

To what extent does THC negatively affect Sleep Architecture?

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Abstract

The purpose of this dissertation is to explore the effects of **THC** (Tetrahydrocannabinol) on **SA** (Sleep Architecture) and to ascertain whether these effects are beneficial or detrimental to cognitive and physical functioning. THC appears to have a profound effect on the **circadian sleep-wake cycle**. THC seems to cause a dramatic increase in **N1**, but no change in **N2**. It seems that **REM** (Rapid Eye Movement) decreases while **WASO** (Wake After Sleep Onset) and **SOL** (Sleep Onset Latency) increase. THC influences **TST** (Total Sleep Time), but the exact effect is unclear, and a conclusion cannot be drawn for **SWS** (Slow Wave Sleep) due to conflicting data. The statistics indicate that THC can negatively affect SA because a decrease in REM reduces memory formation and consolidation, and an increase in SOL and WASO mean greater disturbance during sleep. However, the decrease in REM could benefit **PTSD** patients, and anecdotal evidence shows improvement in **insomnia** symptoms - which would contrast the data on **SC** (Sleep Continuity). So, more research is needed to reach a definite conclusion.

Introduction

Cannabis has been used as a medication for over 5000 years (Bridgeman et al, 2017), and yet we have only just begun to officially research it and its compounds. There are over 100 identified cannabinoids (NIH, 2019) in Cannabis, THC being one of them. THC is a psychoactive compound (DEA, 2020) that may give a euphoric feeling (Raypole, 2019). Used as a medication it can help reduce pain, anxiety, and seizures among other ailments, therefore many people have begun to use it to treat various conditions. So, how does this drug change the underlying mechanisms of our bodies? For example, Sleep. Does THC have an effect? If so, what changes? Is that change beneficial? Detrimental? Can these effects be used to reduce negative symptoms of sleep-related conditions?

This topic is fascinating, not only because of its ties with both ancient and modern pharmacology, but also because of its ties with our everyday lives. Sleep has a huge impact on a number of brain and bodily functions (NIH, 2022) throughout the sleep-wake cycle. The circadian sleep-wake cycle regulates how alert or sleepy you feel in a 24-hour cycle in response to changes in stimuli such as light or temperature (Blume et al, 2019. Okamoto-Mizuno and Mizuno, 2012). Therefore, it is intriguing to investigate how this medication alters something as fundamental as sleep. In this dissertation, I will be answering the burning question of 'To what extent can THC affect Sleep Architecture?'

Aim 1

What is the Endocannabinoid system?

The Endocannabinoid system (ECS) is a complex system that is involved in many important bodily processes such as - learning, memory, emotional processing, immune responses and sleep (Raypole, 2019. Grinspoon, 2021). Endocannabinoids bind to ECS receptors to send signals around the body. Endocannabinoids are produced naturally within our bodies (De Pietro, 2021) for the purpose of interacting with these receptors. Endocannabinoids are specific to the binding site of the receptors, the receptor is comparable to a lock and the Endocannabinoid is the key (Cannabis Clinic, 2022).

Phytocannabinoids are cannabinoids that come from the Cannabis plant (Thomas, 2016) and interact with ECS receptors in a similar manner to Endocannabinoids. The main ECS receptors are CB1 and CB2. CB1 regulates the quantity and activity of most neurotransmitters in our body (Grinspoon, 2021. De Pietro, 2021.) and the CB2 receptor is mainly responsible for immune responses (Cannabis Clinic, 2022).

How does THC interact with the ECS?

THC affects the body through the ECS, interacting with both CB1 and CB2 receptors. THC has a higher affinity for CB1 (Haney, 2022) - meaning it has an influence on homeostatic functions such as memory, coordination and sleep (NIH, 2020). THC can partially activate CB1 receptors because it has a similar shape to Anandamide (AEA) (Zou and Kumar, 2018), which is an endocannabinoid produced in the body to activate CB1 receptors (Scherma et al, 2019), so THC produces many similar behavioural effects to AEA when bound to a CB1 receptor. THC has a longer acting duration and higher potency than AEA (Justinova et al, 2005), so less THC is needed to produce similar effects to AEA.

What is Sleep Architecture?

Sleep Architecture (SA) is the “basic pattern of normal sleep” (Peters, 2022). Sleep has five stages, but can be divided into two main sections: Rapid Eye Movement (REM) and Not Rapid Eye Movement (NREM). REM is one stage. So, NREM accounts for every other stage of sleep: Wake, N1, N2, Slow Wave Sleep (SWS) - with N1 being the lightest sleep, N2 being light sleep and SWS being deep sleep (Patel and Araujo, 2018).

