing memory and learning (Hampson & Deadwyler, 1998). This process lays the basis for reductions in memory commencing cannabis use.

Disagreements exist regarding a comprehensive model of memory; however, most research agrees that two main categories of memory exist: short-term memory (STM), further broken into working or spatial memory, and long-term memory (LTM), further divided into implicit or explicit memory (Camina & Güell, 2016). STM offers the ability to retain and manipulate information for a short period of time whereas LTM provides permanent memory storage, which can be retrieved implicitly or explicitly (Camina & Güell, 2016). Implicit memory is considered unconscious information including skills and habitual behaviors, and explicit memory is information that must be retrieved consciously using an active search process or through cues (Unsworth et al., 2013). Explicit memory is subdivided into episodic memory, the recollections of personal commonplace experiences, and semantic memory, the non-context dependent knowledge about facts, definitions, and concepts (Fillit et al., 2017). Much research over cannabis and memory test for measures of episodic memory and not implicit memory. Two prominent brain regions encompass the memory system: the hippocampus and the prefrontal cortex (PFC), including the lateral and dorsal ventricle PFC. The hippocampus is associated with the processing and consolidation of episodic and semantic memory to long-term memory and process working memory (Girardeau & Zugaro, 2011). Associated with both the hippocampus and prefrontal cortex, working memory refers to spatial and verbal information that is held on to for a relatively short period of time before either being dumped or consolidated (Erikkson et al., 2015).

The central question of this investigation was to determine whether a negative relationship between cannabis and memory exists, and if there is sufficient data to back up the inquiry that cannabis use produces a negative effect on memory processes including memory consolidation and memory recall. An initial search found literature pertaining to cannabis' deficit-causing effect on memory processing, mainly the effects of THC on memory processes. The function of this review will be to evaluate the literature and confirm or refute such claims. Considering the amount of genetic or environmental factors that could influence memory functioning, the reviewed studies only show a correlational relationship, not causation. Studies employed both behavioral tasks and neuroimaging techniques (mainly fMRIs) to gauge a clear relationship and establish statistical significance between users and controls. As such, the results for this paper will focus on the hypothesis that cannabis has a negative effect on memory processes as noted by behavioral memory tasks and or brain imaging showing dysfunctional brain activity during testing. It is also hypothesized that acute cannabis use will show a greater effect on memory processing than long-term or chronic use.

CHAPTER 2

METHODOLOGY

2.1 Materials

This review examined peer-reviewed journal articles from reliable databases and scientific journals. The literature included in the study results are from the databases PsycINFO, PsycARTICLES, PubMed Central, PubMed, Psychology and Behavioral Sciences Collection, and Google Scholar. The formal databases were all accessed via the University of Texas at Arlington's library database system. To ensure all necessary items were included in this review the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) 2020 checklist was employed.

2.2 Procedure

The review was done systematically searching for relevant information based on each result section, which included short-term memory, long-term memory, episodic memory, and animal trials. When relevant, each category was further divided into acute or chronic users and human or animal trials. Searches were completed using systematic keywords including the type of memory (short-term or working or long-term or episodic or recall), the pattern of use (acute or chronic), and finally by subject species (human or mice or rat). Each combination of search terms was employed until all possible combinations had been researched, for example: "chronic cannabis *and* short-term memory *and* human trials" was followed by "acute cannabis use *and* short-term memory *and* human trials" and so forth. Studies were chosen for inclusion based on title and abstract relevancy, the relation of cannabis to memory, a placebo or control group for comparison, relevancy to the category of memory being searched, and validity of the study. Studies were excluded based on; irrelevant titles or abstracts, irrelevancy to the memory type being searched, inclusion of synthetic cannabinoids, or lack of internal or external validity in the study design. Year of publication was not added to the exclusion criteria list as many foundational studies, the key to understanding the history of research on cannabis, are fifty-plus years old. To ensure each study was still relevant, and new data did not contradict original findings, each study published over twenty years ago was counter-checked against any correlating data from the last ten years to ensure relevancy and correctness. Figure 2.1 details the total number of studies included in the review and how many were excluded based off title or abstract solely.

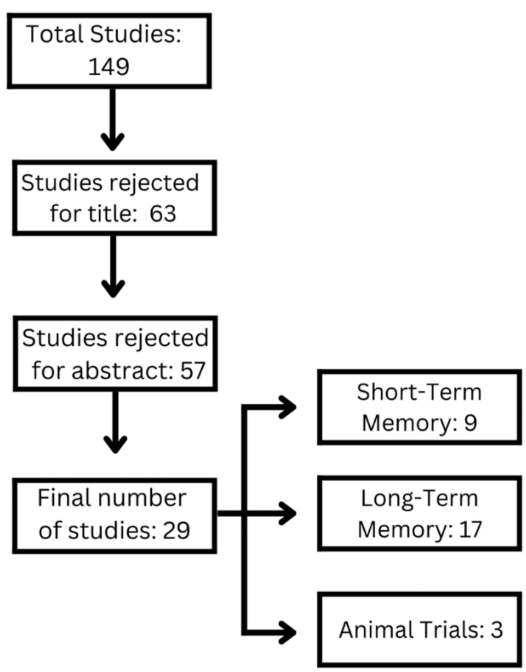

Figure 2.1: Flow chart detailing the selection and elimination process for the scholarly articles included in this review.

