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Campbell, Laura M

Tang, Bin

Watson, C Wei-Ming

et al.

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Cannabis use is associated with greater total sleep time in middle-aged and older adults with and without HIV: A preliminary report utilizing digital health technologies

Laura M. Campbell[1,2], **Bin Tang**[2], **C. Wei-Ming Watson**[1,2], **Michael Higgins**[3], **Mariana Cherner**[2], **Brook L. Henry**[2], **Raeanne C. Moore**[2]

[1]SDSU/UC San Diego Joint Doctoral Program in Clinical Psychology, San Diego, CA

[2]Department of Psychiatry, University of California San Diego, San Diego, CA

[3]Exercise and Physical Activity Resource Center, University of California, San Diego

Abstract

Current literature on the effect of cannabis use on sleep quality is mixed, and few studies have used objectively-measured sleep measures or real-time sampling of cannabis use to examine this relationship. The prevalence of cannabis use among older adults and persons living with HIV has increased in recent years, and poor sleep quality is elevated in these populations as well. However, research examining cannabis-sleep relationships in these populations is lacking. Thus, we aimed to examine the relationship between daily cannabis use and subsequent objectively-measured sleep quality in middle-aged and older adults with and without HIV. In this pilot study, seventeen (11 HIV+, 6 HIV−) adults aged 50–70 who consumed cannabis completed four daily smartphone-based surveys for 14 days, in which they reported their cannabis use (yes/no) since the last survey. Participants also wore actigraphy watches during the 14-day period to objectively assess sleep quality (i.e., efficiency, total sleep time, and sleep fragmentation). In linear mixed-effects models, cannabis use was significantly associated with greater subsequent total sleep time (β=0.56; p=0.046). Cannabis use was not related to a change in sleep efficiency (β=1.50; p=0.46) nor sleep fragmentation (β=0.846, p=0.756) on days with cannabis use versus days without cannabis use. These preliminary results indicate cannabis use may have a positive effect on sleep duration in middle-aged and older adults. However, future studies with larger sample sizes that assess cannabis use in more detail (e.g., route of administration, dose, reason for use) are needed to further understand this relationship.

Keywords

marijuana; sleep health; HIV/AIDS; aging; ambulatory assessment

Correspondence: Raeanne C. Moore, Ph.D., Address: HIV Neurobehavioral Research Program, 220 Dickinson Street, Suite B (8231), San Diego, CA 92103, Phone: 619-543-5378 / Fax: 619-543-1235 / r6moore@health.ucsd.edu.

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The authors report no personal or financial conflicts of interest.

Introduction

As state-based legalization of medical and recreational cannabis has expanded in the U.S., cannabis use has increased in middle-aged and older adults as well as people living with HIV (PWH; Han et al., 2017; Pacek, Towe, Hobkirk, Nash, & Goodwin, 2018). The estimated prevalence of sleep disorders is elevated in both PWH (30-73%; Allavena et al., 2016; Reid & Dwyer, 2005) and older adults (14-38%; Morin, LeBlanc, Daley, Gregoire, & Merette, 2006; Ohayon, 2002) compared to the general population (10%; Ram, Seirawan, Kumar, & Clark, 2010). Common sleep disturbances in PWH include difficulty falling asleep, short sleep duration, and overall insomnia, which have been linked to chronic daytime fatigue, declines in physical and social functioning, greater use of healthcare services, and reductions in health-related quality of life (Reid & Dwyer, 2005).

Literature on the relationship between cannabis use and sleep quality is mixed, with both positive and negative sleep outcomes tied to cannabis use. The variability in findings is likely due to the heterogeneous nature of whole plant cannabis and contextual factors of use such as dose, frequency of use, composition of cannabis product, and motivation/s for use (Babson, Sottile, & Morabito, 2017). There is some evidence that chronic cannabis use is tied to worse sleep outcomes with habituation to sleep-inducing and sleep-enhancing properties leading to increased and problematic cannabis use and cannabis withdrawal-related issues such as trouble falling asleep, waking up during the night, and/or experiencing strange dreams (Gates, Albertella, & Copeland, 2016). Studies show that short-term, low-dose delta-9 tetrahydrocannabinol (THC) cannabis products have a mild sedative effect, decreasing sleep onset latency and rapid-eye movement (REM) sleep and increasing total sleep time and slow wave sleep, while high-doses of THC decrease REM and slow wave sleep, increase sleep onset latency, and have hallucinatory actions (Garcia & Salloum, 2015). Preliminary research on non-intoxicating cannabis compound cannabidiol (CBD) suggests it may have potential therapeutic benefits at medium and high doses for insomnia and REM sleep behavior disorder (Babson et al., 2017).