Light sleep is categorised by sleep spindles and K-complexes, which are sharp bursts of brain activity due to neuronal firing and long, recognisable delta waves respectively. Both of these phenomena are theorised to aid memory consolidation (Patel and Araujo, 2018). Especially procedural memory consolidation, which is involved in the learning and recall of skills (Stanley, 2023). The K-complexes are theorised to be involved in regulating arousal from sleep as well (Gandhi and Emmandy, 2021). But as of right now, scientists don't completely understand the purpose of light sleep (Stanley, 2023).

Deep sleep is identified by slow delta waves. In this stage, the rate of human growth hormone released into the body increases (Dijk, 2009) which suggests this stage's purpose is physical restoration, repair and growth. This stage is important for improving mood, maintaining the body and boosting the immune system (Stanley, 2023. Johnson, 2019). It is more difficult to wake up during this stage, hence the name 'deep sleep' (Purves et al, 2001).

During REM, eyes move rapidly and brain waves are desynchronised (Colten and Altevogt, 2015). Currently, scientists believe that REM's function is emotional and spatial memory formation and consolidation with short-term memories being transferred into long-term ones (Greer, 2024). REM contributes to memory processes by "pruning and maintaining new synapses" (Wei et al, 2017).

To summarise - light sleep is believed to be involved in procedural memory consolidation; deep sleep is involved in physical restoration; and REM sleep is involved in emotional and spatial memory processes.

'Physiology, Sleep Stages' by Patel and Araujo (2018) states that adults should be in NREM for 75% of TST, and REM for 25%. Ideally, adults spend <5% of TST falling asleep (N1), 45% of TST in N2 sleep and 25% in SWS. The average length of a cycle should be 90 minutes. Similarly, 'Sleep Physiology' by Colten and Altevogt (2015) states that 75-80% of TST should be spent in NREM and 20-25% in REM. N1 should last for 2-5%, N2 for 45-55%, and SWS for 13-23% of total sleep time. This article states the average cycle should last for 90-120 minutes. There are many studies which give similar figures, therefore these statistics may be considered reliable. For this project I will mostly be referencing Colton and Altevogt's data because it provides an acceptable range for normal SA, so data that falls outside of these ranges can be considered abnormal.

What is the Endocannabinoid system's role in sleep ?

The CB1 receptor is partially responsible for regulating the circadian sleep-wake cycle, and so it plays a role in sleep. In a study conducted by Vincent Santucci et al (1996), using SR141716A (a CB1 inhibitor) to inhibit the CB1 receptor increased the total time spent awake, and decreased SWS and REM. Similarly, a study conducted by Murillo-Rodríguez et al (1998) found that the administration of AEA, a CB1 agonist, greatly increases SWS and REM, but decreases overall wakefulness (Murillo-Rodríguez, 2020). This gives confidence that the CB1 receptor contributes to sleep regulation - specifically, SWS and REM regulation. SWS and REM are widely considered the two most important stages due to their restorative and consolidative effects.

