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A randomized controlled trial of a manual-only treatment for reduction and cessation of problematic caffeine use

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ABSTRACT

Background: Caffeine Use Disorder was added to *DSM*-5 as a diagnosis for further research, but few studies have been conducted to identify effective treatments. This randomized, controlled clinical trial examined the efficacy of a manual-only treatment program for caffeine cessation and reduction among individuals seeking treatment for problematic caffeine use.

Methods: Individuals meeting at least two proposed *DSM*-5 diagnostic criteria for Caffeine Use Disorder were randomly assigned to receive either immediate treatment or treatment delayed by 7 weeks. The treatment consisted of a manual containing information about caffeine and instructions for gradually reducing caffeine consumption over a period of 6 weeks, with no counseling or additional support. Caffeine consumption and caffeine-related distress were assessed before treatment, 7 weeks after receiving the treatment manual (end-of-treatment), and 20 weeks post-treatment.

Results: The manual-only treatment resulted in significant reductions in participants' self-reported caffeine consumption and caffeine-related distress at end-of-treatment that were sustained at 20-weeks post-treatment. Salivary caffeine levels and community observers corroborated the self-reported reductions in caffeine consumption. Comparisons between the immediate and delayed treatment groups suggest the reductions in caffeine consumption were attributable to the manualized treatment rather than spontaneous with the passage of time.

Conclusions: The present study provides evidence that a gradual caffeine reduction and cessation program may be successfully implemented using a manual-only approach. This time- and cost-effective intervention may be easily adopted by practitioners with limited time or experience with behavioral interventions who want to encourage their patients to reduce caffeine consumption.

1. Introduction

An estimated 89% of adults in the United States consume caffeine daily (Fulgoni et al., 2015). Although moderate caffeine consumption is not generally associated with negative health consequences (Nawrot et al., 2003), approximately 14% of adults consume more than the recommended limit of 400 mg of caffeine per day (Fulgoni et al., 2015; USDA, 2015). Caffeine may negatively affect conditions such as anxiety, insomnia, tachycardia, urinary incontinence, gastrointestinal upset, and is associated with complications during pregnancy (see Temple et al., 2017 or Sweeney et al., 2018 for review). Abrupt cessation of caffeine after regular use can result in a withdrawal syndrome characterized by headache, fatigue, mood disturbances, difficulty concentrating, and flu-like symptoms (e.g., Hughes et al., 1993; Juliano and Griffiths, 2004), and the *DSM*-5 recognizes Caffeine Withdrawal as a diagnosis when these symptoms cause clinically significant distress or impairment (American Psychiatric Association, 2013). Furthermore, some individuals report continued caffeine use despite (1) having a persistent desire or unsuccessful efforts to cut back, and despite (2) having a medical or psychological problem worsened by caffeine (e.g., Hughes et al., 1998; Juliano et al., 2012). These symptoms, combined with (3) caffeine withdrawal or caffeine use to avoid withdrawal, were recently proposed as the key diagnostic criteria for Caffeine Use Disorder, which is included in *DSM*-5 as a condition for further study (Budney et al., 2015; Meredith et al., 2013).

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To date, few studies have been conducted to develop and validate caffeine cessation treatments. Gradual reduction of caffeine use over a period of several weeks has shown to be effective in some prior controlled studies with heavy caffeine consumers and individuals with urinary incontinence (Bryant et al., 2002; Foxx and Rubinoff, 1979; James et al., 1985, 1988), but only one recent investigation treated participants and characterized their problematic caffeine use according to *DSM* criteria. Evatt et al. (2016) evaluated a gradual caffeine cessation treatment among individuals seeking treatment for problematic caffeine use using a wait-list control design. Participants received a one-hour counseling session and received a manual incorporating cognitive-behavioral strategies to reduce caffeine consumption over a period of five weeks. On average, treatment resulted in significant reductions in self-reported caffeine use and salivary caffeine following the manualized intervention, with no significant increases in self-reported caffeine use observed for up to one year of follow-up.

Although the brief intervention assessed by Evatt et al. (2016) is of shorter duration than treatment approaches for other substance use disorders, the requirement of a one-hour individual counseling session may still be considered burdensome for health care professionals with limited time and expertise dedicated to behavioral interventions. Caffeine reduction is recommended for a range of contraindicated conditions, but individuals seeking treatment for problematic caffeine use often report continued use despite recommendations from medical professionals (Hughes et al., 1988; Juliano et al., 2012). Therefore, a very brief and disseminable treatment program for caffeine cessation may have wide clinical utility. Although the treatment manual in the previously published trial provides the basic structure for an effective behavioral intervention, the efficacy of a manual-only intervention without individualized counseling is unknown. The present randomized controlled trial examined the efficacy of simplified, manual-only treatment for caffeine reduction and cessation in individuals seeking treatment for their caffeine use. We hypothesized that the manual-only intervention would be effective for caffeine reduction and cessation in the absence of individualized counseling, and that caffeine-related distress would decrease.

