



Student Works

2021-07-26

Methods to Stop Caffeine Use and Minimize Caffeine Withdrawal Symptoms in the State of Caffeine Dependence: A Literature Review

Morgan Behling
Brigham Young University, mbehling37@yahoo.com

Blaine Winters
Brigham Young University, Blaine-Winters@byu.edu

Follow this and additional works at: <https://scholarsarchive.byu.edu/studentpub>



Part of the [Nursing Commons](#)

BYU ScholarsArchive Citation

Behling, Morgan and Winters, Blaine, "Methods to Stop Caffeine Use and Minimize Caffeine Withdrawal Symptoms in the State of Caffeine Dependence: A Literature Review" (2021). *Student Works*. 322.
<https://scholarsarchive.byu.edu/studentpub/322>

This Peer-Reviewed Article is brought to you for free and open access by BYU ScholarsArchive. It has been accepted for inclusion in Student Works by an authorized administrator of BYU ScholarsArchive. For more information, please contact scholarsarchive@byu.edu, ellen_amatangelo@byu.edu.

Methods to Stop Caffeine Use and Minimize Caffeine Withdrawal Symptoms
in the State of Caffeine Dependence: A Literature Review

Morgan Behling

A scholarly paper submitted to the faculty of
Brigham Young University
in partial fulfillment of the requirements for the degree of
Master of Science

Blaine Winters, Chair

College of Nursing
Brigham Young University

Copyright ©2021 Morgan Behling

All Rights Reserved

ABSTRACT

Methods to Stop Caffeine Use and Minimize Caffeine Withdrawal Symptoms in the State of Caffeine Dependence: A Literature Review

Morgan Behling
College of Nursing, BYU
Master of Science

Caffeine is the most consumed psychoactive drug in the world and those who consume it frequently become dependent. Even if individuals desire to quit caffeine, they may not be able to due to withdrawal side effects, or a lack of knowledge of how to quit. Harmful effects of long-term caffeine consumption include fatigue, irritability, headaches, nausea, and depression. The goal of this literature review was to explore current evidence on different methods to quit or reduce caffeine use and minimize caffeine withdrawal effects in those who are dependent. A literature review of studies from 2014 to 2020 was conducted using the databases CINAHL, PsychInfo and Medline. Using a gradual caffeine dose taper is successful in helping people quit caffeine or reducing caffeine intake and keeping a journal of caffeine intake is a useful tool to promote long-term cessation of caffeine consumption. Exercising for 20 minutes a day helps combat withdrawal effect, by positively increasing mood and alertness. Professional counseling has proven effective in assisting with caffeine withdrawal and providing individuals with information about caffeine may assist in both reducing or stopping caffeine intake. Nurse practitioners should assess patients for caffeine use and desire to reduce caffeine consumption. Strategies identified in this literature review may be helpful in assisting patients quit or reduce caffeine intake while minimizing withdrawal effects.

Keywords: caffeine; withdrawal; nurse practitioner; review

TABLE OF CONTENTS

Title Page	i
Abstract	ii
Table of Contents	iii
Methods to Stop Caffeine Use and Minimize Caffeine Withdrawal Symptoms in the State of Caffeine Dependence: A Literature Review	
	1
Introduction.....	1
Background.....	2
Methods.....	3
Results.....	4
Using an Instructional Manual with or without a Counselor	4
The Role of Placebo in Reducing Withdrawal Symptoms	5
False Genetic Information.....	6
Blinded Dose Taper	6
Aerobic Exercise.....	7
Discussion.....	8
Tapering Caffeine Intake	8
Keeping a Daily Record of Caffeine Use	9
Symptom Reduction.....	9
Additional Resources	9

Conclusion 10

References 11

Appendix A 14

Figure 1 PRISMA Flow Diagram 17

Methods to Stop Caffeine Use and Minimize Caffeine Withdrawal Symptoms
in the State of Caffeine Dependence: A Literature Review

Introduction

Caffeine is the most consumed psychoactive drug in the world. In America, 87% of adults and children regularly consume beverages and foods containing caffeine (Ferre, 2016). With how prevalent caffeine use is, nurse practitioners will frequently care for patients who consume caffeine. Short-term benefits of caffeine consumption include increased alertness, concentration, and improved mood (Nehlig, 2015). Patients report caffeine consumption for reasons such as increasing energy for sports or exercise, increasing their ability to focus, increasing alertness, or simply because they like how it makes them feel (Scuri et. al, 2018). Due to its benefits, some patients will frequently consume caffeine, and become dependent upon it in order to function normally. Caffeine dependence is associated with decreased sleep quality, daytime drowsiness, headaches, and psychological distress (Ogeil & Phillips, 2015).