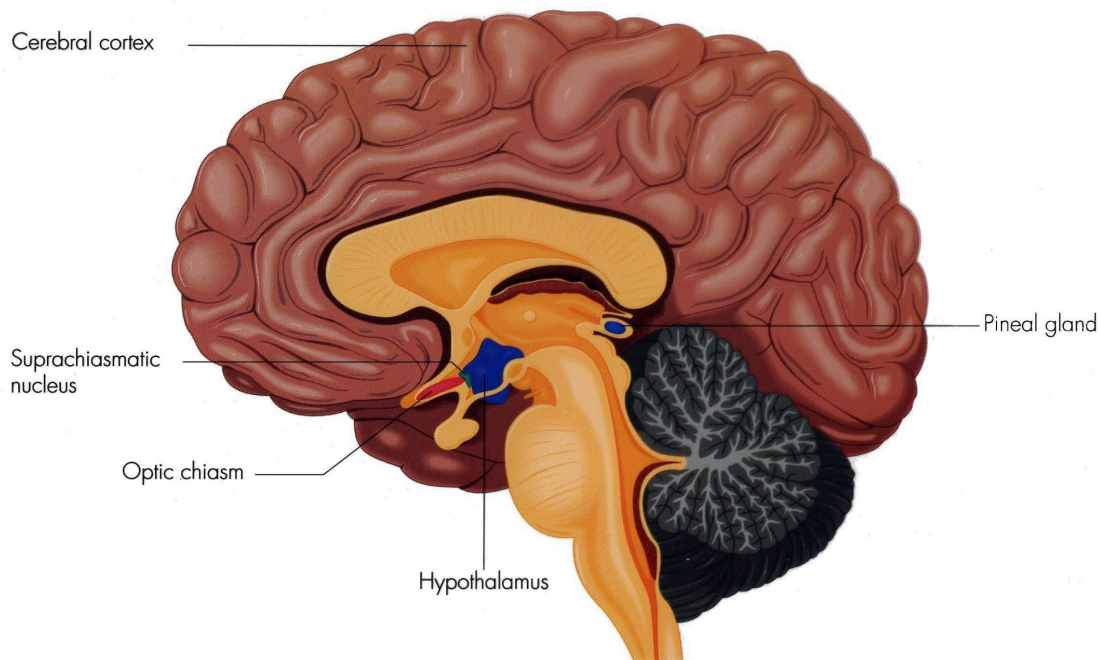


Image 1: Labelled diagram of the brain showing the SCN and Hypothalamus (Wikipedia contributors, 2019).

The SupraChiasmatic Nucleus (SCN), located in the Hypothalamus, is a central pacemaker of the Circadian sleep-wake cycle (Ma and Morrison, 2020). The CB1 receptor is abundant in the SCN and many other areas of the brain relating to sleep (Murillo-Rodríguez, 2008). AEA levels are at their lowest right before sleep and increase through the night until they are at their highest upon waking up the next day (Kesner and Lovinger, 2020). Suggesting that AEA's effect on the CB1 receptor in sleep is involved in regulating the timings during sleep. Murillo Rodríguez et al (2003) discovered that increasing AEA levels also increases “basal forebrain adenosine”, which is said to be an indicator of sleep-wake transitions (Blanco-Centurion et al, 2006).

Therefore, it is suspected that CB1 receptors and its agonists could influence or partially control the homeostatic regulation of circadian rhythm timings. This suggests that THC, like AEA, should have an effect on the timings of transitions between sleep stages, and thus SA.

Aim 2

How does THC affect total sleep time (TST)?

A normal adult's TST should be at least 7 hours - which is 420 minutes (Suni, 2021). A study conducted by UCL (2022) found that 30-50 year olds have an average TST of 7.01 hours (~420 minutes). A systematic review conducted in the UK, US and the Netherlands reported a similar figure of 7.1 hours (~426 minutes) (Kocevska et al, 2020). Both studies have similar results - therefore it can be determined that the average TST of an adult is around 420 minutes.

One study found that 35% of adults in the US get <7 hours a night (CDC, 2022), another study got a similar figure of 1/3 adults getting <7 hours of sleep (Liu et al, 2016). In Kocevskaja et al's review - 25.8% get an average TST of <7 hours. These statistics show that around 30% of adults get less than 420 minutes of sleep a night.

In a study conducted by Pacek et al (2017) ~78% of participants attained <420 minutes of sleep, ~20% had between 420-540 minutes and ~2% slept for >540 minutes. The average TST was 340 minutes. In this study, THC is not taken in isolation - instead Cannabis as a whole was taken - this means other cannabinoids were present. This could affect the results, but currently it cannot be said whether another cannabinoid has an effect on SA due to a lack of research, however, THC is a part of Cannabis and so will still have an effect on SA. This suggests that THC decreases TST. 62.2% of the participants either had insomnia or were on the sub-threshold of insomnia - this could impact the validity of the study.

Duration of sleep was said to 'worsen' after intake of THC according to a PSQI study. A normal PSQI sleep duration should be ~0.44 (Buysse et al, 1988), whereas in this study - the average score was 2.45 (Winiger et al, 2021). This implies they had a lower TST. This supports the conclusion of the previous study that THC decreases TST. But since TST was not explicitly stated, this study is weaker than other studies.

In Vandrey et al's study (2011), the average TST was 451 minutes. This indicates that THC may increase TST. This study is more valid than the previous studies because none of the participants had sleep-related conditions that could skew the results. But, it isn't completely valid due to different quantities of Cannabis used and other drug intake. In a BMJ article, it was found that Cannabis use is associated with TST extremes (BMJ, 2021), which is defined as <360 minutes and >540 minutes. This could explain how different studies have reached different conclusions on the effect of Cannabis on TST.

Overall, THC's effect on TST is critically under-researched and more studies are needed to reach a conclusion, but with the current information available - we can infer that THC has an effect on TST.

How does THC affect sleep continuity?