To-date, the majority of cannabis-sleep studies have assessed sleep quality and/or cannabis use with self-report questionnaires that rely on retrospective recall, which is vulnerable to inaccuracy (Lauderdale, Knutson, Yan, Liu, & Rathouz, 2008; Althubaiti, 2016). Additionally, many studies that have examined the relationship between cannabis and sleep administer cannabis in a lab setting or in clinical trials (Babson, Sottile, & Morabito, 2017), which may lack generalizability to real-world contexts. Studies utilizing digital health technologies in people's everyday lives are needed to investigate these complex relationships. Furthermore, investigations of cannabis use on sleep behaviors are lacking in the context of HIV disease and older age, two populations at high risk for sleep disturbances. Therefore, this ecological momentary assessment (EMA) and actigraphy study aimed to examine the relationship between real-world self-reported cannabis use and subsequent objective sleep quality in middle-aged and older adults with and without HIV. Due to the mixed findings in the literature (as discussed above), as well as the limited literature examining cannabis use and sleep in middle-aged and older adults, we did not have *a priori* hypotheses and therefore took a more exploratory approach.

Methods

Participants

This study examines a subset of participants (11 PWH; 6 HIV-) who endorsed cannabis use at least once over a 14-day period from a larger-scale ongoing EMA study at the HIV Neurobehavioral Research Program (HNRP) at the University of California, San Diego (UCSD) between 2016 and 2019. Participants were recruited from other studies at the HNRP and from the community. Study inclusion and exclusion criteria was kept to a minimum to increase generalizability. All participants were age 50 or older, able to provide written informed consent, and fluent in English. Exclusion criteria included: neurological disease or disorder (e.g., stroke), serious mental illness (e.g., schizophrenia), and history of severe learning disorder. Participants that had a positive alcohol breathalyzer or urine toxicology screening (excluding cannabis) at their laboratory baseline visit were rescheduled. All procedures were approved by UCSD's Institutional Review Board, and all participants demonstrated decisional capacity, provided written informed consent, and were compensated for their time. Bonus compensation was provided for each EMA survey participants completed at the rate of $1/survey.

Procedures

Lab Visits.—At the baseline lab visit, participants completed standardized neuromedical and neurobehavioral assessments (see Heaton et al. (2010) for more details). Medical comorbidities were determined via a combination of clinical interview and review of prescription medications. HIV serostatus was confirmed using a HIV antibody point-of-care rapid test (Mirad, MedMira, Nova Scotia, Canada). A computerized, semi-structured interview was used to determine DSM-IV criteria for current and lifetime mood disorders and substance and alcohol use disorders (Composite International Diagnostic Interview; World Health Organization, 1997). DMS-IV criteria were used because this study took place at a center in which data collection methodology is harmonized across studies, and the center's methodology was instituted prior to the release of the DSM-5. In line with DSM-5 criteria, substance abuse and dependence were combined into one "use disorder" category (see Table 1). Lifetime total cannabis use days and quantity of cannabis use were also collected using the modified timeline follow-back interview (Robinson, Sobell, Sobell, & Leo, 2014).

Participants were given a Samsung smartphone with 4G Android Operating system and the 3-axis ActiGraph GT9X Link wrist accelerometer. A staff member provided an individually tailored 20-30 minute structured training session to orient participants to the smartphone to help ensure survey completion. Participants were asked to carry the smartphone with them throughout the duration of the study, and the smartphone used an encrypted native application framework so data could not be accessed if the smartphone was lost or stolen. Staff also oriented participants to the actigraphy watch, and instructed participants to wear the watch on their non-dominant hand 24 hours/day for the duration of the study except when the watch could get wet (e.g., bathing). Participants were given a smartphone and actigraphy instruction manual and an actigraphy watch log to record when and why they removed the watch as well as what time they went to bed and woke up.

After the participant had completed the 14-day EMA and actigraphy period, the participant completed a follow-up lab visit to return the devices and complete follow-up surveys.

Fourteen-day EMA and actigraphy study period.—Over the fourteen-day EMA study period, participants received alerts four times per day for total of 56 possible data points per participant. The surveys were dispersed throughout the day in four interval periods: morning, midday, afternoon, and evening. Survey times were randomized within each interval period and customized to the participants' sleep-wake schedule. The text messaging notification on the smartphone sounded every two minutes until the survey was answered or until 16 minutes had passed. If the participant did not respond within 16 minutes, the survey was considered "missed".