Caffeine dependence is a worldwide issue. In the International Statistical Classification of Diseases and Related Health Problems, the World Health Organization (WHO) categorizes caffeine as a psychostimulant that produces withdrawal and dependence disorders (Budney & Emond, 2014). In addition, the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders identifies caffeine withdrawal as a formal disorder (Budney & Emond, 2014).

Caffeine withdrawal symptoms include headache, fatigue, low energy, irritability, anxiety, poor concentration, depressed mood, and tremors (Ogeil & Phillips, 2015). Many patients report these negative withdrawal symptoms as the primary reason they continue caffeine intake, even when they have a desire to quit. The purpose of this literature review is to examine

different methods for quitting or decreasing caffeine intake and managing caffeine withdrawal symptoms.

Background

Caffeine works by increasing and enhancing dopamine signaling in the brain through increased dopamine receptor availability. Other stimulant drugs such as cocaine function similarly. Dopamine controls various physiological functions throughout the body and in the brain by acting on receptors D1, D2, D3, D4, and D5 (Mishra et al., 2018). These receptors help control and regulate human motivation, concentration, psychomotor speed, concentration, and the ability to experience pleasure (Dunlop & Nemeroff, 2007).

In addition, dopamine is the primary neurotransmitter involved in the reward pathway in the brain, which is made possible in part by the euphoric effects of dopamine (Dunlop & Nemeroff, 2007). Illegal substances and prescription drugs with high addiction potential work through the same reward pathway. Some drugs, like prescription medications, inhibit the dopamine transporter (Mishra et. al, 2018), which is the protein responsible for removing dopamine from the neural synapse.

Caffeine specifically increases dopamine signaling in the brain by increasing dopamine receptor availability (Volkow et. al, 2015). Caffeine has been found to increase the availability of D2 and D3 receptors in the putamen and ventral striatum (Volkow et. al, 2015). Studies have shown that increases in D2 and D3 receptor availability in the ventral striatum, caused by ingesting caffeine, are what temporarily increase alertness in caffeine-consuming individuals (Volkow et. al, 2015). By increasing the availability of these dopamine receptors, more dopamine can bind to receptors, which then increases dopaminergic signaling in the brain, thus increasing the overall effect of dopamine (Mishra et. al, 2018). However, these effects of

increased dopamine are only temporary. Over time, with long-term consumption of caffeine, the brain will stop producing as much dopamine as normal (Mishra et. al, 2018). Instead, it begins to compensate, relying on increasing amounts of caffeine to achieve normal amounts of dopamine and dopaminergic signaling. As a result, caffeine withdrawal symptoms occur, such as tiredness, fatigue, and irritability.

Methods

A literature review was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The databases searched were Medline, CINAHL Complete, and PsychInfo. An article search was completed from the years 2014 to 2020. The terms, “caffeine AND addiction or withdrawal or stop” were used, which yielded 430 research articles. To limit the population to adults, the results were further narrowed by adding the terms, “NOT child or adolescent,” which yielded 366 results. By adding the terms, “NOT rat or rodents or mice or animal and NOT alcohol or nicotine,” the search was narrowed one final time to exclude all studies on animals, and all articles that examined caffeine use along with alcohol or nicotine use. One hundred forty-six articles remained, and once duplicates were removed the article list decreased to 134. After title and abstract review, 115 articles were excluded for not meeting the purpose of the review. Articles that solely discussed caffeine side effects, caffeine use, or caffeine consumption were eliminated. Nineteen full-text articles were assessed for eligibility. Articles included directly examined methods to decrease or stop caffeine intake and improve caffeine withdrawal symptoms. In total, seven articles met the inclusion criteria for this review (See Figure 1 and Appendix A).