CHAPTER 3

RESULTS

The following studies include only the trials from each study relevant to memory and cannabis use as several studies included testing measures such as learning and attention, which are not included in the central hypothesis of this review and as such are not reported. Characteristics of the studies selected include systematic processes of testing, control or placebo groups, and trials directly focused on the connection between cannabis and memory. Table 3.1 details each of the 29 studies included in the results.

Study	Memory Type	Cannabis Use	Subjects	Test Employed	Effects Observed/Not Observed
Darley et al., 1973	ST	Acute	Human	Word Recognition Test	RTs increased significantly with THC intoxication.
Bossong et al., 2012	ST	Acute	Human	Sternberg	Significant effect of THC on WM performance, load capacity, and abnormal brain activity under intoxication.
Ilan et al., 2004	ST	Acute	Human	N-Back Test	THC intoxication increased low load RTs, lower accuracy in high load, and increased total brain activity during testing.
Tervo-Clemmens et al., 2018	ST	Chronic	Human	Sternberg	Greater cannabis use was associated with lower WM accuracy.
Jager et al., 2006	ST	Chronic	Human	Sternberg	Accuracy and RT differences between controls and users were not significant.
Cousijn et al., 2014	ST	Chronic	Human	N-Back Test	No significant effects were found between users and non-users.

Kanayama et al., 2004	ST	Chronic	Human	Posner Cueing Task	Users showed abnormal elevated brain activity during testing indicating the brain must compensate for the inhibition of THC.
Cousijn et al., 2014	ST	Chronic	Human	N-Back Test	Users had more difficulty performing the task, accuracy decreased with increasing load.
Kroon et al., 2022	ST	Chronic	Human	N-Back Test	Heavy cannabis users display less activity in WM regions during testing.
Chen & Mackie, 2020	ST	Acute	Animal	T-maze with free and forced choices	Testing after short delays (10-15 seconds) showed significantly reduced WM abilities in intoxicated mice.
Blaes et al., 2019	ST	Acute	Animal	Delayed response WM task	Accuracy was reduced significantly under intoxication.
Hampson & Deadwyler, 2000	ST	Acute	Animal	Delayed Non-Match to Sample	As THC dosage increased, accuracy decreased. Hippocampal neuronal firing was shown to be significantly delayed.
Bossong et al., 2012	LTM	Casual	Human	Image Recall Test	A significant main effect was found between drug use and memory performance.
Morgan et al., 2010	LTM	Casual	Human	Prose Recall test	Users who smoke high THC cannabis strands performed worse on recall than other users, who also performed worse than non-users.
Heishman et al., 1997	LTM	Acute	Human	Free Recall test	As cannabis use increased, word recall decreased, even when being presented the same word lists repetitively.
Hooker & Jones, 1987	LTM	Acute	Human	COWAT	Errors and omissions from the word lists were significantly higher after intoxication.
Miller & Cornett, 1978	LTM	Acute	Human	Word Recall	Differences between those dosed with THC and those not dosed were significant, there was also a significant difference between high and low dosages of THC.

Miller et al., 1976	LTM	Acute	Human	Word Recall	Cued recall was superior to uncued recall across groups, and intoxicated users performed worse than controls. Intrusions were also significantly high in the intoxicated group.
Miller et al., 1977	LTM	Acute	Human	Word Recall	The experimental group showed significantly more external intrusion errors than controls. Both groups showed if the item was not recalled during IFR, then it would not be recalled in the FR portion.
Miller et al., 1979	LTM	Acute	Human	Word Recall & Recognition	Recognition memory showed no significant main effect. However, intrusion errors were higher for the intoxicated group compared to controls.
Battisti et al., 2010	LTM	Chronic	Human	Word Recall	Intoxicated users performed worse than controls. However, participants self-reporting to longer histories of cannabis performed better than those with shorter histories.
Solowij et al., 2011	LTM	Chronic	Human	RAVLT	Cannabis users performed statistically worse than controls for recall and recognition memory tasks.
Darley et al., 1973	LTM	Acute	Human	Word Recall	Immediate recall did not show a significant effect, but delayed recall showed significant differences between users and non-users.
Darley et al., 1974	LTM	Acute	Human	Word Recall	Recall accuracy was determined as state-dependent, whether or not stimuli had been seen before or during intoxication.
Ranganathan et al., 2017	LTM	Acute	Human	RAVLT	There was a significant effect of THC on both RAVLT and recall testing measures compared to controls.