Sleep Continuity (SC) is important because an irregular or disrupted SC can negatively affect SA. SC is “the amount and distribution of sleep versus wakefulness in a given sleep period” (Mezick, 2013). In more quantitative terms, SC is a combination of Sleep Onset Latency (SOL) and Wake After Sleep Onset (WASO).

The adult's average SOL should fall between 5 and 30 minutes (Charles, 1993). Zolovska (2013), similarly states that SOL is usually less than 20 minutes. Considering the reproducibility of this statistic, SOL should be <30 minutes (Charles, 1993). The average WASO of adults was found to be 36.9 minutes (Quante, 2018), this is 8.8% of the average TST of 420 minutes and WASO should be no more than 10% of TST.

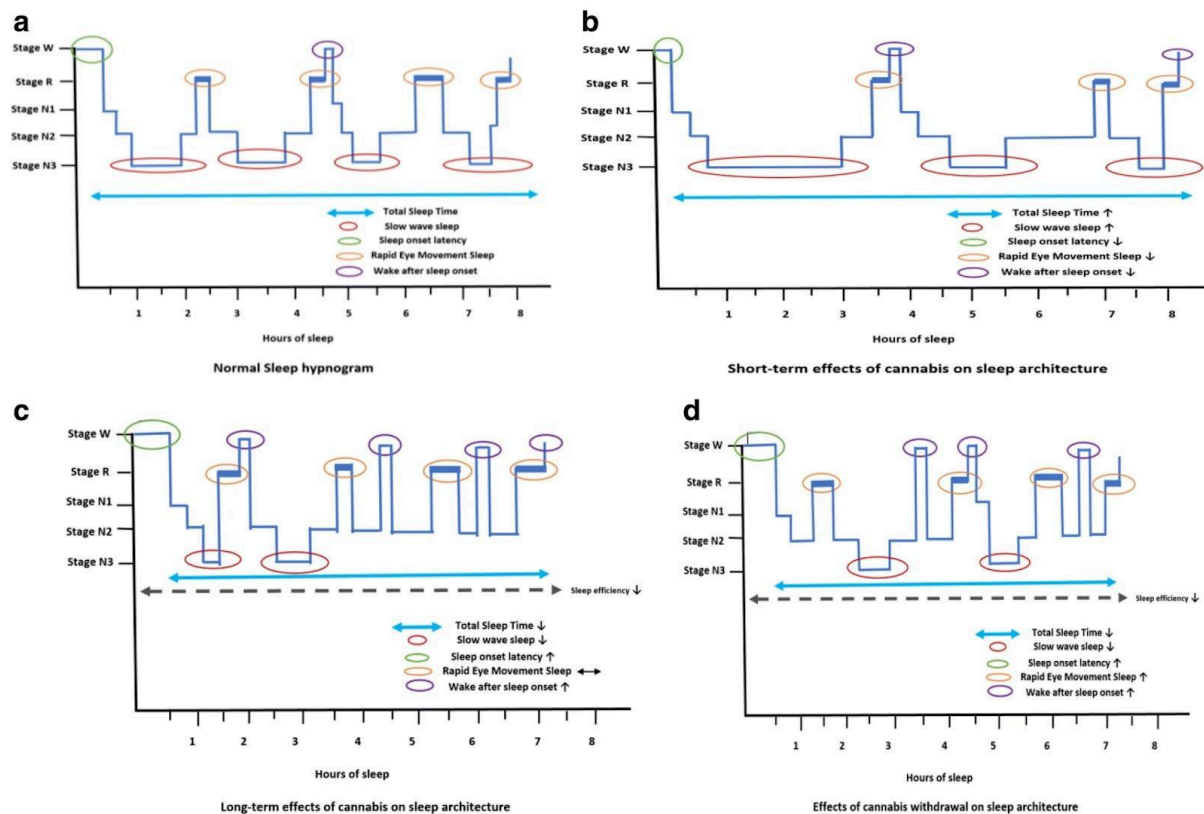
In a study conducted by Bolla et al (2008), the average SOL of a control group was 5 minutes and 22 minutes for the Cannabis group. Despite the 22 minutes being within the acceptable range - it is an increase when compared to the control group which leads us to believe that THC could increase SOL. There was no significant WASO difference between groups. Both groups' WASO was within 10% of TST.