Results

Using an Instructional Manual with or without a Counselor

Two studies examined the effectiveness of using an instructional manual to help caffeine-dependent patients abstain. The manual contained information such as a list of caffeine content in various food and drinks, general information about caffeine, behavioral strategies to decrease caffeine intake, and a journal with a graph for patients to record their daily caffeine intake. One study provided only the manual to participants while the other included the manual and a 60-minute counseling session (Evatt et al., 2016; Sweeney et al., 2019). During the counseling session, the counselor taught participants about caffeine dependence, withdrawal symptoms, and coping strategies to overcome stress and the desire to consume caffeine (Evatt et al., 2016). The participants in both studies recorded daily caffeine intake in a journal during and after the study (Sweeney et al., 2019). Both studies had participants gradually decrease caffeine intake in order to minimize withdrawal effects (Sweeney et al., 2019). The first study instructed patients to taper their caffeine consumption to 75% of their normal caffeine in the first week, 50% in their second week, 25% during the third week, 12.5% during the fourth week, and to as little as possible the fifth week (Evatt et al., 2016). The second study did not specify the exact details of the caffeine taper but gave the participants the general information on how to taper in the manual (Sweeney et al., 2019).

Both studies found the caffeine taper and instructional manual to be effective in reducing or eliminating caffeine intake up to the 1-year mark. Both found journaling to be helpful in reducing caffeine intake. The session with the counselor also was successful in reducing caffeine intake. Those who had a session with a counselor on average reduced their caffeine by

slightly more (77% reduction) than those who did not meet with a counselor (75% reduction), up to a year afterwards (Sweeney et al., 2019).

The Role of Placebo in Reducing Withdrawal Symptoms

The role of using placebo caffeine to help manage caffeine withdrawal symptoms was also studied. One study evaluated 89 adults, who self-identified as moderate to heavy coffee drinkers (Mills et al., 2016). The participants were required to drink three cups of coffee in a 24 hour period, and then go 24 hours without any caffeine intake. After 24 hours without caffeine intake the participants blood pressure was measured, and they completed the Caffeine Withdrawal Symptom Questionnaire (CWSQ) test to assess their withdrawal symptoms. The CWSQ test measures symptoms such as fatigue, mood disturbances, personal motivation, nausea, and headache. A low score indicates mild withdrawal symptoms, while a high score indicates more intense withdrawal symptoms. Patients completing the questionnaire then drank a cup of decaffeinated coffee. Half the group was told the coffee was decaffeinated, and half was told the coffee was caffeinated. After 45 minutes, participants had their blood pressure measured, and completed the CWSQ. Participants who believed they drank caffeinated coffee had a reduction of 14.6 points on the CWSQ test after drinking the beverage, while the group believing they drank decaffeinated coffee had only a 5.5-point reduction (Mills et al., 2016). There was no statistically significant change in blood pressure in either group (Mills et al., 2016).

In another study, the effect of caffeine content on withdrawal symptoms was evaluated (Mills et al., 2017). The researchers found that patients who believed they were drinking caffeine when they were actually not, reported a lower CWSQ score than those who knew they were consuming a decaffeinated drink. These findings were validated by Juliano et al. (2019) who discovered participants who believed they were drinking caffeine when actually given a

decaffeinated drink experienced less withdrawal symptoms than those who knew they were consuming a decaffeinated beverage (Juliano et al., 2019).