2. Methods

2.1. Participants

The Johns Hopkins University School of Medicine Institutional Review Board approved all study procedures. Participants were recruited from the greater Baltimore, Maryland area using advertisements via local newspapers/magazines, radio, public transport, paper flyers in the community, online (e.g., Facebook), as well as word-of-mouth referral. Advertisements offered the opportunity for treatment at no cost and did not indicate monetary compensation. Written informed consent was obtained at an in-person screening and intake session (intake) at the study site located on the Johns Hopkins Bayview Medical Center campus. Eligible participants: (1) were 18–70 years old, (2) were fluent in written and spoken English, (3) consumed caffeine at an average dose of ≥200 mg of caffeine per day, (4) fulfilled at least two *DSM*-5 diagnostic criteria for Substance Use Disorder as applied to caffeine (i.e., the minimum threshold indicating mild substance use disorder according to *DSM*-5), (5) expressed a desire to reduce or eliminate caffeine consumption. We chose to require only two DSM criteria in order to make the treatment available to more individuals seeking assistance, as the *DSM* research criteria for Caffeine Use Disorder were designed to be somewhat conservative as more data on clinical samples are acquired (Budney et al., 2015). Individuals were excluded if they had a significant medical condition, psychiatric disorder/symptoms (e.g., severe untreated depression), or evidence of substance use disorder other than caffeine (i.e., positive urine drug test or self-reported problematic substance use). Pregnant or breastfeeding women or women who were not using an effective means of birth control (e.g., condoms) were excluded. Caffeine is distributed to breast milk and amniotic fluid, and pregnant or breastfeeding participants may require special consideration during caffeine reduction treatment.

2.2. Design

Eligible participants were randomized to either an immediate or a delayed treatment group. Urn randomization stratified age (< 45 years old; ≥45), sex (Male; Female), and initial caffeine consumption (< 400 mg daily; ≥400 mg). Study sessions were conducted individually. Participants in Immediate Treatment group received the treatment manual (treatment session) at another visit to the study site within a few days of their intake session, whereas those in the Delayed Treatment group returned to the study site and received the manual after a 7-week delay. Individuals in both groups completed an end-of-treatment assessment at the study site approximately 7 weeks after receiving the manual. A final assessment was conducted via phone 20-weeks after end-of-treatment (20 weeks post).

2.3. Treatment

At the treatment session, study staff met briefly with the participant (i.e., less than five minutes) to give them the treatment manual (See Supplemental Materials). The manual contained information about caffeine, cognitive behavioral strategies for caffeine reduction, an index with caffeine content for common items, a diary with corresponding blank graphs for plotting daily caffeine consumption, and instructions for calculating weekly goals. Strategies in the manual, such as identifying antecedents and high-risk situations for caffeine use, were modeled on the principles of relapse prevention (Marlatt and Gordon, 1985). Each participant was verbally instructed to keep caffeine consumption the same as usual during the first week and track their consumption in the diary section of the manual. They were also told to use their caffeine consumption for Week 1 as the starting point and follow the instructions in the manual to calculate their weekly goals. A bonus was provided for returning the diary at the end-of-treatment assessment, though it was not required that participants complete the diary to earn the bonus. Participants earned $25 for the screening/intake visit (regardless of whether they qualified), and eligible participants could earn up to $375 for completing the treatment portion of the study. Specifically, eligible participants could earn $25 for completing the treatment session, $150 for completing the end-of-treatment session, a $50 bonus for returning the treatment manual, $75 for completing take-home questionnaires following the end-of-treatment session, and $75 for completing the telephone interview and returning mail-in questionnaires at 2 weeks post-treatment. Study payment was not contingent on caffeine reduction.