Vandrey et al (2011) found that the SOL of participants after Cannabis intake was 8 minutes which is within the healthy range. The average TST was 419 minutes and the average WASO was 45 minutes, this is 11% of TST and therefore above the acceptable range. This indicates that THC intake increases WASO. Increases in WASO can lead to a greater appetite and energy need. It can also decrease tolerance to stress which can lead to a worse mood (Medic et al, 2017). Cognitive and emotional functioning are also impacted by a disturbed night of sleep (Van Someren, 2015). From this information, an increase in WASO seems to have similar negative effects to decreasing all sleep stages.

Pacek et al (2017) found that Cannabis increases SOL with the average being 31.1 minutes with 31% of participants having a SOL >30 minutes. An increase of SOL can be considered negative. An increase in WASO is also seen, with it being on average 54.7 minutes with 51.7% of participants having WASO >30 minutes. Considering the average TST was around 340 minutes, this is above 10%. This study suggests that THC increases both SOL and WASO.

Both Vandrey et al's and Pacek et al's studies conclude that THC intake increases WASO, whereas Bolla et al's data shows no change in WASO. Similarly to WASO, SOL also seems to increase with THC intake because both Bolla et al and Pacek et al recorded an increase in SOL, although Vandrey et al found that there is no change. So, with the current information - it seems that THC increases both SOL and WASO. However, the difference in findings may be explained by Pacek et al's participants having pre-existing sleep-related conditions, and that each study is measuring a slightly different variable - so they are not completely comparable. Replication studies are needed to confirm the effect of THC on SC.

What are the effects of THC withdrawal on SA?



Hypnograms of SA under different conditions (Kaul et al, 2021)

Around 76% of adults report disturbed sleep during Cannabis withdrawal (Budney, 2004), which could lead to higher rates of relapse. As seen on the hypnograms above, SWS is decreased compared to normal SA but similar to long term THC use, these decreases mean less rejuvenation and a weaker immune system. REM seems to be similar, if not slightly decreased (Kaul et al, 2021).

On the second night of withdrawal in Cohen-Zion et al's study (2009) - N1 and SWS had no significant difference when compared to the control group. REM of the Cannabis-users was 3.6% higher than the control group, this could be due to REM rebound. REM rebound is where REM% is increased after a period of REM suppression (Feriante and Singh, 2020), which can be induced by alcohol or THC intake (Roehrs and Roth, 2001. Summer and Rehman, 2021). This is supported by anecdotal reports of vivid or strange dreams (Summer and Rehman, 2021) during withdrawal. REM rebound suggests that REM decreases with the intake of THC because REM increases after cessation. REM rebound could be due to either THC or alcohol withdrawal - more research is needed to determine if THC does cause REM rebound. An increase in REM would be considered positive in terms of consolidation, but it could have negative effects in terms of nightmares due to the vivid dreams (Owens, 2020).

Since both the control and values are within the acceptable range, functioning would not change drastically. N2 for the control group is 54.6% and 51.6% for the withdrawal group - this could infer that THC withdrawal causes N2 to decrease.

Mean PSG Outcomes By Study Condition.

	Placebo		Extended-Release Zolpidem	
	Cannabis Use	Cannabis Abstinence	Cannabis Use	Cannabis Abstinence
Total Sleep Time (min)	451 (10)	419 (9.6) *	464 (10)	419 (10) *
Sleep Efficiency	.89 (.01)	.85 (.01) *	.91 (.01)	.88 (.01) *
Sleep Latency (min)	8 (1)	29 (5) *	8 (1)	22 (3) *
REM Latency (min)	103 (8)	71 (5) *	90 (6)	83 (5)
Wake After Sleep Onset (min)	45 (6)	44 (6)	40 (6)	36 (5)
% Stage 1 Sleep	10 (1)	8 (1) *	9 (1)	8 (1)
% Stage 2 Sleep	50 (1)	46 (1) * [‡]	49 (1)	51 (1) [‡]
% Stage 3/4 Sleep	15 (1)	16 (1)	16 (1)	15 (1)
% REM Sleep	25 (1)	30 (1) * [‡]	26 (1)	26 (1) [‡]

*Denotes a significant abstinence effect

[‡]Denotes a significant difference between abstinence conditions

Table 1 - Effect of THC on SA under the effect of Zolpidem compared to a placebo (Vandrey et al, 2011).

As shown in table 1, Cannabis withdrawal has seemingly no effect on SWS, and a minimal effect on N1. N2 has a 4% decrease when compared to Cannabis use and 46% is below the acceptable range - this could negatively influence procedural memory consolidation. REM increases to 30%, which is above the healthy range. This may be positive in terms of increased memory consolidation, but it could mean decreased time spent in other stages. This increase in REM suggests REM rebound. In this study, SWS seems to stay the same in both the withdrawal and Cannabis use placebo groups (Vandrey et al, 2011).