False Genetic Information

The effect of genetic counseling and false genetic information on caffeine withdrawal symptoms has been studied. One study analyzed how withdrawal response during cessation of caffeine is affected when a participant is told they have a certain gene related to caffeine withdrawal (Mills et al., 2017). Ninety-three caffeine users were tested with a false DNA test, which was obtained through a swab of the cheek. The participants then met with a researcher who informed them that the presence of a specific allele on the dopamine receptor gene had been found to greatly increase caffeine withdrawal symptoms. Three days later, the participants were called with their false genetic test results and were told whether they tested positive or negative for the gene. The participants were again informed of the effects of this gene on caffeine withdrawal. Those told they tested positive for the gene were warned they may be more susceptible to intense caffeine withdrawal symptoms. Then participants were instructed to go for 24 hours without caffeine and measure their withdrawal symptoms on a self-reported caffeine withdrawal scale. After the 24-hour period, participants were instructed to drink a cup of coffee and report their withdrawal symptoms again. The Post-Beverage and Pre-Beverage CWSQ scores were compared, and the differences were not statistically significant ($\chi^2(1) = 0.18$, $p = 0.671$) (Mills et al., 2017). Overall, the false genetic information had no effect on caffeine withdrawal symptoms.

Blinded Dose Taper

One study aimed to test the effect of a blinded dose taper on caffeine withdrawal effects. In this study, three groups of caffeine-dependent participants had their daily intake of caffeine

gradually decreased from 300mg per day to 0mg during a 4-day period (Mills et al., 2018). The first day the participants were given 300mg of caffeine, the second day 200mg, the third day 100mg, and the fourth day 0mg. Participants in the designated “open reduction group” knew how much caffeine they received. Participants in the blinded group were not given any information regarding the amount of caffeine they received. A third group was designated “the deceptive group,” and were given inaccurate information regarding their caffeine intake. Twice daily, all study participants completed the CWSQ test to monitor their withdrawal symptoms. The test was completed in the morning and afternoon. In the morning, there was no significant difference in the CWSQ scores between the three groups (Mills et al., 2018). However, in the afternoon, the open reduction group experienced a mean increase of 6.95 points on the CWSQ test per day, the deceptive reduction group increased by 2.12 points per day, and the blinded group increased by 2.73 points per day (Mills et al., 2018). According to these data, the caffeine dose information reported to participants greatly influenced their withdrawal symptoms. The deceptive group was told their caffeine was decreased by a lot less than it actually was, and they reported the least amount of caffeine withdrawal symptoms.

Aerobic Exercise

One study examined the effect of aerobic exercise on caffeine withdrawal. In the study, caffeine-dependent participants consumed no caffeine for 12 hours. After consuming no caffeine for 12 hours, the participants’ CWSQ scores increased by an average of 14.88 points from baseline (Morava et al., 2019). The participants were randomly assigned to either consume caffeine or exercise by briskly walking for 20 minutes. The participants in the caffeine consumption group had a mean reduction of 12.91 points on the CWSQ after ingesting caffeine. The exercise group had a mean reduction of 8.07 points on the CWSQ test (Morava et al., 2019).

These results support the assertion that brisk exercise has utility in reducing caffeine withdrawal symptoms. Specifically, the participants indicated that the exercise gave them extra energy, put them in a better mood, and increased their alertness. The exercise participants also showed a short-term increase in their working memory (Morava et al., 2019).

Discussion

Nurse practitioners should routinely assess a patient's caffeine usage as well as any desire to discontinue caffeine ingestion, which is especially important if caffeine use is problematic, contraindicated, or causing unwanted side effects. Patients should be educated regarding the withdrawal effects of caffeine, as well as the health benefits of discontinuing caffeine. Benefits to quitting caffeine include increased energy, less fatigue, better sleep at night, less headaches, less irritability, and better focus.

Although the use of a placebo and false genetic information in mitigating caffeine withdrawal symptoms have been studied and included in this literature review, this specific information may not be helpful to a nurse practitioner, as it would be difficult to apply in a clinical setting. It also would not be ethical for a nurse practitioner to mislead a patient by using placebos or false genetic information.

Tapering Caffeine Intake

One strategy identified in quitting caffeine use while decreasing caffeine withdrawal symptoms is to gradually decrease caffeine intake. One study found it effective for participants to consume 75% of their normal caffeine in the first week, 50% in the second week, 25% during the third week, 12.5% during the fourth week, and as little as possible the fifth week (Evatt et al., 2016). This strategy could easily be implemented in a clinical setting.