Duperrouzel et al., 2019	LTM	Casual	Human	WMS-IV	Immediate recall was more erroneous one year after baseline testing suggesting long-term effects of cannabis use.
Smith et al., 2015	LTM	Chronic	Human	WMS-III	EM performance was significantly worse than controls
Ilan et al., 2004	LTM	Acute	Human	Verbal Recall	THC decreased memory accuracy
Doss et al., 2020	LTM	Acute	Human	Mnemonic Similarity Test	THC decreased memory accuracy due to encoding errors

Table 3.1: Comprehensive table of studies included in the results. Key: EM – Episodic Memory, WM – Working memory, LTM – Long-term memory, STM – Short-term memory, COWAT – Controlled Word Association Task, RAVLT, Rey Auditory Verbal Learning Task, WSM – Weschler Memory Scale.

3.1 Short-Term Memory

Under the umbrella of short-term memory, working memory (WM) showed the most statistically significant results. Nine studies of interest were identified investigating WM procedures. More specifically, three studies used modified Sternberg tasks, four used N-back tasks, and two employed perception and recognition measures. Of the Sternberg style studies, only Bossong et al., 2012 performed tests with acutely intoxicated users while the other two studied casual users who were not intoxicated during the time of the study. All three of these studies concluded that WM functioning was impaired in cannabis users. The results of the acute intoxication study determined hyperactivity during low load tasks, a positive relationship between reaction times and load, as well as a significant difference in accuracy between controls and users (Bossong et al., 2012). Conversely, Tervo-Clemmens et al., 2018 determined reaction times and accuracy was actually higher in causal and chronic cannabis users than non-user controls. As the users from this study were not intoxicated while tested, the postulation was cannabis related deficits may stabilize over time leading to short-lived harm on WM. Negating these results, Jager et al., 2006 concluded WM may be more effected over time as cannabis use continues, determined by an increase in brain activity when load decreased. Comparisons against controls revealed non-users displayed an expected reduction in brain activity as load decreased. For the N-back studies, only one study used acute intoxication measures, while the other three completed all testing measures with non-intoxicated chronic users. The acute intoxication study found a significant difference between controls and experimental groups, likely due to the intoxication measure, which suggests acute intoxication shows the most profound effects on memory (Ilan et al., 2004). The three studies performed using non-intoxicated participants did not find any significant differences between experimental and control groups on behavioral tasks, again suggesting acute cannabis intoxication produces the most significant memory deficits (Cousijn et al., 2014; Cousijn et al., 2014; Kroon & Cousijn, 2022). Cousijn et al., 2014 also employed fMRIs in addition to the behavioral measures finding no significant change of the hippocampi network functionality over time in cannabis users. Another study by Cousijn et al., 2014 also employed fMRI techniques determining users had more difficulty performing the WM tasks as they had a substantial increase in brain activity during trials compared to controls, which suggests additional brain activity is needed to compensate for deficiencies in regions associated with WM. Confirming that conclusion, Kroon & Cousijn 2022 determined cannabis word association (e.g., 'marijuana,' 'high,' 'blunt,' 'smoke,' etc.) cued the brain to decrease activity in WM associated regions. which could lead to interference in other cognitively demanding circumstances. Lastly, two studies examined perception and recognition measures where Darley et al., 1974 reflected earlier results stating reaction times increased after THC intoxication, the postulation for such was an increase in time needed to adequately encode the information. Kanayama et al., 2004 again confirmed users must compensate with other brain regions to perform the same WM tasks as a non-user, which was determined through a short-delayed task and fMRI. Concerning WM, the final studies' results reflected the hypothesis of this review when users were acutely intoxicated while testing, but not when chronic users were tested while not intoxicated.

3.2 Long-Term Memory

Thirteen studies were found directly related to recall measures of LTM. Of these, 10 employed immediate free recall (IFR) measures, 11 used delayed free recall (DFR) measures, six included criteria for recognition memory, and nine included measures for intrusion or interference errors, 12 studies used verbal learning, encoding, and retrieval tasks, while one used imagery. The results unanimously concluded that cannabis negatively affected retrieval (recall) for delayed recall measures and almost entirely for immediate recall measures. Two studies did not find significance for IFR as one concluded no significant difference between testing conditions, IFR versus DFR, and another did not find differences between users and controls for IFR (Darley et al., 1973; Miller et al., 1979). More specifically, Miller et al., 1979 found no significant difference in recall accuracy between IFR, DFR, and final free recall measures within groups (experimental or placebo), however, they did determine a significant difference between the placebo and cannabis groups. The implication of which is cannabis users performed no different with IFR as they did with DFR and the same for the placebo group; however, when comparing the two testing groups, the cannabis group performed worse than the placebo group in each trial condition. Conversely, Darley et al., 1973, determined no significant difference between control and experimental groups in recall accuracy, even though the experimental group was acutely intoxicated at the time of testing. This result contradicts earlier findings indicating acute intoxication produces statistically significant differences in performance on memory tasks. Interestingly, two studies found rehearsal of the given stimuli, word lists in both instances, did not improve recall accuracy within the experimental groups (Heishman et al., 1997; Darley et al., 1974). An explanation for such a result may be due to state differences dependent on whether a participant was intoxicated, or not, when initially presented with the stimuli list (Darley et al., 1974). The combined results for recognition memory were varied with four studies confirming a reduction in recognition of previously given word lists, while one other found no significance reduction in recognition accuracy compared to controls (Solowij et al., 2011, Miller et al., 1979; Miller et al., 1977; Miller et al., 1976; Miller & Cornett, 1978). Darley et al. (1974), however, found that recognition measures were not state dependent, implying whether the participant was intoxicated or not, their recognition accuracy was no different.