2.4. Measures

At the intake session, participants completed a structured clinical interview with study staff assessing *DSM*-5 substance use disorder criteria as applied to caffeine to determine eligibility and describe the pattern of caffeine-related distress in the sample. Table 1 lists the nine research criteria for Caffeine Use Disorder as proposed in *DSM*-5 and as assessed in the present study. To meet an individual diagnostic criterion, participants must have endorsed the item as occurring within the past 12-months with sufficient frequency or intensity. The proposed threshold for a diagnosis of Caffeine Use Disorder is for an individual to meet all of the first three diagnostic criteria (Table 1) along with distress or impairment (American Psychiatric Association, 2013). As stated previously, we required participants to meet only two diagnostic criteria for Caffeine Use Disorder for inclusion. This ensured some *DSM*-defined caffeine-related distress, while not being overly restrictive given that the research criteria for Caffeine Use Disorder are tentative. A questionnaire assessing all sources of caffeine (e.g., coffee, tea, soft

Table 1
Assessment of DSM-5-proposed caffeine use disorder criteria within the sample enrolled in caffeine reduction treatment.

DSM-5 Caffeine Use Disorder research criteria	Number and percent of randomized sample (n = 36) [1] meeting individual *DSM* criteria at Intake		Visual analog scale (0-10) agreement on corresponding Caffeine Use Disorder questionnaire for past 7 days for completers [2] (*Mean, SD)*		
	n	%	Intake	End-of-Treatment	20 Weeks Post
1. A persistent desire or unsuccessful efforts to cut down or control caffeine use.	34	94.4%	7.3 (2.6)[3]	7.5 (3.1)	5.6 (3.8)*
2. Continued caffeine use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by caffeine.	27	75.0%	4.2 (4.1)	1.6 (2.4)**	0.6 (1.2)***
3. Withdrawal, as manifested by either of the following:	35	97.2%			
a The characteristic withdrawal syndrome for caffeine.			5.2 (4.1)[4]	4.8 (3.7)	1.8 (2.7)**
b Caffeine (or a closely related substance) is taken to relieve or avoid withdrawal symptoms.			7.3 (2.9)	2.8 (3.1)***	1.0 (1.8)***
4. Caffeine is often taken in larger amounts or over a longer period than was intended.	22	61.1%	5.2 (3.4)	2.5 (3.2)**	1.8 (2.3)***
5. Recurrent caffeine use resulting in a failure to fulfill major role obligations at work, school, or home.	5	13.9%	1.2 (2.3)	0.6 (1.1)	0.4 (0.8)
6. Continued caffeine use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of caffeine (e.g., arguments with spouse about consequences of use, medical problems, cost).	4	11.1%	2.1 (3.2)	1.1 (2.0)	0.4 (0.7)**
7. Tolerance, as defined by either of the following:	28	77.8%			
a A need for markedly increased amounts of caffeine to achieve desired effect.			5.0 (3.9)	0.7 (1.0)***	0.7 (1.8)***
b Markedly diminished effect with continued use of the same amount of caffeine.			4.7 (3.9)	1.7 (2.5)**	2.3 (3.5)*
8. A great deal of time is spent in activities necessary to obtain caffeine, use caffeine, or recover from its effects.	28	77.8%	4.4 (3.3)	1.6 (2.1)**	1.8 (3.0)**
9. Craving or a strong desire or urge to use caffeine.	12	33.3%	7.1 (2.6)	4.0 (3.3)***	2.9 (3.5)***
Met criteria for Caffeine Use Disorder (at least #1-3)	26	72.2%			

[1] Data in this column show the percent of the randomized sample (n = 36) who met the proposed diagnostic criteria for Caffeine Use Disorder within the past 12 months as in the DSM-5. DSM-5 describes Caffeine Use Disorder as a problematic pattern of caffeine use leading to clinically significant impairment or distress, as manifested by at least items 1–3 of the above occurring within a 12-month period.

[2] Data in the 3 rightmost columns show mean VAS rating of the extent of agreement ranging from 0 (not at all) to 10 (very strongly agree) with the diagnostic criteria as experienced within the past 7 days for those participants who completed the study and returned the questionnaires at 20 Weeks Post (n = 28). Two participants did not provide VAS rating for either items 3b or 7b (n = 26 for these items) and one participant did not provide a VAS rating for item 7a (n = 27 for this item). Asterisks indicate a significant reduction post-treatment (End-of-Treatment or 20 Weeks Post) relative to Intake where: * $p < .05$, ** $p < .01$, *** $p < .001$. There was only one significant decrease in VAS ratings prior to receiving the treatment manual (Intake vs. Treatment session; data not shown for Treatment session); participants rating of using caffeine to avoid withdrawal (item 3b) was significantly lower at the treatment session ($M = 5.3$, $SD = 3.1$; $F(1,24) = 7.6$; $p < .05$) relative to intake.

[3] Calculated using maximum VAS agreement within subject out of two items: 1. a persistent desire, 2. unsuccessful efforts to cut down.

