Spring 2017

Caffeine Withdrawal and Dependence: A Review

Alexander Roberts
arr68@zips.uakron.edu

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Alexander Roberts

Sponsor: Dr. Ronald Levant

Readers: Shana Pryor, Ginelle Wolfe

The University of Akron

Williams Honors College

Abstract

With the prevalence of caffeine use increasing in modern lifestyles, it is important to look at the symptoms of caffeine use, including withdrawal and dependence, and whether these symptoms have implications for addiction. A limited number of assessments have been developed to assess caffeine withdrawal. In order to make a call for more assessments and programs to be developed to assist with healthy caffeine use, this literature review observed recent studies focusing on withdrawal and dependence. Ozsunger et al. (2009) classified caffeine withdrawal into three categories of symptoms. Three years later, Juliano et al. (2012) used an experimental approach to develop a larger classification with seven clusters of withdrawal symptoms. Rogers et al. (2013) observed the effects of withdrawal on daily functionality. Juliano et al. (2012) assessed and interviewed participants who were physically dependent on caffeine in order to suggest further treatments for caffeine dependence. Evatt et al. (2015) developed a program for treatment for an individual problematically consuming caffeine.

INTRODUCTION

Caffeine plays a large role in many people's lifestyles. With the modern society's obsession with coffee, anyone living in an urban area can find a major coffee shop within a five-minute drive. The University of Akron alone has four Starbucks locations on campus. The price of coffee can add up significantly over time. Purchasing a Grande coffee with no cream or flavor every day would cost someone approximately $860 a year. Although caffeine is consumed almost every day by people who drink coffee, it is empirically unclear as to whether or not someone can be addicted to caffeine. There are at least four methods for assessing caffeine addiction in *The Diagnostic and Statistical Manual of Mental Disorders, 5th Edition* (DSM-5), including **Caffeine-Related Disorders (503) 305.90 (F15.929)** and Caffeine Intoxication (503) **292.0 (F15.93)** (2013). It may also be possible to apply the general definition of addiction to caffeine addiction. According to the American Society of Addiction Medicine's (2011) public policy statement:

> "Addiction is characterized by inability to consistently abstain, impairment in behavioral control, craving, diminished recognition of significant problems with one's behaviors and interpersonal relationships, and a dysfunctional emotional response. Like other chronic diseases, addiction often involves cycles of relapse and remission."

Simply put, addiction is an inability to stop using a drug. Dependence, however, occurs when "the body adapts to the drug, requiring more of it to achieve a certain effect (tolerance) and eliciting drug-specific physical or mental symptoms if drug use is abruptly ceased (withdrawal)" (2018). The purpose of this literature review is to provide a brief overview of what current research has been published and to make a call for areas of future research. One topic that came up frequently when researching caffeine was withdrawal, with some literature focusing on

physical dependence.

REVIEW OF LITERATURE

WITHDRAWAL

An important component to understanding caffeine withdrawal is to understand how the symptoms of withdrawal have been organized. In 2009, Ozsungur, Brenner, and El-Sohemy developed a system for grouping symptoms of withdrawal into three clusters, using a sample of nearly 850 participants between the ages of twenty and twenty nine. The sample was pooled from the University of Toronto's student body (Ozsungur et al., 2009). This sample selection may provide some bias because it would be very easy for a convenience sample of college students to not accurately represent the population of people who intake caffeine. However, convenience bias may have been greatly reduced due to the large size of the sample.

Ozsungur et al. (2009), provided participants with an assessment and a questionnaire of caffeine consumptions and habits. "Caffeine intake was assessed using a semi-quantitative food frequency questionnaire (FFQ), which is a method that has been shown to be a valid and reliable approach…" (Ozsungur et al., 2009, p. 542). Ozsungur et al.'s (2009) use of this measure showed how evidence for validity and reliability were assessed. In the FFQ, participants were asked how many cups of coffee or other caffeinated beverages they consumed per week or per day, depending on the frequency of consumption. They were also assessed on the frequency they drank coffee when they were not home or at work. The questionnaire, focusing on habits related to caffeine consumption, provided participants with fourteen symptoms of caffeine withdrawal and asked them to rate the severity of the symptoms they experienced within two days of not consuming any caffeinated beverage. Because this questionnaire was targeted toward

participants who regularly consumed coffee, only approximately 300 participants' data were analyzed from 495 participants (Ozsungur et al., 2009).