Only four studies tested cannabis users while not intoxicated whereas the other nine studies included acute measures, several of which found significant differences between THC concentrations. Specifically, three of the acute intoxication studies indicated higher concentrations of THC produced more significant deficits in recall accuracy than participants given lower THC concentrations (Morgan et al., 2010; Heishman et al., 1997; Miller & Cornett, 1978). Miller and Cornet (1978), showed an increasing rate of memory error as THC concentration increased across three experimental groups, noting a positive relationship between the measures as confirmed by Morgan et al. (2010). Interestingly, Battisti et al. 2010 determined participants, who self-reported as having extensive cannabis use histories correctly recalled a greater number of words than participants who self-reported to having shorter histories of cannabis use.

Focusing on encoding errors specifically, two studies reported deficits related to the pretest and posttest trials between intoxicated and non-intoxicated groups (Bossong et al., 2012; Ranganathan et al., 2017). Bossong et al. 2012 specifically determined a change in normal brain activity during encoding, suggesting that alterations to cognition from cannabis intoxication produce deficits in later recall of information. Raganathan et al. 2017 confirmed this by determining, via a pre-test/post-test model, that experimental participants could not accurately recall the stimuli as the stimuli was never properly encoded. Comparisons between control and experimental groups and pre and post tests indicated items learned before intoxication were recalled adequately while items learned after intoxication could not be recalled, implying a state-dependent encoding error (Bossong et al., 2012; Ranganathan et al., 2017).

Considered a function of long-term memory, episodic memory (EM) was investigated by four of the final studies. Duperrouzel et al. 2019 employed the Logical Memory and Design Subsets from the Weschler Memory scale giving participants two short stories and later asking them to recall as much as possible showing significant decreases in LTM after a delayed recall measure was used. Smith et al. 2015also used subsets from the Weschler Memory scale but investigated the relationship between cannabis use disorder (CUD) and EM. The results confirmed EM performance was significantly worse for participants who had a history or current diagnosis of CUD. The last two studies were performed while users were acutely intoxicated administering 3mg or 15 mg of THC respectively, employing either a repetitive word task or mnemic similarity task designed to test perception (Ilan et al., 2004; Doss et al., 2020). Both studies concluded EM was negatively affected after THC intoxication as users made more errors in attempting to recall the stimuli.

3.3 Animal Trials

Three animal trial studies were found, all of which focused on WM. Chen & Mackie 2020 used C57BL/6L mice dosed with 3mg/kg of THC daily for three weeks in early life. Mice were trained utilizing a T-maze while trials occurred before and during THC intoxication, the premise was to gauge how well the mice could navigate the maze after intoxication and a short delay. The results indicated encoding, and retrieval of WM were impaired under THC intoxication with males showing significant memory deficits after a 15-second delay and females after just 10 seconds (Chen & Mackie, 2020). Both Blaes et al. 2019 and Hampson & Deadwyler 2000 utilized Long-Evans Rats given 0.3-3 mg/kg or 0.5-2 mg/ml of THC respectively, and employed variations of lever matching task, which granted a food reward if the correct level was selected. While both studies concluded THC significantly impaired the rats' ability to remember the correct lever, Hampson & Deadwyler 2000 went further to surgically implant wire electrodes on the rats' brains measuring the neuronal firing rate of the hippocampus, concluding THC intoxication not only reduces WM accuracy but lowers hippocampal firing during intoxication. Blaes et al. 2019 concluded that a significant memory reduction was only evident at the 3 mg of THC dosage, reaffirming the previously stated results determining a negative relationship between memory accuracy and THC quantity.

CHAPTER 4

DISCUSSION

The purpose of this study was to determine if a negative relationship existed between cannabis use and memory functioning and if acute intoxication was more significant than long-term or chronic use. The results reflected the hypothesis and confirmed the existence of such relationships. The literature indicated nearly every part of the memory system was adversely affected by cannabis, not just a singular function, corresponding with previous meta-analyses and literature reviews on the topic (Colizzi et al., 2016; Batalla et al., 2014; Ranganathan & D'Souza, 2006; Schoeler et al., 2016).