[4] Calculated using maximum VAS agreement within subject out of five items: 1. headache, 2. fatigue or drowsiness, 3. depressed mood or irritability, 4. difficulty concentrating, and 5. nausea, vomiting, or muscle pain/stiffness.

drinks, energy drinks, chocolate, medicines) was used to determine eligibility with regard to typical caffeine use.

Caffeine consumption over time was assessed using a 7-day Timeline Follow-Back (Sobell and Sobell, 1992) completed at each assessment; i.e., 1. intake, 2. treatment, 3. end-of-treatment, 4. 20 weeks post. At each assessment, participants completed paper questionnaires assessing: the State-Trait Anxiety Index (STAI; Spielberger et al., 1970), the Beck Depression Inventory-II (BDI-II; Beck et al., 1996), and visual analog scale (VAS) agreement (i.e., 0 = not at all to 10 = very strongly agree) with *DSM*-5 Substance Use Disorder criteria as applied to caffeine as experienced in the past seven days. We used endorsement of *DSM* criteria as experienced in the past seven days as a continuous measure of self-reported caffeine-related distress, which could be assessed repeatedly over time during study participation. This is preferable to repeatedly assessing the presence or absence of *DSM*-symptoms as occurring over the past 12-months, which may be relatively insensitive to changes in caffeine-related distress due to study intervention. At end-of-treatment sessions, participants also completed a treatment acceptability questionnaire. A community observer (e.g., spouse, friend) nominated by the participant provided estimates of participant's caffeine consumption at about the time of treatment and end-of-treatment sessions. Saliva samples collected at the treatment and end-of-treatment sessions were analyzed for quantitative estimates of salivary caffeine via gas chromatography (Shi et al., 1993). Timeline Follow-Back was conducted over the phone at 20 weeks post, and the other paper questionnaires were mailed to the participants with a return envelope and postage.

2.5. Data analyses

Baseline demographic differences between groups were assessed using independent samples *t* tests or chi square analyses for the randomized sample (n = 36; see Results for a description of participant flow). Changes in outcomes across assessments were examined using planned contrasts in repeated measures ANOVAs with the within-subjects factor of Session (i.e., 1. intake, 2. treatment, 3. end-of-treatment, 4. 20 weeks post) and between-subjects factor of Group (i.e., Immediate Treatment or Delayed Treatment) for participants who completed the study (n = 29) so that reductions in caffeine consumption would not be attributable to differential attrition of high caffeine consuming participants. Planned contrasts compared outcomes at intake relative to each subsequent session and tested for Group by Session interactions. For example, effects for outcomes attributable to the passage of time in the Delayed Treatment group would be detected by a significant Group by Session interaction between 1. intake and 2. treatment sessions (e.g., if the Delayed Group reduced caffeine intake prior to treatment to a significantly greater extent relative to the Immediate Treatment group). Paired *t* tests compared salivary caffeine for those participants who provided a saliva sample before and after treatment (n = 31). Differences in caffeine consumption between the Immediate and Delayed Treatment groups at approximately seven weeks post-intake (i.e., 3. end-of-treatment for the Immediate Group vs. 2. treatment for the Delayed Group) were compared using an independent samples *t*-test for study completers (n = 29).

3. Results

3.1. Participants

Three-hundred and ten individuals were assessed for eligibility via telephone, 82 provided written consent and were assessed for eligibility at the in-person intake session, and 36 were randomized to either the Immediate (n = 17) or Delayed Treatment (n = 19) over a period of approximately 2.5 years. The most common reasons for exclusion prior to treatment (other than those lost to follow-up) included no desire to reduce caffeine use (n = 52), evidence of co-occurring substance use or psychiatric disorders (n = 44), low caffeine consumption (n = 42), and too few Caffeine Use Disorder criteria endorsed (n = 38). A detailed participant flow diagram is shown in Supplemental Materials.

Of the randomized participants, 36 (100%) attended the treatment session and received the manual, 31 (86.1%) attended the end-of-treatment session, 29 (80.5%) were reached for the 20 weeks post phone session (at which past-week caffeine use was assessed), and 28 (77.8%) mailed back the paper questionnaires. Randomized participants were 55.6% female (44.4% male), 63.9% White (30.6% Black or African-American, 2.8% Asian, 2.8% Other), and 91.7% Non-Hispanic (5.6% Hispanic, 2.8% Unknown). Mean age was 45.8 years (SD = 12.9). Mean typical caffeine consumption at intake was 755.2 mg per day (SD = 373.1; Range = 203–1956 mg per day). The primary source of caffeine for most participants was coffee, but a sub-sample (n = 6) received caffeine primarily from soft drinks, tea, or energy drinks. It was common for participants to receive caffeine from multiple sources (e.g., coffee and tea). There were no significant differences in demographic information or typical caffeine consumption between groups at intake. Detailed demographic information is shown in Supplemental Materials.