After analyzing the data found from the assessment and the questionnaire, Ozsungur et al. (2009) found three significant clusters into which withdrawal symptoms could be grouped: "fatigue and headache," (p. 544) (e.g., drowsiness and inability to focus) "dysphoric mood," (p. 544) (e.g., anxiety and depressed moods) and "flu-like somatic" (p. 544) (e.g., nausea and muscle pain). Most participants experienced symptoms within the fatigue and headache cluster, with less participants experiencing dysphoric moods and even less participants experiencing flu-like somatic symptoms. Although the clustering of symptoms was useful, Ozsungur et al. (2009) did not discuss how they determined the nomenclature of the three clusters in which to organize symptoms.

This study contained a few other significant limitations, which could be addressed in future research. "Subjects who responded 'Yes, I used to consume them regularly but do not anymore'... were also excluded from all analyses" (Ozsungur, 2009, p. 543). By removing analyses of participants who have abstained from consuming caffeine recently, Ozsungur et al. (2009) removed any possibility of observing long-term symptoms of withdrawal. However, by asking participants to recall more recent information, thus lowering recall bias, the data may have been more valid and reliable. Ozsungur et al. also excluded data of participants with mood disorders, which eliminated any observation of interactions between psychopathology and caffeine consumption.

Three years after Ozsungur et al.'s (2009) study, Juliano, Huntley, Harrell, and Westerman (2012) studied a method to categorize symptoms of caffeine withdrawal into seven clusters, compared to Ozsungur et al.'s (2009) three clusters. Juliano et al. (2012) administered

three questionnaires to only 213 participants with an average age of 24. The size of the sample

increased the possibility of error. Although the sample size was smaller than the previous study,

Juliano et al. (2012) gathered data from participants from both a university setting and a public

setting in Washington, DC, via advertisements and flyers. This provided their study with a more

representative sample.

Unlike Ozsungur et al. (2009), Juliano et al. (2012) took an experimental approach to

their study. The three questionnaires provided to participants assessed their caffeine consumption

habits, withdrawal symptoms, and cravings for caffeine and sweets. The effect of cravings was

appropriately given its own questionnaire because "there is insufficient evidence that craving is a

valid symptom of caffeine withdrawal" (Juliano et al., 2012, p. 233). Most participants were

asked to take the questionnaires after not consuming caffeine for sixteen hours, while one

subgroup took the questionnaire both halfway through the sixteen hour window and after the

window. Saliva samples were taken to confirm that participants had successfully not consumed

any caffeine. The participants who completely abstained from consuming caffeine during the

sixteen hours were separated into two other subgroups. One subgroup consumed decaffeinated

coffee and filled out the questionnaires again. The other subgroup consumed decaffeinated

coffee with a flavorless caffeinated solution added (so that they were not aware that they were

consuming caffeine). The design of this experiment was made even more appropriate because of

its double-blind conditions. Neither the experimenters nor the participants knew which group

was consuming caffeine, which may have effectively decreased observer bias and a placebo

effect. This experimental approach was much more extensive than Ozsungur et al.'s (2009)

assessment consisting of one questionnaire.

Juliano et al. (2012) more thoroughly explained their methods of data analysis. Using

principal components analysis, they found seven significant factors: "1: Fatigue/drowsiness; 2.

Low alertness/difficulty concentrating; 3. Mood disturbances; 4. Low sociability/motivation to

work; 5. Nausea/upset stomach; 6. Flu-like feelings; and 7. Headache" (Juliano et al., 2012, p.

231). Although they found seven significant factors using principal components analysis,

principle axis factoring would have been a more reliable analysis of data to use. Juliano et al.

(2012) found that there was not a significant difference in severity of withdrawal systems

between any of the subgroups. However, they found that participants who were regular coffee-

drinkers prior to the study experienced had significantly stronger symptoms than participants

who did not regularly drink coffee (2012).