The short-term memory results predominantly studied WM processes and determined acute intoxication produced the most significant deficits to memory. As there were variable results concerning non-intoxicated chronic users, it is potential a tolerance to cannabis and reduction to its adverse effects could develop over time (Cousijn et al., 2014; Kanayama et al., 2004; Tervo-Clemmens et al., 2018). Conflictingly, Jager et al. 2006 concluded there may be more adverse effects of cannabis on WM over time, especially with increased use and THC concentrations. Two studies in the WM category of results employed encoding and delayed recall measures, which do not necessarily fit the criteria to be considered WM tasks (Norris, 2017; Kanayama et al., 2004, Darley et al., 1973). However, both studies explicitly stated their inquiry was STM or WM and as such were included in the WM section of this review.

As for the effort needed to mediate memory tasks, several studies determined, via fMRI, that users displayed significantly less activity in WM associated brain regions compared to controls during the memory tasks. Conversely, users displayed a substantial increase in general brain activity during recall or recognition measures, an abnormal phenomenon contrasted against the lack of extensive brain activity in non-users (Ilan et al., 2004; Cousijn et al., 2014). This is not to conclude a change in network functionality in WM due to sustained cannabis use (Cousijn et al., 2014). For instance, Hampson & Deadwyler 2000 did not find any significant effect of cannabis on hippocampal neuron networks, implying cannabis affects the hippocampus in ways other than neuronal firing. Kroon and Cousijn's study implied the reduction of brain activity, from exposure to cannabis associated words, leads to major concerns over cannabis' interference in cognitively demanding circumstances.

In the LTM section a significant effect of cannabis on memory processes was also discovered. While most studies found a significant effect of cannabis on memory, two studies did not reach significance, either due to trial type or group type. The postulation for both was an inability to retrieve stored information from LTM due to initial encoding errors Raganathan et al., 2017; Darley et al., 1973). Three recall-based studies determined encoding was the catalyst for errors in recall, intrusions, or recognition (Bossong et al., 2012; Ranganathan et al., 2017; Hooker & Jones, 1987). An interesting result from one study discovered that participants who self-reported as having a longer lifetime history use of cannabis had greater recall accuracy than participants who had a shorter histories of cannabis use (Battisti et al., 2010). The postulation of such a result is that long-term or chronic users experience stabilization of the brain over time and thus allow for better memory accuracy. Essentially the longer the brain must adapt to cannabis conditions, the better it will become at compensating to complete memory tasks adequately. The EM results showed recall, association, and recognition measures as components of the studies' testing methods, and while they differed, each showed a significant effect of cannabis on memory and a statistically significant difference between control and experimental groups (Ilan et al., 2004; Doss et al., 2020; Duperrouzel et al., 2019; Smith et al., 2015). In the animal trial category, each study confirmed the findings of human studies but allowed for a more controlled model via electrode implantation, high concentrations of THC, and repeated measures or testing. The benefit of these animal studies lends to future research allowing for more intensive testing via animal subjects.

4.1 Limitations

Limitations to this review include most prominently the lack of data. Each study reviewed utilized significantly different testing measures to garner results. As such, a meta-analysis of the data would result in sparse results with each analysis holding a very small effect size due to a lack of studies per analysis. Other limitations of this model of research include access errors with a need for institutional access to enough databases or journals to read the literature in its entirety.

4.2 Future Research

Future research should include better longitudinal studies to gauge the effect of cannabis over time as well as study the age of on set. Many of the results showed only a significant effect of cannabis on memory processes when acutely intoxicated, thus longitudinal studies would further provide a valid way to continually retest the users and determine such effects. As longitudinal designs are difficult to employ, more achievable research may focus on using brain imaging and chemical testing measures to understand the effect of cannabis on memory not only at the behavioral level but also at the cognitive and neurochemical levels. Further, while this study focused only on organic cannabis, it is losing popularity as the preferred choice of cannabis due to a rise in synthetic cannabis (Hassamal & Hassamal, 2021). Synthetic cannabis produces up to several hundred times the THC concentration and potency as organic strands. Therefore, it would be beneficial to study the form of cannabis most readily consumed recreationally.