The EMA survey included a question that queried about substance use: "*Since the last alarm, have you taken or used any of the following substances? (check all that apply): Caffeine, Tobacco, Herbal supplements, Weight-loss supplements, Alcohol, Cannabis/marijuana, Cocaine/crack, Crystal/meth, Ecstasy/Molly, Heroin, Other street drug(s), Prescription drugs not prescribed to me, and No substance/drug use."* The convergent validity of the alcohol and marijuana portion of this question has been previously reported in this sample, and have shown to be correlated to number of days of past use and quantity of use (Paolillo et al., 2017).

Objective Sleep Measures

The wrist-worn ActiGraph GT9X Link device was used to objectively assess sleep quality and has been previously shown to distinguish sleep versus wakefulness when worn at night (Cole, Kripke, Gruen, Mullaney, & Gillin, 1992). ActiGraph data was processed by co-author MH at UCSD's Exercise and Physical Activity Resource Center, adhering to best practices for processing this dynamic data. The time window to assess sleep versus awake was assessed on a minute-by-minute basis using a rolling window (Cole et al., 1992; Sadeh, Sharkey, & Carskadon, 1994). Participants were asked to record the time they went to bed (i.e. tried to fall asleep) and time they first awoke in daily written logs in order to determine number of minutes in bed. If participant sleep records were missing entirely, sleep onset and awake time were manually determined by a specially trained research assistant. The first minute of 0 movement counts after a drop from 1000 counts was considered the start and the minute before an increase from 0 counts to over 1000 counts was considered the end. Manual detection methods for determining time in bed is outlined by Full et al. (2018). Values derived include: (1) total sleep time – the number of minutes asleep; (2) sleep efficiency – the number of minutes asleep divided by number of minutes in bed (ranges from 0-100 with higher values indicating more efficient sleep); and (3) sleep fragmentation index – an index of restlessness during sleep (ranges from 0-100 with higher values indicating more fragmented sleep; Knutson, Van Cauter, Zee, Liu, & Lauderdale, 2011; Loewen, Siemens, & Hanly, 2009).

Statistical Analyses

Cannabis use was classified per day into two groups: use (at least once in the day) and no use. A participant was considered to have used cannabis during a day if they self-reported

cannabis use on the second, third, or fourth survey of that day or first survey of the next day. This methodology was selected because the survey asks "*since the last survey*", and, after looking at the survey times and sleep times, the morning survey of the next day was more likely to represent the previous night than that morning. Objective sleep measures were compared between cannabis use (i.e., use vs. no use), using a linear mixed-effects regression with subject-specific random intercepts, controlling for study day. The same model was then adjusted for potential confounders, including alcohol use, caffeine use, tobacco use, and HIV status, which were selected using the Akaike information criterion (AIC; Akaike, 1974), a model selection criterion considering both model fit and complexity in evaluating a model. The models were reduced with backward elimination method based on the AIC values. Weekday versus weekend day (i.e., Friday and Saturday) were not included as covariates given that only a small proportion of the sample was employed (11.8%). Upon examination, sleep and cannabis use did not differ on weekdays vs. weekends (matched T-tests p's>0.10). Lower AIC value indicates better model. Results were considered statistically significant at $p<0.05$. Statistical analyses were implemented using R version 3.5.1 (2018).

Results

Overall Sample Characteristics

Participant demographic and clinical characteristics are presented in Table 1. Only 19.5% (n=17) of participants from the parent study endorsed cannabis use during the study period. On average, these seventeen participants were 57.8 years old, with 14.5 years of education, 52.9% white, and primarily male (82.4%). Two participants (11.8%) met criteria for a current cannabis use disorder, and seven (41.2%) participants met criteria for lifetime cannabis use disorder.

EMA, cannabis use, and sleep characteristics are presented in Table 2. The median number of surveys completed was 50 out of 56 possible surveys (89% adherence), and the median percent of surveys in which cannabis was endorsed was 28.3%. The median number of days with sleep data was 11 days. The National Sleep Foundation recommends ≥85% sleep efficiency and between 7-9 hours of sleep for middle-aged adults (Hirshkowitz et al., 2015; Ohayon et al., 2017). On days with both EMA and sleep data, the median percent efficiency was 77.2%. On average, 82.4% (n=14) participants had less than 85% efficiency. The average total sleep time in hours was 5.3 hours. Fourteen participants (82.4%) had less than 7 hours of sleep, and no participants had greater than 9 hours of sleep. Three participants reported that they were prescribed sleep medications.