3.2. Caffeine Use Disorder criteria

Table 1 shows the percent of the randomized sample (n = 36) meeting each proposed diagnostic criterion for Caffeine Use Disorder. The majority of the sample (72.2%) met criteria 1–3 and thus would have met the proposed threshold for Caffeine Use Disorder. All of those who met criteria for Caffeine Use Disorder also met additional criteria beyond criteria 1–3. The most commonly endorsed criteria among all participants were withdrawal (97.2%) and a persistent desire or unsuccessful efforts to cut down or control caffeine use (94.4%).

Table 1 also shows mean VAS rating of the extent of agreement with each Caffeine Use Disorder criteria (past seven days) for those participants who completed the paper assessments through 20 weeks post (n = 28). Across all criteria, there were no significant reductions in VAS ratings of symptoms prior to receiving the treatment manual (intake vs. treatment session; data not shown for treatment session) with the exception of a significant reduction in agreement for using caffeine to avoid withdrawal (see Table 1, item 3b). However, when comparing ratings at end-of-treatment or 20 weeks post relative to intake, several significant reductions in VAS ratings across a number of caffeine-related distress symptoms were observed, including reductions in ratings for a persistent desire or unsuccessful efforts to cut down, continued caffeine use in spite of a recurrent physical or psychological problem, continued caffeine use in spite of recurrent social or interpersonal problems, withdrawal, tolerance, using more caffeine or over a longer period than intended, spending a great deal of time using, obtaining, or recovering from the effects of caffeine, and craving (see Table 1).

3.3. Reductions in caffeine use

Fig. 1 shows mean daily caffeine intake as reported on the 7-day Timeline Follow-Back for those individuals who completed the study through 20 weeks post. The data show robust reductions in reported caffeine use at the end-of-treatment sessions for both groups (i.e., 84% overall reduction in caffeine use relative to intake). These reductions were greater than reductions in caffeine use that occurred between intake and the treatment sessions (9%), and were generally sustained over the 20-weeks post-treatment (i.e., 75% overall reduction at 20-weeks post relative to intake). Consistent with this, within-subjects

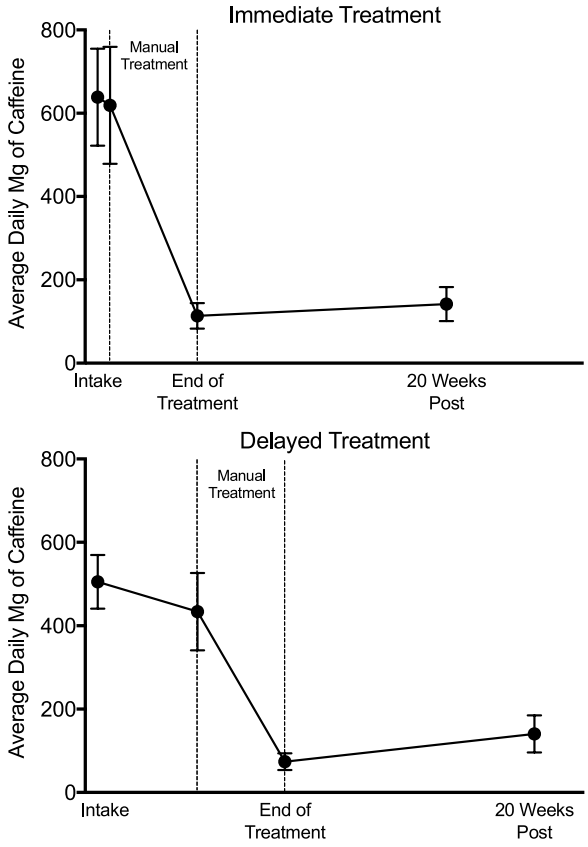

Fig. 1. Mean (± SEM) daily caffeine intake in milligrams (mg) as reported on the Timeline Follow-Back on the screening session (Intake), the session at which the treatment manual was given (Manual Given), 7 weeks after receiving the treatment manual (End of Treatment), and 27 weeks after receiving the treatment manual (20 Weeks Post). Top panel shows the group that received the manual within a few days after screening (Immediate Treatment), and the bottom panel shows the group in which treatment was delayed by 7 weeks (Delayed Treatment). Data shown are for $n = 29$ individuals who completed the study.