Keeping a Daily Record of Caffeine Use

Another strategy identified to assist in quitting caffeine use is to keep a daily record of caffeine intake. This is something that could easily be implemented by a nurse practitioner. Nurse practitioners can encourage patients wanting to quit caffeine to keep a daily journal of their ingested caffeine. The patient may also record how they felt, how they slept, any withdrawal effects, and any stressors in their life. If significant issues are noted via journaling, the nurse practitioner could then teach coping strategies, or refer the patient for counseling in an attempt to resolve the identified problems.

Symptom Reduction

There are several strategies nurse practitioners can recommend to reduce caffeine withdrawal symptoms. Exercise is one effective strategy to help reduce caffeine withdrawal symptoms (Morava et al., 2019). Specifically, briskly walking for 20 minutes was associated with a lower CWSQ score, and was found to increase participants alertness and energy. In addition, it put participants in a better mood, and increased their short-term memory. Daily exercise should be recommended while a patient is tapering caffeine use in an attempt to mitigate withdrawal symptoms. Other helpful interventions may include over-the-counter pain medications for headaches, instruction regarding sleep hygiene, and a prescription for short-term anti-nausea medication.

Additional Resources

This literature review also identified several resources a nurse practitioner can provide to their patients in their efforts to quit or reduce caffeine consumption. A nurse practitioner can give their patient a manual or handout with information about how to reduce caffeine intake, what withdrawal symptoms to expect, and strategies to help reduce caffeine intake. In addition, a

nurse practitioner can recommend a patient start seeing a counselor to help with any underlying issues that may contribute to caffeine intake.

Conclusion

The purpose of this review was to identify strategies for decreasing caffeine dependence or reducing caffeine intake, and minimizing withdrawal symptoms while doing so. Based on research findings, several strategies were identified. Exercise helps in reducing caffeine withdrawal symptoms. Using a gradual caffeine dose taper is successful in helping people quit caffeine or reduce their caffeine intake, while simultaneously mitigating withdrawal symptoms. Meeting with a counselor to discuss ways to overcome the temptation to use caffeine, as well as providing individuals with a written manual with information about caffeine has proven effective in reducing caffeine consumption. Keeping a journal of caffeine intake, and having participants continue to record their caffeine intake after treatment is associated with long-term success in quitting caffeine.

References

- Budney, A. J., & Emond, J. A. (2014). Caffeine addiction? Caffeine for youth? Time to act! *Addiction, 109*(11), 1771-1773. <https://doi.org/10.1111/add.12594>
- Dunlop, B. W., & Nemeroff, C. B. (2007). The role of dopamine in the pathophysiology of depression. *Archives of General Psychiatry, 64*(3), 327–337.
<https://doi.org/10.1001/archpsyc.64.3.327>
- Evatt, D. P., Juliano, L. M., & Griffiths, R. R. (2016). A brief manualized treatment for problematic caffeine use: A randomized control trial. *Journal of Consulting and Clinical Psychology, 84*(2), 113–121. <https://doi.org/10.1037/ccp0000064>
- Ferre, S. (2016). Mechanisms of the psychostimulant effects of caffeine: Implications for substance use disorders. *Psychopharmacology, 233*(10), 1963-1979.
<https://doi.org/10.1007/s00213-016-4212-2>
- Juliano, L. M., Kardel, P. G., Harrell, P. T., Muench, C., & Edwards, K. C. (2019). Investigating the role of expectancy in caffeine withdrawal using the balanced placebo design. *Human Psychopharmacology: Clinical and Experimental, 34*(2).
<https://doi.org/10.1002/hup.2692>
- Mills, L., Boakes, R. A., & Colagiuri, B. (2016). Placebo caffeine reduces withdrawal in abstinent coffee drinkers. *Journal of Psychopharmacology, 30*(4), 388–394.
<https://doi.org/10.1177/0269881116632374>
- Mills, L., Boakes, R. A., & Colagiuri, B. (2018). The effect of dose expectancies on caffeine withdrawal symptoms during tapered dose reduction. *Journal of Psychopharmacology, 33*(8), 994–1002. <https://doi.org/10.1177/0269881118817158>

Mills, L., Dar-Nimrod, I., & Colagiuri, B. (2017). Effect of genetic information and information about caffeine content on caffeine withdrawal symptoms. *Scientific Reports*, 7(1).