Kaul et al's study shows a clear decrease in SWS compared to a normal SA, and Cohen-Zion et al's study the SWS% was similar to that of a non-user. So, all three studies show a different trend regarding SWS and withdrawal. Therefore, a conclusion cannot be reached about the effect of withdrawal on SWS - replication studies are needed.

Overall, the effects of withdrawal on SA is difficult to determine because cannabinoids can remain in the system for up to 30 days after cessation (Wagener, 2019). The current data suggests that REM increases during withdrawal - this could indicate the occurrence of REM rebound, which indicates that the intake of THC suppresses REM. An increase in REM may be considered positive due to increased memory formation and consolidation, but negative in terms of increased dream vividity.

N2 appears to decrease during Cannabis withdrawal - this would be negative due to decreased procedural memory consolidation. Cohen-Zion et al's and Vandrey et al's studies show contradictory results regarding N1, with the former claiming N1 is similar to the SA of a

healthy, non-Cannabis user and the latter stating that N1 is similar to the N1 of a Cannabis user.

The effect of THC withdrawal on SWS cannot be concluded either due to each study showing contrasting results as well. More research is needed to determine the effect of withdrawal on SWS and N1.

What effect does THC have on the sleep stages?

THC is similar to AEA - as explored earlier. The administration of AEA in a human hippocampus significantly increases time spent in SWS and REM (Kesner and Lovinger, 2020). Similar results have been noted in studies of rats and AEA (Low et al, 2023), which lends confidence to these findings. Since THC has a similar effect to AEA, the expected result is that THC will increase SWS and possibly REM.

Vandrey et al (2011) administered Cannabis and a placebo of zolpidem to the study's participants. On average, they spent 10% of TST in N1, 50% in N2, 15% in SWS and 25% in REM. These statistics are similar to the expected SA of someone not taking THC. The main difference is that N1% is abnormally high. REM is at the higher end of the expected range and SWS is at the lower end of the range - but they are still within the healthy ranges. From this evidence, it cannot be concluded that THC affects SWS, N2 or REM, but it can be concluded that THC is associated with an increase in N1.

Pacek et al (2017) also found SA was similar to that expected of a non-THC user - with N1 being 6.6%, N2 55.1%, SWS 20.6%, REM 17.7%. N1 is, again, outside of the normal range, which gives us confidence that Cannabis does increase N1. The N2 statistic is 5.1% higher than the previous study and 0.1% outside of the normal range - but this 0.1% is negligible. The SWS falls within the normal range, which infers THC has no remarkable effect on SWS. REM is below the healthy range by 2.3%, which could indicate that THC decreases REM.

In Bolla et al's study in 2008, 14/17 of the participants had taken THC within a day of the experiment. Therefore, the readings taken on the first night are not considered withdrawal due to many exogenous cannabinoids still circulating the system. But, any readings taken after night 1 would be classified as withdrawal. For the Cannabis-using group, SWS was 7% and REM was 21%. Compared to the control group which had an average SWS of 15% and a REM of 21%. There is a significant decrease in SWS compared to the control group, and 7% is outside of the acceptable range for SWS. So, we can infer that THC decreases SWS. REM% was the same for both groups and 21% is within the acceptable REM range. This leads us to conclude that THC has no significant effect on REM.

In 2004, Nicholson et al conducted a study with both a placebo and THC group. Both groups had similar N2% and were within the healthy range. But N1% was abnormally high in both placebo and THC at around 10% for both. Therefore, the effect of THC on N1 is unclear in this study. SWS was 17% in the placebo group and 19% in the THC group. Both groups are within the normal SWS range, but the values do suggest that THC could increase SWS.

REM for the Cannabis group (16.6%) was 3% lower than the placebo group (19.6%). This infers that THC could decrease REM, which is supported by the observation of REM rebound during Cannabis withdrawal.

From the current data, THC appears to have a profound effect on N1, with the available data indicating an increase when compared to normal SA. N1 is critically under-researched, so we cannot say that an increase in N1 is positive or negative. Currently, the only known negative could be less time spent in other stages. As stated earlier, there seemed to be no remarkable difference between a non-user's N2% and a user's N2%. Since there seems to be no change, this means there should be no change in procedural memory recall or arousals during the night.