REFERENCES

Adams, I. B., & Martin, B. R. (1996). Cannabis: Pharmacology and toxicology in animals and humans. *Addiction, 91*(11), 1585. https://doi-org.ezproxy.uta.edu/10.1111/j.1360-0443.1996.tb02264.x

Atakan Z. (2012). Cannabis, a complex plant: different compounds and different effects on individuals. *Therapeutic Advances in Psychopharmacology*, *2*(6), 241–254. https://doi.org/10.1177/2045125312457586

Batalla, A., Crippa, J. A., Busatto, G. F., Guimaraes, F. S., Zuardi, A. W., Valverde, O., Atakan, Z., McGuire, P. K., Bhattacharyya, S., & Martín-Santos, R. (2014). Neuroimaging studies of acute effects of THC and CBD in humans and animals: a systematic review. *Current Pharmaceutical Design*, 20(13), 2168–2185. https://doi.org/10.2174/13816128113199990432

Battisti, R. A., Roodenrys, S., Johnstone, S. J., Respondek, C., Hermens, D. F., & Solowij, N. (2010). Chronic use of cannabis and poor neural efficiency in verbal memory ability. *Psychopharmacology*, 209(4), 319–330. https://doi.org/10.1007/s00213-010-1800-4

Blaes, S. L., Orsini, C. A., Holik, H. M., Stubbs, T. D., Ferguson, S. N., Heshmati, S. C., Bruner, M. M., Wall, S. C., Febo, M., Bruijnzeel, A. W., Bizon, J. L., & Setlow, B. (2019). Enhancing effects of acute exposure to cannabis smoke on working memory performance. *Neurobiology of Learning and Memory*, *157*, 151–162. https://doi.org/10.1016/j.nlm.2018.12.00

Bossong, M. G., Jansma, J. M., van Hell, H. H., Jager, G., Oudman, E., Saliasi, E., Kahn, R. S., & Ramsey, N. F. (2012). Effects of δ9-tetrahydrocannabinol on human working memory function. *Biological Psychiatry, 71*(8), 693–699. https://doi.org/10.1016/j.biopsych.2012.01.00

Bossong, M. G., Jager, G., van Hell, H. H., Zuurman, L., Jansma, J. M., Mehta, M. A., van Gerven, J. M., Kahn, R. S., & Ramsey, N. F. (2012). Effects of Δ9-tetrahydrocannabinol administration on human encoding and recall memory function: a pharmacological FMRI study. *Journal of Cognitive Neuroscience*, *24*(3), 588–599. https://doi.org/10.1162/jocn_a_00156

Camina, E., & Güell, F. (2017). The neuroanatomical, neurophysiological and psychological basis of memory: current models and their origins. *Frontiers In Pharmacology, 8*(438). 10.3389/fphar.2017.00438.

Carlini, E. A. (2004). The good and bad effects of (-) trans-delta-9-tetrahydrocannabinol (Δ^9 - THC) on humans. *Toxicon, 44,* 461-467. 10.1016/j.toxicon.2004.05.009

Chen, H.-T., & Mackie, K. (2020). Adolescent Δ9-tetrahydrocannabinol exposure selectively impairs working memory but not several other mPFC-mediated behaviors. *Psychopharmacology*. https://doi.org/10.3389/fpsyt.2020.576214

Colizzi, M., McGuire, P., Pertwee, R. G., & Bhattacharyya, S. (2016). Effect of cannabis on glutamate signaling in the brain: A systematic review of human and animal evidence. *Neuroscience and Biobehavioral Reviews, 64*, 359–381. https://doi.org/10.1016/j.neubiorev.2016.03.01

Cousijn, J., Vingerhoets, W. A., Koenders, L., de Haan, L., van den Brink, W., Wiers, R. W., & Goudriaan, A. E. (2014). Relationship between working-memory network function and substance use: a 3-year longitudinal fMRI study in heavy cannabis users and controls. *Addiction Biology*, *19*(2), 282–293. https://doi.org/10.1111/adb.1211

Cousijn, J., Wiers, R. W., Ridderinkhof, K. R., van den Brink, W., Veltman, D. J., & Goudriaan, A. E. (2014). Effect of baseline cannabis use and working-memory network function on changes in cannabis use in heavy cannabis users: a prospective fMRI study. *Human Brain Mapping*, *35*(5), 2470–2482. https://doi.org/10.1002/hbm.22342

Darley, C. F., Tinklenberg, J. R., Roth, W. T., & Atkinson, R. C. (1974). The nature of storage deficits and state-dependent retrieval under marihuana. *Psychopharmacologia*, *37*(4), 139–149. https://doi.org/10.1007/BF00437420

Darley, C. F., Tinklenberg, J. R., Hollister, T. E., & Atkinson, R. C. (1973). Marihuana and retrieval from short-term memory. *Psychopharmacologia*, *29*(3), 231–238. https://doi.org/10.1007/BF0041403

Darley, C. F., Tinklenberg, J. R., Roth, W. T., Hollister, L. E., & Atkinson, R. C. (1973). Influence of marihuana on storage and retrieval processe in memory. *Memory & Cognition*, *1*(2), 196–200. https://doi.org/10.3758/BF03198094