<https://doi.org/10.1038/s41598-017-08678-4>

Mishra, A., Singh, S., & Shukla, S. (2018). Physiological and functional basis of dopamine receptors and their role in neurogenesis: Possible implication for parkinson's disease.

Journal of Experimental Neuroscience, 12(1), 1–8.

<https://doi.org/10.1177/1179069518779829>

Morava, A., Fagan, M. J., & Prapavessis, H. (2019). Effects of caffeine and acute aerobic exercise on working memory and caffeine withdrawal. *Scientific Reports*, 9(1).

<https://doi.org/10.1038/s41598-019-56251-y>

Nehlig, A. (2015). Effects of coffee/caffeine on brain health and disease: What should I tell my patients? *Practical Neurology*, 16(2), 89-95. [https://doi.org/10.1136/practneurol-2015-](https://doi.org/10.1136/practneurol-2015-001162)

[001162](https://doi.org/10.1136/practneurol-2015-001162)

Ogeil, R. P., & Phillips, J. G. (2015). Commonly used stimulants: Sleep problems, dependence and psychological distress. *Drug and Alcohol Dependence*, 153(1), 145-151.

<http://doi.org/10.1016/j.drugalcdep.2015.05.036>

Scuri, S, Petrelli, F, Tesauro, M, Carrozzo, F, Kracmarova, L, & Grappasonn, I. (2018) Energy drink consumption: A survey in high school students and associated psychological effects. *Journal of Preventive Medicine and Hygiene*, 59(1), 75-79.

<https://doi.org/10.15167/2421-4248/jpmh2018.59.1.898>

Sweeney, M. M., Meredith, S. E., Juliano, L. M., Evatt, D. P., & Griffiths, R. R. (2019). A randomized controlled trial of a manual-only treatment for reduction and cessation of

problematic caffeine use. *Drug and Alcohol Dependence*, 195, 45–51.

<https://doi.org/10.1016/j.drugalcdep.2018.10.034>

Volkow, N., Wang, G., Logan, J., Alexoff, D., Fowler, J., Thanos, P., Wong, C., Casado, V., Ferre, S., & Tomasi, D. (2015). Caffeine increases striatal dopamine D2/D3 receptor availability in the human brain. *Translational Psychiatry*, 5(4), 1–6.

<https://doi.org/10.1038/tp.2015.46>

Appendix A

Citation	Design	Purpose of the Study	Sample Size	Methods	Results
(Evatt et al., 2016)	Randomized Control Trial	The purpose of this study was to develop and test a therapist-guided manualized treatment for caffeine use including cognitive-behavioral therapy and five weeks of gradually tapering down caffeine consumption.	67	Individuals seeking treatment for problematic caffeine use were randomized using a waitlist-control design to receive immediate treatment or delayed treatment, which was six weeks later. A one-hour long treatment session designed to help individuals quit or reduce caffeine consumption was provided by a trained counselor along with a take-home booklet. After the treatment session, participants completed daily diaries of caffeine consumption for 5 weeks. They returned for follow-up assessments at 6, 12, and 26 weeks and had a telephone interview at 52-weeks post-treatment.	Treatment resulted in a significant reduction in self-reported caffeine use and salivary caffeine levels. No significant posttreatment increases in caffeine use were observed for up to 1-year follow-up. Comparisons to the waitlist-control condition revealed that reductions in caffeine consumption were due to treatment and not the passing of time.
(Morava et al., 2019)	Quasi-experimental experiment	The purpose of this study was to compare the effects of acute moderate intensity aerobic exercise to caffeine on working memory and caffeine withdrawal symptoms.	59	There were two phases to this study. In phase one, non-caffeine and caffeine consumers completed a working memory assessment, followed by acute exercise and caffeine intake. In Phase II, caffeine consumers from Phase I underwent the working memory assessment and reported caffeine withdrawal symptoms following a 12-hour deprivation period	Twenty minutes of acute aerobic exercise was effective in decreasing caffeine withdrawal symptoms. Exercise and caffeine administration improved working memory accuracy in caffeine and non-caffeine consumers.
(Sweeney et al., 2019)	Randomized control trial	The purpose of this study was to examine the usefulness of a manual-only treatment program for caffeine cessation and reduction among individuals seeking treatment for problematic caffeine use.	36	Individuals 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.	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. 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.