Cannabis and Sleep Relationships

Table 3 displays the results for all mixed-effects linear regression models. Cannabis use was related to greater subsequent total sleep time (β=0.559; p=0.046). However, there was no significant relationship between cannabis use and subsequent sleep efficiency (β=1.497; p=0.461) or cannabis use and subsequent sleep fragmentation index (β=0.846; p=0.756). HIV status, alcohol use, caffeine use, and tobacco use were added to the models as covariates, and selected based on the AIC. After model selection with AIC, none of the potential covariates were retained in the models.

Discussion

While studies have highlighted that EMA is a feasible way to examine substance use (e.g.,Paolillo et al., 2018; Shiffman, 2009), few studies have used multiple sources of digital health technologies to examine cannabis and health behaviors in the real world. Participants demonstrated good adherence to completing the EMA surveys and wearing the actigraphy watch, indicating that using both concurrently among older adults with and without co-morbid medical conditions is feasible. Our results suggest cannabis use is associated with greater than a half an hour increase in sleep time. However, cannabis use was not associated with an increase or decrease in efficiency or sleep fragmentation. While being mindful of the small sample size and unknown cannabinoid content of the cannabis used, these results contribute to the decidedly mixed literature examining sleep and cannabis use that has focused primarily on younger participants in lab-based settings or using retrospective questionnaires (Babson et al., 2017).

The majority of participants in this study had poor objective sleep quality (i.e., <85% efficiency, <7 hours of sleep). In both older adults and PWH, poor sleep quality has been associated with a variety of negative outcomes such as worse cognitive functioning, everyday functioning, and quality of life (Babson, Heinz, & Bonn-Miller, 2013; Magee, Caputi, & Iverson, 2011; Mahmood, Hammond, Nunez, Irwin, & Thames, 2018; Nebes, Buysse, Halligan, Houck, & Monk, 2009). The first line medications to treat insomnia, benzodiazepines and z-drugs, have been associated with negative cognitive (e.g., memory loss) and physical (e.g., falls) events, particularly in older adults (Glass, Lanctôt, Herrmann, Sproule, & Busto, 2005). Recent clinical trials have shown that cannabinoids (THC and combined THC/CBD preparations) may have a positive effect on sleep in multiple populations including PWH (Bedi et al., 2010; Kuhathasan et al., 2019). However, there is a need for further trials to determine the most advantageous composition and dosing of cannabis products that may be efficacious sedative-sparing treatments for insomnia. In particular, CBD, a non-psychoactive cannabinoid, could be especially useful if proved effective for treating sleep problems in neurocognitively vulnerable populations (e.g., PWH and older adults). These types of trials may benefit from real-time behavioral assessments to show whether cannabinoid based treatments result in similar (or improved) sleep outcomes compared to treatment with sedative/hypnotic medications, and whether such treatment results in better neurocognitive outcomes.

There are limitations to this study. First, while there were several EMA surveys in which cannabis use was endorsed, only seventeen people were included in this study, thus limiting power to detect associations and the generalizability of the study. Demographically, the majority of the sample was male, which is reflective of the HIV population in the surrounding community and the national HIV population (Centers for Disease Control and Prevention, 2017); therefore, larger studies with more diverse samples are needed. Additionally, we did not have the power to test interaction effects to understand whether sleep-cannabis relationships differ by HIV status. This is an important question for follow-up work given that other studies have found the relationship between cannabis and subjective sleep quality differs by HIV status (Lim & Thames, 2018). Second, in order to limit participant burden, the EMA study did not assess cannabis use in detail. Future studies

should examine additional cannabis use characteristics such as dose, route of administration, time of use, composition of cannabis product, and reason/s for use in order to further understand the relationship between cannabis and sleep. Third, although we used lagged analyses, causality should not be assumed. Cannabis use may be associated with other variables that are also related to sleep that may confound this relationship.

Overall, this study demonstrates that coupling smartphone-based EMA and actigraphy devices to examine the relationship between cannabis use and sleep in the real-world can provide novel insights into the temporal relationships of these behavioral co-factors. In our small sample, findings showed cannabis use was associated with longer sleep duration later that night but was not associated with sleep efficiency nor sleep fragmentation. As recreational and medicinal cannabis use continues to rise, new methodologies that utilize technology such as digital phenotyping (e.g., utilizing phone sensors, keyboard interaction; Stange et al., 2018; Zulueta et al., 2018) will prove useful to further characterize and investigate the relationship between cannabis use in the real world and health behaviors across the lifespan.

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Table 1.