contrasts showed significantly lower reported caffeine use at end-of-treatment ($F(1, 27) = 62.9$, $p < .001$, $\eta_p^2 = 0.70$) and 20-weeks post ($F(1, 27) = 54.3$, $p < .001$, $\eta_p^2 = 0.67$) relative to intake. Session x Group interactions assessing group differences in caffeine consumption changes over time were not significant ($ps \geq .27$), which would have detected any differences in caffeine consumption between intake and treatment sessions that were attributable to the passage of time in the delayed treatment group. Further, at approximately seven weeks post-intake for both groups, pre-treatment caffeine consumption in the Delayed Group was significantly greater than end-of-treatment caffeine consumption in the Immediate Group ($t(27) = 3.00$, $p < .01$; $d = 1.17$).

Participants' caffeine consumption relative to the recommended dietary limit of 400 mg of caffeine per day was also evaluated (USDA, 2015). At intake, 86% of participants reported consuming more than 400 mg per day on average according to a questionnaire assessing typical caffeine consumption, and 64% of participants reported consuming more than the recommended daily dietary limit of caffeine in the past week on the Timeline Follow-Back. Of those retained at the end-of-treatment, none reported consuming caffeine in excess of recommended dietary limits. Of those retained at 20 weeks post-treatment, 7% reported mean daily dietary caffeine consumption in excess of the recommended dietary limits.

Estimates of salivary caffeine collected from participants at end-of-treatment ($n = 31$) were also consistent with significant reductions in caffeine consumption pre- and post-treatment ($t(29) = 3.31$, $p < .01$, $\eta_p^2 = 0.27$).[1] Median salivary caffeine pre-treatment was 3253.1 ng/mL ($M = 3476.3$, $SD = 2512.0$) and post-treatment median was 1036.6 ng/mL ($M = 1663.4$, $SD = 2054.8$). Community observers generally corroborated participant self-report; 87% percent of observers ($n = 27$) noted a decrease in the participant's caffeine consumption following the intervention whereas 13% ($n = 4$) indicated they were not sure or did not notice a reduction.

3.4. Treatment acceptability

Treatment acceptability and treatment adherence were good. Mean ratings at end-of-treatment (as reported on a 0–10 VAS) indicated that participants "read all or most of the Guide to Caffeine Reduction and Cessation" (i.e., treatment manual), $M = 8.7$, $SD = 2.2$, "liked learning about caffeine use, caffeine dependence, and caffeine withdrawal from the guide," $M = 8.0$, $SD = 2.3$, "completed all or most of the Caffeine Diary in the Guide," $M = 8.6$, $SD = 2.6$, and overall found "the guide was helpful during my attempt to reduce or quit caffeine," $M = 8.5$, $SD = 2.1$.

3.5. Secondary measures

There were no significant changes in depression or anxiety over time as assessed by the BDI-II and the State/Trait anxiety subscales of the STAI (mean data presented in Supplementary Table 2).

4. Discussion

The results of the present study support the efficacy of a manual-only treatment for gradual caffeine reduction in individuals presenting with problematic caffeine use. Participants showed significant reductions in self-reported caffeine consumption following treatment with only brief instructions on how to use the treatment manual. Reductions in caffeine consumption were corroborated by the analysis of salivary caffeine levels and community observers before and after treatment. The reductions in caffeine use following treatment in both groups were much greater than reductions in caffeine consumption observed during the 7-week period prior to treatment in the Delayed Treatment group, which served as a control condition to assess any spontaneous reductions following intake. Reductions in caffeine consumption after treatment remained at levels significantly lower than intake up to 20 weeks post-treatment, although at 20 weeks post, both groups had received the intervention and as such it is possible the results were in part attributable to the passage of time. Further, VAS ratings of Caffeine Use Disorder symptoms in the past week were significantly reduced following treatment. This suggests that the extent to which participants experienced caffeine-related distress as reflected in symptoms of Caffeine Use Disorder was significantly reduced due to the study intervention. Importantly, mean typical daily caffeine consumption prior to intervention was above the recommended dietary limit of 400 mg per day. Prior to the intervention, 86% of participants reported typically consuming greater than the USDA-recommended dietary limit of 400 mg of caffeine per day and 64% reported consuming on average more than 400 mg per day in the past week on the Timeline Follow-Back. By contrast, fewer than 10% of participants at 20 weeks post-