Unlike N2, SWS% is inconsistent between studies. When compared to AEA, SWS should increase, this conclusion is supported by Nicholson et al's study. If this is correct - it would mean more time would be spent in reparation and rejuvenation. It could also mean a decrease in WASO because it is harder to wake up during SWS. This study is the most valid, but no other study here supports this conclusion. Bolla et al's study implies that THC decreases SWS. This would have a negative impact on the body because it would mean a lowered immune response and less energy restoration. In the long term, it could mean longer recovery times and possibly stunted growth. In Pacek et al's and Vandrey et al's study, the SWS was within range, which suggests that THC has no effect on SWS%. We cannot confidently determine THC's effect SWS with the current data. More studies are needed with THC administered in isolation to understand THC's effect on SWS.

The AEA hypothesis predicts that REM% should increase. But no research currently supports this - therefore THC probably does not increase REM%. Nicholson et al's and Pacek et al's studies show a clear decrease in REM% with values that fall outside of the acceptable range. Since two studies show the same trend - this increases the reliability of the conclusion, but Pacek et al's study includes treatment-seeking participants - which means that pre-existing conditions could affect the validity. If REM were to decrease, it could mean worsened memory formation and consolidation (Summer, 2021). Bolla et al's and Vandrey et al's studies showed that REM% falls within the acceptable range. This data also seems reliable and lends confidence to this conclusion. No significant change in REM would mean no significant positive or negative effect. With the available research, a conclusion cannot be reached regarding THC's effect on REM - but considering REM rebound during withdrawal, the conclusion that THC decreases REM seems slightly more plausible.

From the information available, it can be inferred that THC increases N1 - but it cannot be ascertained whether this is positive or negative due to lack of research on N1. THC seems to have no effect on N2. A definite conclusion regarding REM cannot be reached, but considering REM rebound - it seems that THC could decrease REM. This would be negative for most people because it means less memory consolidation. THC's effect on SWS cannot be determined due to conflicting data.

Aim 3

Is THC's effect on SA detrimental to a healthy person?

From a TST standpoint, an increase could be beneficial or detrimental. It would mean more time spent in each stage - which would increase consolidation and rejuvenation. But an extreme increase in TST could increase the risk of health issues such as - CHD, Type 2 Diabetes and Depression (Johns Hopkins Medicine, 2019). Whereas, a decrease in TST would mean decrease time in all stages. An extreme lack of sleep can cause similar health issues to an excessive amount of sleep (NIH, 2022). Therefore, we can conclude that THC may have a detrimental effect on SA.

In terms of SC, THC has an overall negative effect. Both WASO and SOL seem to increase. An increase in WASO means more disrupted sleep - this leads to a decrease in each sleep stage, and an increased SOL could mean less TST.

THC's effect on SWS and REM cannot be confidently determined. But it seems as though THC could decrease REM - this would be negative. This means decreased consolidation and worsened retention. For SWS, a decrease would be negative because of a reduced immune response and less restoration. An increase would be positive because it means waking up feeling more refreshed. THC appears to have a possibly detrimental effect on rejuvenation and cognitive abilities if both SWS and REM decreases. If SWS increases, THC could have a positive effect on rejuvenation. An increased N1 can have a negative effect in terms of decreased time in other stages. N2 remains unchanged - meaning no particular detrimental or beneficial effect.

Additionally, withdrawal effects would be detrimental as well. It is important to consider withdrawal when taking THC because unless someone uses Cannabis indefinitely - they will go through withdrawal at some point. Compared to a normal SA, an increased REM would be considered positive. Whereas, a decrease in N2 would be detrimental. There is not enough data to comment on SWS or N1.

Overall, THC could be detrimental to functioning and health for a normal person in regards to SA. But more studies with less external variables that can affect results are needed to reach a confident conclusion.

Is THC's effect beneficial or detrimental to SA of people with different conditions?

For a person with PTSD, THC could be used as a possible treatment because a decrease in REM would be positive. Numerous studies have shown that REM increases in PTSD patients, so taking THC could decrease REM% to be within an acceptable range (Pace-Schott et al, 2015). This would be significant because REM is associated with vivid dreams. (Dal Sacco, 2022). A symptom of PTSD is nightmares and flashbacks, these flashbacks are worse during REM, therefore a decrease in REM would mean a decrease in nightmare frequency and intensity. There is evidence for it decreasing daytime flashbacks as well (Fraser, 2009). Although, during withdrawal nightmares can return - therefore a continuous treatment of THC may be needed.

Additionally, a tolerance to THC could be developed - meaning the dose of THC would need to increase over time. This could be an issue for patients in the long term - so a treatment of THC alongside therapy could be beneficial. Overall, THC is an effective medication for

controlling sleep-related PTSD symptoms - and for most PTSD patients the benefits of THC intake outweigh the negatives.