Doss, M. K., Weafer, J., Gallo, D. A., & de Wit, H. (2020). Δ^9-Tetrahydrocannabinol during encoding impairs perceptual details yet spares context effects on episodic memory. *Biological psychiatry. Cognitive Neuroscience and Neuroimaging*, *5*(1), 110–118

Duperrouzel, J. C., Hawes, S. W., Lopez-Quintero, C., Pacheco-Colón, I., Coxe, S., Hayes, T., & Gonzalez, R. (2019). Adolescent cannabis use and its associations with decision-making and episodic memory: Preliminary results from a longitudinal study. *Neuropsychology, 33*(5), 701–710. https://doi.org/10.1037/neu0000538

Eriksson, J., Vogel, E. K., Lansner, A., Bergström, F., & Nyberg, L. (2015). Neurocognitive Architecture of Working Memory. *Neuron*, *88*(1), 33–46. https://doi.org/10.1016/j.neuron.2015.09.020.

Fillit, H. M., Rockwood, K., Young, J., & Brocklehurst, J. C. (2017). *Brocklehurst's textbook of Geriatric Medicine and Gerontology* (8th edition). Elsevier. https://www.sciencedirect.com/topics/neuroscience/explicit-memory.

Hampson, R. E., & Deadwyler, S. A. (2000). Cannabinoids reveal the necessity of hippocampal neural encoding for short-term memory in rats. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *20*(23), 8932–8942. https://doi.org/10.1523/JNEUROSCI.20-23-08932.2000

Hampson, R. E., & Deadwyler, S. A. (1998). Role of cannabinoid receptors in memory storage. *Neurobiology of Disease*, *5*(6 Pt B), 474–482. https://doi.org/10.1006/nbdi.1998.022

Hassamal, S., & Hassamal, S. (2021). The rise in synthetic cannabinoids and cathinones. *Psychiatric Times, 38*(7). https://www.psychiatrictimes.com/view/synthetic-cannabinoids-cathinone

Heishman, S. J., Arasteh, K., & Stitzer, M. L. (1997). Comparative effects of alcohol and marijuana on mood, memory, and performance. *Pharmacology, Biochemistry, and Behavior*, *58*(1), 93–101. https://doi.org/10.1016/s0091-3057(96)00456-x

Hooker, W. D., & Jones, R. T. (1987). Increased susceptibility to memory intrusions and the Stroop interference effect during acute marijuana intoxication. *Psychopharmacology*, *91*(1), 20–24. https://doi.org/10.1007/BF0069092

Ilan, A. B., Smith, M. E., & Gevins, A. (2004). Effects of marijuana on neurophysiological signals of working and episodic memory. *Psychopharmacology, 176*(2), 214–222. https://doi.org/10.1007/s00213-004-1868-9

Jager, G., Kahn, R. S., Van Den Brink, W., Van Ree, J. M., & Ramsey, N. F. (2006). Long-term effects of frequent cannabis use on working memory and attention: an fMRI study. *Psychopharmacology*, *185*(3), 358–368. https://doi.org/10.1007/s00213-005-0298-

Kanayama, G., Rogowska, J., Pope, H. G., Gruber, S. A., & Yurgelun-Todd, D. A. (2004). Spatial working memory in heavy cannabis users: a functional magnetic resonance imaging study. *Psychopharmacology*, 176(3-4), 239–247. https://doi.org/10.1007/s00213-004-1885-8

Kroon, E., Kuhns, L., & Cousijn, J. (2022). Context dependent differences in working memory related brain activity in heavy cannabis users. *Psychopharmacology*, 239(5), 1373–1385. https://doi.org/10.1007/s00213-021-05956-y

Lu, H-C., Mackie, K. (2021). Review of the endocannabinoid system. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, 6(6), 60-615. https://doi.org/10.1016/j.bpsc.2020.07.016

Meyer, J. S., & Quenzer, L. F. (2019). Psychopharmacology: Drugs, the brain, and behavior (3rd ed.). Oxford University Press.

Miller, L. L., & Cornett, T. L. (1978). Marijuana: dose effects on pulse rate, subjective estimates of intoxication, free recall and recognition memory. *Pharmacology, Biochemistry, and Behavior*, 9(5), 573–577. https://doi.org/10.1016/0091-3057(78)90205-8

Miller, L., Cornett, T., Brightwell, D., McFarland, D., Drew, W. G., & Wikler, A. (1976). Marijuanaand memory impairment: the effect of retrieval cues on free recall. *Pharmacology, Biochemistry, and Behavior*, *5*(6), 639–643. https://doi.org/10.1016/0091-3057(76)90305-1

Miller, L. L., Cornett, T. L., & Wikler, A. (1979). Marijuana: effects on pulse rate, subjective estimates of intoxication and multiple measures of memory. *Life Sciences*, *25*(15), 1325–1330. https://doi.org/10.1016/0024-3205(79)90398-9