[1] Values that were below the lowest value of quantitation (100 ng/mL; $n = 7$) were conservatively included in the analysis as 99 ng/mL. Values that were above the highest calibration standards (5000 ng/mL; $n = 9$) were included in the analyses (though values this high ought to be generally considered estimated rather than exact quantitation), because high values might be expected with higher caffeine consumers. Saliva samples from one participant were excluded from analysis because the pre-treatment value (46383.9 ng/mL) exceeded the next highest estimate (9340.7 ng/mL) by more than four standard deviations and was suspected to be a result of mouth contamination. Excluding this participant did not affect significance of the statistical results.

treatment reported caffeine consumption in excess of 400 mg per day on the Timeline Follow-Back. On the other hand, it should be noted that rates of caffeine metabolism and tolerance between individuals may be highly variable, and symptoms such as caffeine withdrawal may occur at dietary doses much lower than 400 mg per day (e.g., Evans and Griffiths, 1999).

Overall, the results of this trial are promising for the manual-only treatment approach, especially given that the intervention was designed to be executed with minimal time and expertise. The gradual, manualized reduction program for individuals with problematic caffeine use was effective for a previous treatment study (Evatt et al., 2016), but the manual was also accompanied by a one-hour behavioral therapy session which may be impractical in some healthcare settings. Although it is possible additional counseling as administered in the prior study may provide further benefits, both studies showed meaningful decreases in caffeine consumption, which suggests the manual alone is sufficient. Similar to prior studies (e.g., Juliano et al., 2012), almost half (47%) of the randomized sample had previously been advised by a medical authority to quit or cut back on their caffeine use (e.g., primary care provider, cardiologist, urologist, mental health therapist, obstetrician), suggesting the need for caffeine cessation intervention tools among a diverse group of clinicians. That the recommendation of a healthcare professional was insufficient to reduce caffeine use in these individuals emphasizes the importance of developing behavioral interventions for caffeine cessation and illustrates how the caffeine reduction treatment manual may have significant clinical impact if effectively disseminated.

Potential challenges to wider application of the manualized treatment must be considered. First, we note that the sample in the present study was motivated to reduce caffeine consumption. As such, the success of the intervention may not generalize to a less motivated clinical sample. Even so, we would note that participants frequently reported multiple failed attempts to cut down prior to treatment, despite wanting to cut down and despite of the problems that caffeine was causing them. Indeed, a desire to quit and inability to quit are proposed to be defining characteristics of Caffeine Use Disorder. Thus, the degree of motivation to quit in the present sample ought not undermine the generality of the intervention for those with *DSM*-defined impairment related to their caffeine use. Participants in the present study were free from co-morbid substance use disorders and psychiatric disorders. Psychiatric patients with excessive caffeine consumption may benefit from a similar cessation program, especially those with sleep abnormalities or anxiety, but further research with this population is needed. Participant retention in the present study was generally good, but the small sample size precludes a thorough examination of predictors of treatment attrition. Compensation for participation was relatively modest given the time commitment and duration of follow-up. Future research may consider increased compensation for study participation or advertisements that indicate compensation in addition to free treatment to encourage study engagement and retention. The efficacy of the intervention program in a larger, more diverse sample and in specific populations with co-morbid substance use and psychiatric conditions is warranted. Regardless, the sustained reduction in caffeine consumption in the present study, as well as the intervention's cost- and time-effectiveness is encouraging for broader application.

5. Conclusions

In summary, this randomized controlled trial demonstrated the efficacy of a manual-only intervention for problematic caffeine use with reductions in caffeine use sustained over 20 weeks. Given the acceptability and simplicity of the intervention, the treatment manual may be a valuable tool for practitioners across a range of clinical settings who advise caffeine reduction or cessation in the case of problematic caffeine use or contraindicated medical conditions.

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Contributors

Mary M. Sweeney managed data collection, led the analyses, and prepared the manuscript. Steven E. Meredith assisted in study design, managed data collection, and revised the manuscript. Laura M. Juliano assisted in study design and revised the manuscript. Daniel P. Evatt assisted in study design and revised the manuscript. Roland R. Griffiths oversaw data collection, obtained funding, designed the study, and revised the manuscript. All authors have approved the manuscript.

Conflict of interest

No conflict declared.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.drugalcdep.2018.10.034.