Overall, this seemed to be a more thorough study, with a few points of hesitation. With

the analysis of more assessments, Juliano et al. (2012) discussed more specific clusters of

symptoms than did Ozsungur et al. (2009). Juliano et al. (2012) took an experimental approach

with a more representative sample in order to decrease sampling error. However, the sample size

needed to be larger to further decrease the chance of error. They also did not thoroughly explain

the symptoms of each cluster and how or when specific symptoms occurred in participants after

abstaining from caffeine. Like Ozsunger et al. (2009), Juliano et al. (2012) did not study the

effects of withdrawal in a long-term setting.

Rogers, Heatherly, Mullings, and Smith (2013) also took an experimental approach to

studying withdrawal symptoms. However, unlike the previous studies, which classified

symptoms into clusters, Rogers et al. (2013) observed the effects of withdrawal on daily

functionality. This study collected data from 369 participants, "aged between 18 and 62" (Rogers

et al., 2013, p. 231). Although this could be a decent sample size, power analysis of the sample

was not provided, as well as statistical information, including mean age and methods of

gathering participants for data collection. Like previous studies, this may have been a convenience sample found on a college campus. Participants were given a questionnaire to assess their caffeine consumption habits so that they may be placed in one of two caffeine-consumption groups: "non-low" or "medium-high" (Rogers et al., 2013, p. 231). Both groups were split into two subgroups, with one subgroup consuming caffeine and the other consuming a placebo. Each subgroup consumed coffee with caffeine or placebo, tasting identical, once in the morning and again in the afternoon. The coffees tasted identical with the use of a caffeine solution and placebo that had little to no noticeable flavor. Like in Juliano et al.'s (2012) study, the caffeine/placebo treatments were consumed under double-blind conditions to control for observer bias and placebo effect.

Rogers et al. (2013) provided participants with multiple tests for data collection. First, participants were asked to tap on a space bar in thirty-second intervals. To observe "mental awareness, sleepiness, and anxiety/jitteriness" (p. 231), Rogers et al. (2013) provided participants with items from a scale developed in a previous study. Participants were asked to rank these scale items from zero to nine. To observe effects on recognition, participants were given a five-digit sequence of numbers. While quickly looking at of thirty five-number sequences strobed on a computer screen, participants were asked to indicate if they saw the original sequence of numbers on each screen. Rogers et al. (2013) by asking participants to press the space bar as soon as they observed a small star pop up on the computer screen. Participants repeated each test four times.

Using analyses of variance (ANOVAs) and post-hoc Tukey's tests, Rogers et al. (2013) found a number of significant results. Memory recognition was the only variable that was not significantly affected by caffeine withdrawal. Rogers et al. (2013) found that "the difference

between caffeine and placebo treatments was larger for medium-high consumers, with the striking result being lower mental alertness, greater sleepiness, and… poorer performance on all tasks in medium-high consumers than in the other three groups" (p. 233). This indicated that people who regularly consume caffeine experience stronger withdrawal symptoms upon caffeine abstinence than people who do not regularly consume caffeine.

One surprising finding of this study was that caffeine consumption did not effectively increase levels of mental alertness in participants who don't drink a lot of caffeine. Rogers et al. (2013) also found that caffeine brought alertness and performance back up to a "normal state of affairs" (p. 235), but did not increase levels beyond that. "The present results demonstrate adverse effects of overnight caffeine withdrawal…, which increase in severity as withdrawal continues into the afternoon" (Rogers et al., 2013, p. 235). Unlike in the previous studies, this was the first mention of how quickly one begins to experience withdrawal.

Overall, Rogers et al. (2013) developed a thorough experimental design with simplistic yet effective data analyses. Rogers et al.'s (2013) use of ANOVA and Tukey's tests made the "data analysis" section of this study easier to read and understand for readers with less knowledge of advanced statistical analyses, such as undergraduate students. Rogers et al. (2013) also provided readers with simple and effective figures to illustrate their results. However, they did not provide any geographical or statistical statistics of the sample. Rogers et al. (2013) also did not mention any methods used to maintain variability or reliability, so one may be hesitant to generalize their results to a population of regular caffeine consumers.

DEPENDENCE

As previously stated, withdrawal is a component of physical dependence of caffeine.