Miller, L. L., McFarland, D., Cornett, T. L., & Brightwell, D. (1977). Marijuana and memory impairment: effect on free recall and recognition memory. *Pharmacology, Biochemistry, and Behavior*, *7*(2), 99–103. https://doi.org/10.1016/0091-3057(77)90191-

Morales, P., & Reggio, P.H. (2019). CBD a new hope?. *ACS Medicinal Chemistry Letters*, *10*(5), 694-695. 10.1021/acsmedchemlett.9b00127

Morgan, C. J., Schafer, G., Freeman, T. P., & Curran, H. V. (2010). Impact of cannabidiol on the acute memory and psychotomimetic effects of smoked cannabis: naturalistic study. *The British Journal of Psychiatry: The Journal of Mental Science*, 197(4), 285–290. https://doi.org/10.1192/bjp.bp.110.077503.

Norris D. (2017). Short-term memory and long-term memory are still different. *Psychological Bulletin*, 143(9), 992–1009. https://doi.org/10.1037/bul0000108

Ranganathan, M., & D'Souza, D. C. (2006). The acute effects of cannabinoids on memory in humans: a review. *Psychopharmacology, 188*(4), 425–444. https://doi.org/10.1007/s00213-006-0508-

Ranganathan, M., Radhakrishnan, R., Addy, P. H., Schnakenberg-Martin, A. M., Williams, A. H., Carbuto, M., Elander, J., Pittman, B., Andrew Sewell, R., Skosnik, P. D., & D'Souza, D. C. (2017). Tetrahydrocannabinol (THC) impairs encoding but not retrieval of verbal information. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, *79*(Pt B), 176–183. https://doi.org/10.1016/j.pnpbp.2017.06.019

Schoeler, T.; Kambeitz, J.; Behlke, I.; Murray, R.; Bhattacharyya, S. (2016). The effects of cannabis on memory function in users with and without a psychotic disorder: Findings from a combined meta-analysis. *Psychological Medicine, 46*, 177–188

Smith, M. J., Cobia, D. J., Reilly, J. L., Gilman, J. M., Roberts, A. G., Alpert, K. I., Wang, L., Breiter, H. C., & Csernansky, J. G. (2015). c. *Hippocampus, 25(*9), 1042–1051. https://doi.org/10.1002/hipo.22427.

Solowij, N., Jones, K. A., Rozman, M. E., Davis, S. M., Ciarrochi, J., Heaven, P. C., Lubman, D. I., & Yücel, M. (2011). Verbal learning and memory in adolescent cannabis users, alcohol users and non-users. *Psychopharmacology*, 216(1), 131–144. https://doi.org/10.1007/s00213-011-2203-x

Substance Abuse and Mental Health Services Administration. (2021). Key substance use and mental health indicators in the united states: results from the 2020 national survey on drug use and health. Center for Behavioral Health Statistics and Quality, *Substance Abuse and Mental Health Services Administration*, (HHS Publication No. PEP21-07-01-003, NSDUH Series H-56). https://www.samhsa.gov/data/

Terry-McElrath, Y. M., O'Malley, P. M., Patrick, M. E., & Miech, R. A. (2017). Risk is still relevant: Time-varying associations between perceived risk and marijuana use among US 12th grade students from 1991 to 2016. *Addictive Behaviors*, *74*, 13–19. 10.1016 https://europepmc.org/article/PMC/5535803.

Tervo-Clemmens, B., Simmonds, D., Calabro, F. J., Day, N. L., Richardson, G. A., & Luna, B. (2018). Adolescent cannabis use and brain systems supporting adult working memory encoding, maintenance, and retrieval. *NeuroImage, 169*, 496–509. https://doi.org/10.1016/j.neuroimage.2017.12.04

Unsworth, N., Brewer, G. A., & Spillers, G. J. (2013). Working memory capacity and retrieval from long-term memory: the role of controlled search. *Memory & Cognition*, *41*(2), 242–254. https://doi.org/10.3758/s13421-012-0261-x

Wilkinson, S. T., Yarnell, S., Radhakrishnan, R., Ball, S. A., & D'Souza, D. C. (2016). Marijuana Legalization: Impact on Physicians and Public Health. *Annual Review of Medicine*, *67*, 453–466. https://doi.org/10.1146/annurev-med-050214-013454

BIOGRAPHICAL INFORMATION

Kiera Wingo is currently set to receive an Honors Bachelor of Science in Psychology from the University of Texas at Arlington (UTA). She is graduating Summa Cum Laude in May 2023 before heading to graduate school to continue her interests in the field of psychology and neuroscience. Several of her research interests include psychopharmacology, biochemical bases of behavior, and mental or physical trauma and its relatedness to cognition and behavior. While at UTA Kiera has been engaged with student organizations, undergraduate research, the honors college, and has been an assistant to the university advancement team operating the university's social media channels. Outside of academics, Kiera enjoys hiking, traveling, and playing video games.