References

American Psychiatric Association, 2013. Diagnostic and Statistical Manual of Mental Disorders: DSM-5. American Psychiatric Association, Washington, D.C.
Beck, A.T., Steer, R.A., Brown, G.K., 1996. Manual for the Beck Depression Inventory-II. Psychological Corporation, San Antonio, TX.
Bryant, C.M., Dowell, C.J., Fairbrother, G., 2002. Caffeine reduction education to improve urinary symptoms. Br. J. Nurs. 11, 560–565.
Budney, A.J., Lee, D.C., Juliano, L.M., 2015. Evaluating the validity of caffeine use disorder. Curr. Psychiatry Rep. 17, 74.
Evans, S.M., Griffiths, R.R., 1999. Caffeine withdrawal: a parametric analysis of caffeine dosing conditions. J. Pharmacol. Exp. Ther. 289, 285–294.
Evatt, D.P., Juliano, L.M., Griffiths, R.R., 2016. A brief manualized treatment for problematic caffeine use: a randomized control trial. J. Consult. Clin. Psychol. 84, 113–121.
Foxx, R.M., Rubinoff, A., 1979. Behavioral treatment of caffeinism: reducing excessive coffee drinking. J. Appl. Behav. Anal. 12, 335–344.
Fulgoni, V.L., Keast, D.R., Lieberman, H.R., 2015. Trends in intake and sources of caffeine in the diets of US adults: 2001–2010. Am. J. Clin. Nutr. 101, 1081–1087.
Hughes, J.R., Oliveto, A.H., Bickel, W.K., Higgins, S.T., Badger, G.J., 1993. Caffeine self-administration and withdrawal: incidence, individual differences and interrelationships. Drug Alcohol Depend. 32, 239–246.
Hughes, J.R., Oliveto, A.H., Liguori, A., Carpenter, J., Howard, T., 1998. Endorsement of DSM-IV dependence criteria among caffeine users. Drug Alcohol Depend. 52, 99–107.
Hughes, J.R., Amori, G., Hatsukami, D.K., 1988. A survey of physician advice about caffeine. J. Subst. Abuse 1, 67–70.
James, J.E., Paull, I., Cameron-Traub, E., Miners, J.O., Lelo, A., Birkett, D.J., 1988. Biochemical validation of self-reported caffeine consumption during caffeine fading. J. Behav. Med. 11, 15–30.
James, J.E., Stirling, K.P., May Hampton, B.A., 1985. Caffeine fading: behavioral treatment of caffeine abuse. Behav. Ther. 16, 15–27.
Juliano, L.M., Evatt, D.P., Richards, B.D., Griffiths, R.R., 2012. Characterization of individuals seeking treatment for caffeine dependence. Psychol. Addict. Behav. 26, 948–954.
Juliano, L.M., Griffiths, R.R., 2004. A critical review of caffeine withdrawal: empirical validation of symptoms and signs, incidence, severity, and associated features. Psychopharmacology (Berl.) 176, 1–29.
Marlatt, G.A., Gordon, J.R., 1985. Relapse Prevention: Maintenance Strategies in the Treatment of Addictive Behaviors. Guilford Press, New York, NY.
Meredith, S.E., Juliano, L.M., Hughes, J.R., Griffiths, R.R., 2013. Caffeine use disorder: a comprehensive review and research agenda. J. Caffeine Res. 3, 114–130.
Nawrot, P., Jordan, S., Eastwood, J., Rotstein, J., Hugenholtz, A., Feeley, M., 2003. Effects

of caffeine on human health. Food Addit. Contam. 20, 1–30.
Shi, J., Benowitz, N.L., Denaro, C.P., Sheiner, L.B., 1993. Pharmacokinetic-pharmacodynamic modeling of caffeine: tolerance to pressor effects. Clin. Pharmacol. Ther. 53, 6–14.
Spielberger, C.D., Gorsuch, R.L., Lushene, R.E., 1970. State-Trait Anxiety Inventory. Consulting Psychologists Press, Palo Alto, CA.
Sobell, L.C., Sobell, M.B., 1992. Timeline follow-back. In: Litten, R., Allen, J. (Eds.), Measuring Alcohol Consumption. The Humana Press Inc., Totowa, NJ, pp. 41–72.
Sweeney, M.M., Juliano, L.M., Ferré, S., Griffiths, R.R., 2018. The pharmacology of caffeine. In: Miller, S.C., Fiellin, D.A., Rosenthal, R.N., Saitz, R. (Eds.), The American Society of Addiction Medicine Principles of Addiction Medicine, Sixth Edition. Wolters Kluwer, Philadelphia, PA.
Temple, J.L., Bernard, C., Lipshultz, S.E., Czachor, J.D., Westphal, J.A., Mestre, M.A., 2017. The safety of ingested caffeine: a comprehensive review. Front. Psychiatry 8, 80.
USDA, 2015. Scientific Report of the 2015 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture. https://health.gov/dietaryguidelines/2015-scientific-report.