(Mills et al., 2017)	2 × 2 × (2) mixed design	The purpose of this study was to test the effect of genetic information and information about the caffeine content of a beverage on caffeine withdrawal, specifically if: (1) being informed that one has tested positive for a gene related to caffeine withdrawal can produce an exaggerated caffeine withdrawal response during abstinence; (2) belief that one has consumed caffeine leads to a reduction in withdrawal symptoms when no caffeine is consumed.	93	There were two two-level, between-subject factors: Priming (Gene positive or Gene negative conditions) and Caffeine Information (Told Caffeine or Told Decaf condition). The two-level within-subjects factor was time, with one measurement being taken after 24 hours without consuming caffeine (Pre-Beverage) and the other being taken 45 minutes after a cup of decaffeinated coffee (Post-Beverage). The outcome of interest was self-reported caffeine withdrawal symptoms.	Participants given decaffeinated coffee who were allowed to believe they had consumed caffeinated coffee showed a significantly greater reduction in reported caffeine withdrawal symptoms than participants who knew they had been given decaffeinated coffee. The genetic information had no effect on caffeine withdrawal symptoms.
(Juliano et al., 2019)	2 by 2 balanced placebo design	The purpose of this study was to investigate psychological influences on drug withdrawal symptomatology using a caffeine-based model.	87	Using the 2 × 2 balanced placebo design caffeine dose (given caffeinated vs decaffeinated coffee) was crossed with dose expectancy (told caffeine vs. decaf) among 87 (16-hr abstinent) regular coffee consumers in a 2-day study, in order to test caffeine cravings and withdrawal symptoms.	Participants in the decaf group reported greater caffeine cravings than those in the told caffeine both 45 minutes and 8 hour post manipulation. Those given decaf reported greater withdrawal symptoms and showed poorer cognitive performance both 45 minutes and 8 hour post manipulation, with effects for headache and flu-like symptoms first emerging 8 hour post manipulation. Giving the participants caffeine alleviated all withdrawal symptoms and cognitive decrements within 45 minutes.
(Mills et al., 2018)	A mixed between- and within-subjects design.	The purpose of this study was to test whether blinding participants to caffeine dose reductions leads to less severe withdrawal symptoms	48	Three groups of coffee drinkers had their dose of caffeine tapered from 300 mg per day to 0 mg over the course of five days and reported withdrawal symptoms twice daily. Groups were given different information about how much caffeine they were receiving. An Open Reduction group was given accurate information about dose reductions. A Blind Reduction group was given no dose information whatsoever. A Deceptive Reduction	The Open Reduction group reported more intense caffeine withdrawal symptoms than the Deceptive Reduction group on the days with the greatest discrepancy between actual dose and informed dose, indicating a nocebo effect of open versus deceptive reductions. In addition, the rate of increase in intensity of reported

				group was misinformed about the dose, with instructions suggesting that the dose remained on 300 mg for three days then dropped to 0 mg.	withdrawal symptoms in the Blind Reduction and Deceptive Reduction groups was less than that of the Open Reduction group.
(Mills et al., 2016)	2 by 2 mixed design	The purpose of the study was to use caffeine as a model to test the effect of expectancy on withdrawal symptoms, specifically whether the belief that one has ingested caffeine is sufficient to reduce caffeine withdrawal symptoms and cravings in abstinent coffee drinkers.	89	24 hour abstinent regular coffee drinkers completed the caffeine withdrawal symptom questionnaire (CWSQ) before and after receiving decaffeinated coffee. One half of the participants were led to believe the coffee was regular caffeinated coffee (the 'Told Caffeine' condition) and one half were told that it was decaffeinated (the 'Told Decaf' condition).	Participants in the Told Caffeine condition reported a significantly greater reduction in the factors of cravings, fatigue, lack of alertness and flu-like feelings of the CWSQ, than those in the Told Decaf condition.

Figure 1

PRISMA Flow Diagram