Juliano and Daniel observed the effects of dependence in multiple recent studies, with Richards and Griffiths (2012). They gathered participants who identified as dependent on caffeine and who were interested in receiving help for abstaining from caffeine consumption. Juliano et al. (2012) "sought to identify and characterize individuals who were interested in treatment for problematic caffeine use" (p. 949). 275 participants around the Washington, D.C. area who consumed at least 100mg of caffeine a day (2012) were eligible to participate in a phone screening. Of these participants, 94 participants consented to a structured interview. The interviewed participants were mostly European American with a mean age of 41 years (2012). Although the mean age was higher than most studies on college students, the European American statistic may have prevented the findings to be significantly representative of other races/ethnicities.

The phone screening included multiple questionnaires that assessed their general demographics, medical history, caffeine consumption habits, history of trying to abstain from consuming caffeine, and how quickly they consumed caffeine after waking up in the morning. Other reports, like the Beck Depression Inventory, were used to observe mood and anxiety in the participants. "Following self-report assessments, the Structured Clinical Interview for *DSM-IV* Axis-I disorders… was administered by a master's or doctoral level [student] clinician" (Juliano et al., 2012, p. 949). Structured interviews are often higher in validity than unstructured interviews. Graduate level administering was an appropriate design of the study to further increase validity.

Using the assessments and interviews, Juliano et al. (2012) found significant data to characterize participants who were interested in receiving assistance with caffeine dependence. 81% of participants consumed a caffeinated beverage within one hour after waking up. Over

50% of participants were serious about wanting to reduce caffeine consumption, while over 70% were unable to commit to caffeine reductions for at least a week (2012). According to Juliano et al. (2012), "96% of participants reported two or more caffeine withdrawal symptoms when abstaining from caffeine" (p. 51). Depression, anxiety, and mood disorders were identified in a small percentage of the sample. Caffeine dependence was not significantly correlated to the type of caffeinated beverage consumed or gender. Unlike previous studies, Juliano et al. (2012) found that soda was the most frequently consumed beverage within the sample, implying that coffee is not the only beverage that causes dependence and withdrawal symptoms. 43% of participants were instructed to reduce caffeine consumption, but few of them were given specific directions to successfully do so (2012). Juliano et al. (2012) suggest that further research is needed to develop programs for effectively reducing caffeine consumption.

A few limitations were identified in Juliano et al.'s (2012) study on dependence. First, 80% of participants were European American. This lack of diversity may prevent the data from being generalizable to populations of ethnic and racial minorities. The mean age of the sample was 41 years, which may have affected some of the results. For example, although participants were instructed to decrease caffeine consumption, this finding may not be applicable to younger generations because some of the older participants may have more heart problems. However, this has been the largest mean age, making it the most generalizable to people older than young adults. The small sample that was interviewed may affect the validity of the findings, but the use of a structured interview provided a valid measurement to the study. Although there were a small number of limitations, this study on dependence provided an elaborate identification of habits and characteristics of people who are dependent on caffeine.

Evatt, Juliano, and Griffiths (2016) sought to develop a program for individuals who are

believed to be problematically consuming caffeine based upon the results of the previous study conducted by Juliano et al. (2012). Of the 94 participants interviewed by Juliano et al. (2012), 67 participants were offered an opportunity to participate in a caffeine reduction program for a reward of $70. The participants were separated into two groups, one group being treated approximately two weeks after the interview and another group being treated approximately six weeks after the interview. The purpose of the groups being interviewed a month apart was to control for time between the two groups (2016).

The program, administered by a trained bachelor's level student clinician, included a manual for processes to reduce or quit caffeine consumption. "The manual consisted of several treatment components designed to assist the participant designed to assist the participant to commit to a treatment goal, outline a plan for reducing caffeine over time, and use tools to cope with issues that may arise when reducing caffeine consumption" (Evatt et al., 2016, p. 116-117). Using the manual, the clinician helped participants understand the advantages and disadvantages of consuming caffeine in order to further understand the reasons individuals quit consuming caffeine. After the session, participants were instructed to gradually consume smaller amounts of caffeine for four weeks in order to reduce strength of withdrawal symptoms. According to Evatt et al. (2016), participants were also instructed to track their caffeine consumption habits daily in "caffeine diaries" (p. 117) throughout the five weeks.