Participant characteristics (n=17)

	Mean (SD), Median [IQR], or n (%)
Demographic Variables	
Age (years), M (SD)	57.8 (6.1)
Male, n (%)	14 (82.4%)
Race/Ethnicity	--
Non-Hispanic White, n (%)	9 (52.9%)
African American, n (%)	6 (35.3%)
Hispanic, n (%)	1 (5.9%)
Other, n (%)	1 (5.9%)
Education (years), M (SD)	14.5 (1.9)
Employed, n (%)	2 (11.8%)
Household Income, n (%)	--
<$10,000	2 (11.8%)
$10,000-$19,999	9 (52.9%)
$20,000-$34,999	4 (23.5%)
$35,000-$49,999	0 (0%)
$50,000-$74,999	2 (11.8%)
Number of other people living in household, median [IQR]	0 [0, 1]
Percent of time spent alone, median [IQR]	72.5% [39.0%, 81.5%]
Medical characteristics	
Hypertension, n (%)	9 (52.9%)
Diabetes mellitus, n (%)	3 (17.6%)
Hepatitis C, n (%)	1 (5.9%)
BMI >30, n (%)	6 (35.3%)
Psychiatric functioning	
LT MDD, n (%)	13 (76.5%)
Current MDD, n (%)	3 (17.6%)
LT alcohol use disorder, n (%)	10 (58.8%)
Current alcohol use disorder, n (%)	1 (5.9%)
LT cannabis use disorder, n (%)	7 (41.2%)
Current cannabis use disorder, n (%)	2 (11.8%)
Other current substance use disorder, n (%)	0 (0%)
HIV Characteristics [a]	
AIDS, n (%)	6 (54.5%)
Current CD4, median [IQR]	787 [688, 821]
Nadir CD4, median [IQR]	216 [98, 300]
Duration of HIV infection (years), median [IQR]	24.4 [15.7, 28.0]
On ART, n (%)	10 (90.1%)
Undetectable viral load, n (%) [b]	9 (100%)

Note: BMI, body mass index; LT, lifetime; MDD, major depressive disorder;

[a] Based on the subset of participants with HIV infection (n=11);

[b] n=9

Table 2.

Sleep and Substance Use Variables

	Median [IQR], or n (%)
Sleep Variables	
Number of nights of sleep data, median [IQR]	11 [9, 13.5]
Average Percent Efficiency, median [IQR]	77.2% [67.4%, 82.9%]
Efficiency Standard Deviation, median [IQR][a]	8.8 [5.1, 11.6]
<85% Efficiency, n (%)	14 (82.4%)
Average Total Sleep Time (hours), median [IQR]	5.3 [4.8, 6.5]
Total Sleep Time Standard Deviation, median [IQR][a]	0.87 [0.80, 1.63]
<7 hours Total Sleep Time, n (%)	14 (82.4%)
Average Sleep Fragmentation Index, median [IQR]	38.6 [31.9, 49.8]
Sleep Fragmentation Standard Deviation, median [IQR][a]	13.9 [9.9, 17.0]
Prescribed Sleep Medications	3 (17.6%)
Returned sleep log, n (%)	12 (70.5%)
EMA Cannabis Use Variables	
Number of surveys completed [b], median [IQR]	50 [46.5, 52]
Percent of surveys in which cannabis use was endorsed	28.3% [4.4%, 48.0%]
Percent of days in which cannabis use was endorsed	76.9% [42.9%, 92.9%]
Cannabis Use Characteristics	
LT total days of cannabis use, median [IQR]	2564 [684, 10712]
LT total quantity of cannabis use (grams), median [IQR]	1728 [102, 5396]

Note:

[a] A standard deviation was calculated for each participant's objective sleep quality measures over the time they wore the actigraphy watch. This represents the median [IQR] of those values.

[b] total number of surveys possible = 56

LT=Lifetime

Table 3.

Relationship between cannabis use and objective sleep quality

	Unstandardized Coefficient	95% CI	Standardized Coefficient	*p*-value
Model 1: Efficiency				
Cannabis Use (ref: no use)	1.497	[−2.475, 5.470]	0.149	0.461
Day	0.027	[−0.386, 0.439]	0.003	0.899
Model 2: Total Sleep Time				
Cannabis Use (ref: no use)	0.559	[0.015, 1.104]	0.394	0.046
Day	0.024	[−0.034, 0.082]	0.017	0.425
Model 3: Sleep Fragmentation Index				
Cannabis Use (ref: no use)	0.846	[−4.469, 6.161]	0.062	0.756
Day	−0.456	[−1.018, 0.106]	−0.033	0.114