In terms of data - THC seems detrimental to those with insomnia due to the increased WASO, but anecdotal evidence opposes this. THC is often used as a treatment for insomnia (Walsh et al, 2021). The symptom relief from the use of THC in comparison to no THC is considered statistically significant with a -4.5 symptom relief rating in the range of 0 to -10 (Vigil et al, 2018). This study has 409 participants and shows that THC is used as an effective sleep-aid despite what the SA data suggests.

Conclusion

A clear conclusion was difficult to reach due to conflicting data and the low validity levels of studies. Research on THC and SA is in its early phases - so the majority of studies aren't measuring the exact same variable. For example, some studies administer a specific amount and concentration of THC themselves and observe the results in a controlled setting - such as Nicholson et al, 2004. Despite this study being one of the oldest used in this dissertation, it is one of the most valid because in this study an exact amount of THC serum was administered to patients 30 minutes before they went to sleep and data was collected after an adaptation night to help the participants adjust to the new environment. This study was double-blind with a placebo group for comparison of SA.

But, some studies are less valid - such as Pacek et al's study in 2017. Despite this study being one of the most recent, it is one of the least valid studies I have used because the participants were unattended during the study and were "treatment seekers" with pre-existing sleep-related conditions. Additionally, they were expected to supply and use their own Cannabis - so the dose and concentration of THC wasn't controlled. So, it is not certain that the effects seen were due to THC - but considering our current knowledge on Cannabinoids, it can be assumed THC had an influence on the results recorded. External factors such as those listed above could skew the results. Overall, the validity of this study is low. If this area was well researched, this study would be dismissed - but since there are only 17 trials with the keywords 'Cannabis and SA', and 3 trials with the keywords 'THC and SA', this is one of the best studies available currently.

THC intake seems to increase N1 but doesn't seem to have an effect on N2. For SWS and TST, a conclusion cannot be reached due to the different data presented in the studies. In the case of REM, from SA statistics alone a conclusion cannot be reached - but considering REM rebound during withdrawal, it seems as though THC could decrease REM. From data alone, THC seems to have a negative effect on SA. But, an insufficient amount of research has been conducted to understand the effects of an N1 increase, so we do not know if this is negative apart from the possible decrease of time spent in other stages. No change in N2 is neither positive nor negative.

For SWS, a decrease would be negative because of reduced immune response and lower energy levels and an increase would be positive for the opposite reasons. A decrease in REM would be considered negative for most people due to decreased memory consolidation and formation, but for people with PTSD this would be beneficial because it would mean reduced nightmares and less daytime flashbacks. Whereas, for people with insomnia the clinical data contradicts the anecdotal data, so a conclusion on whether THC is beneficial or detrimental cannot be reached.

The SA data indicates that SOL and WASO increase - which would be considered negative because this could decrease TST and lead to disturbed sleep. Unlike the clinical data, anecdotal data suggests that THC helps improve symptoms of insomnia in patients. This disparity between statistical and anecdotal evidence shows that more research is needed to deduce the effect of THC on SA.

To further this field of research, more studies need to be conducted in controlled environments with THC administered in isolation - this would increase confidence in the results and lead to valid conclusions. Despite there being more resources online for SA than THC, there are still many things we do not understand about SA - such as the purpose of N1. So, more studies need to be conducted on both THC's effect on SA and the individual areas of Sleep and THC as well. To truly conclude the extent to which THC can negatively affect sleep architecture, more research is needed.

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Appendix

Glossary

SA - Sleep Architecture

MJ - Marijuana

REM - Rapid Eye Movement

NREM - Not Rapid Eye Movement

SWS - Slow Wave Sleep (deep sleep)

SOL - Sleep Onset Latency

SE - Sleep Efficiency

SC - Sleep continuity

WASO - Wake After Sleep Onset

TST - Total Sleep Time

TIB - Time In Bed

EEG - Electroencephalograph (sleep graph)

PSQI - Pittsburgh Sleep Quality Index (subjective measure of sleep quality)

THC - Tetrahydrocannabinol

ECS - Endocannabinoid System

AEA - Anandamide

CB1 - Cannabinoid Receptor 1

CB2 - Cannabinoid Receptor 2

SCN - Suprachiasmatic nucleus

CHD - Coronary Heart Disease

Memory processes - formation, consolidation and retrieval of memories (Harvard University, 2023)

Agonist - A substance that activates a receptor