The caffeine diaries, as well as measured salivary caffeine levels, were used to measure the two groups' caffeine consumption before and after treatment. Evatt et al. (2016) found significant differences between the results of the two treatment administration groups. The group given treatment two weeks after interviews consumed significantly less caffeine five weeks after treatment than the group that was treated six weeks after interviews. Caffeine consumption levels

were measured in participants across four follow-up assessments taken throughout the next fifty-two weeks. "Among the twenty-seven participants who achieved their individual goal, nine (33%) relapsed to levels above their treatment goal..." (Evatt et al., 2016, p. 119).

A few limitations were found in this study. First, Evatt et al. (2016) did not describe how caffeine consumption was to be measured in the caffeine diaries by participants. Participants may have indicated consuming more or less caffeine than they actually consumed. Also, the use of independent diaries may have increased the possibility of response bias, the possibility that participants recorded consuming less caffeine for more favorable data. Although there were a few limitations, Evatt et al. (2016) provided a framework for developing more intensive treatments for reducing caffeine consumption. A further developed treatment plan with a larger sample size could provide significant implications for future studies on physical dependence.

DISCUSSION

This literature review critiqued multiple studies focusing on caffeine withdrawal and dependence. Caffeine withdrawal has been studied thoroughly, with observations of symptoms, categorization, and possibilities of symptom reduction. However, it was much more difficult to locate literature observing dependence.

A few criticisms could be found in most to all of the literature. Each study observed symptomology over a short period of time, approximately one to two days after abstinence from coffee consumption. Although this is an effective time to study withdrawal because symptoms begin overnight (Rogers et al., 2013), no literature has observed the effects of withdrawal over time. Another pattern across the literature was having a small sample sizes. The sample sizes often were below 200, and mean ages of approximately eighteen to twenty years old. A majority

of the samples consisted of mostly college students. Sampling mostly college students is a

method of convenience, which increases sampling error when attempting to generalize results to

a population. Almost all of the literature focused on coffee as the main source of coffee

consumption. Juliano et al. (2012) looked at other sources of caffeine such as soda. In doing so,

Juliano et al. (2012) was able to study participants who consumed caffeine in sources other than

coffee. Multiple studies excluded participants from data analysis because of their limited coffee

consumption, but they have been consuming caffeine in soda or chocolate.

Although the literature contained a number of criticisms, limitations can be found in the

literature review as well. Many of the studies in the literature review were over five years old.

Although there was a lack of studies from 2015-2018, this may have been due to limitations in

database access. Some current literature has begun observing effects of caffeine consumption on

anxiety disorders in rats. O'Neill et al. (2016) found that adolescent rats showed more anxiety-

induced behaviors as adults. Hughes et al. (2017) found higher levels of anxiety and lower levels

of attention in adult male rats than in females. These findings are interesting and further studies

observing caffeine and anxiety in humans would have significant implications, including

developing stronger withdrawal programs for adults suffering from anxiety.

Juliano et al. (2012) found that although participants had been previously advised to

reduce caffeine consumption, no programs existed that assisted participants with long term

caffeine abstinence. Because some people suffer health problems from consuming caffeine (due

to complications with sugar, not caffeine), it is necessary that more programs on caffeine

reduction are developed and implemented into the medical field. Evatt et al. (2016) developed a

five-week program in which participants independently tracked and reduced caffeine

consumption. Of the 67 participants, 27 participants met their personal goal after the five-week

program, but only nine of them relapsed. This suggests two possibilities. First, having a personal goal may motivate an individual more to continue reducing their caffeine consumption. Second, reducing caffeine consumption might require more extensive clinician involvement to keep participants on track to meet their goals.

In order for the programs to be more beneficial, it is also necessary that future research focuses on developing methods for measuring and assessing dependence across multiple sources of caffeine. In doing so, professionals will be able to best determine caffeine habits, whether or not these habits are unhealthy, and to develop a personalized plan for abstaining from caffeine consumption. In the words of Juliano et al. (2012), "future research is necessary to determine the likelihood of achieving success with caffeine reduction and/or cessation" (p. 952). Using Evatt et al.'s (2016) treatment as a framework may be a successful first step in developing more advanced and possibly more effective treatment plans.

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Completed Honors Project

Alexander Roberts