

BRIEF REPORT

The Addictive Properties of Soft Drink Consumption Using a CTA Animal Model for Addiction

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This study further developed a behavioral model for addiction to test the APA's seventh criteria for dependency. The model was used to investigate two potential addictive properties, either caffeine or sweetener, of soft drinks. For a period of 14 days, animals orally self-administered Coke®, Caffeine Free Coke®, Diet Coke®, or Caffeine Free Diet Coke® and consumption was recorded daily. On day 15, rats were water deprived, exposed to 20 ms of 10% apple juice mixture, and administered an intraperitoneal injection of .15 M lithium chloride at 2% of body weight to provide a conditioned taste aversion. On day 16, animals were given access to 10% apple juice/treatment mixture and alternative soft drink; consumption was recorded. Results of this study showed animals consumed substances containing sugar paired with apple juice more than those containing caffeine. These findings suggest sugar to be a more addictive property of soft drinks compared to caffeine.

Key Terms: Addiction, Soft Drink, Caffeine, Sugar, Dependence, Conditioned Taste Aversion, Rats

The study of drug abuse and addictive substances holds an invested interest among clinicians, the government, employers, and the general population. Drug abuse is an indiscriminate threat that compromises the safety of the community, creates financial strain, and takes a destructive emotional toll on the user and their family. For a drug to be classified as a "drug of abuse," (or addiction as used with animals) it must meet three of seven criterion established by the American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR, 2000): (1) tolerance, (2) withdrawal, (3) increased drug administration for longer periods than intended, (4) inability to reduce or control drug use-binging, (5) spending considerable time acquiring, using, and/or recovering from drug use, (6) significant impact on daily activities, (7) continued use despite adverse _____

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Department of Psychology Austin Peay State University Clarksville, TN 37044-4537 Telephone: (931) 221-1045 Email: hockb@apsu.edu physical or psychological effects. Animal models of addiction have generally utilized the APA's first four criteria, emphasizing tolerance and withdrawal, in evaluating the addictive properties of substances (Schmidt, Schmidt & Hock, 2008). However, these four criteria are only a subset of the APA's definition of drug abuse and may be limited in providing evidence for the potential abuse of some substances. This subset focuses on evidence for physical dependency or addiction, but there is a behavioral component contributing to drug abuse that requires consideration as well.

Measuring Addiction

Animal models of addiction attempt to mimic human dependency as closely as possible. It has been determined that animals will self-administer drugs as humans do (Willner, 1997). However, popular methods rely on surgical techniques and lengthy conditioning procedures (For Reviews, see Schmidt et al., 2008; Willner), whereas, we previously proposed a more efficient, non-invasive, behavioral model using conditioned taste aversion (CTA) to measure addiction based on the APA's

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seventh criteria (Schmidt et al.). In this model, animals are offered free access to the substance daily for a short interval over two weeks. On the conditioning day (day 15) a novel substance (i.e. Apple Juice) is paired with lithium chloride (LiCl) to induce illness, and the apple juice is later presented (day 16) with the original substance and an alternative. If the animals continue consuming the original substance that is mixed with apple juice, despite the experienced illness, the animals are thought to exhibit addiction. This model emphasizes the importance of measuring motivation, not just consumption, in identifying substance abuse. One limitation of this model, as previously described (Schmidt et. al), is that our procedure only uses drugs that can be administered orally. However, by demonstrating the seventh criterion for substance abuse this model offers additional opportunities for future research to measure underlying behavioral motivations in substance abuse and possibly lend support for improved classification of substances.

Soft Drinks and Health Outcomes

Soft drinks are widely consumed despite the negative impact on health outcomes. Numerous studies link high volumes of soft drink consumption to obesity, which is consequently related to increased incidence of type II diabetes, metabolic dysfunction, cardiovascular disease, and cancers (Bray, Nielson & Popkins, 2004; Wolff and Dansinger, 2008; Vartanian, Schwartz & Brownell, 2007). Specific nutritional concerns of soft drink consumption involve the negative correlation with milk consumption-resulting in reduced intake of calcium, fruit and protein intake, and overall increased daily caloric intake with each soft drink beverage consumed (Bray et al.; Wolff and Dansinger, 2008; Vartanian et al.). Although the extent of the effects of soft drink consumption requires further investigation (Wolff and Dansinger), the negative and unpleasant effects related to soft drink consumption display a serious concern-Are soft drinks addictive? While soft drinks may not be an addictive substance in their entirety, specific properties of the beverage, such as the high content of caffeine and sugar, may play a role in promoting continued consumption despite the obvious detrimental effects on health.

Caffeine

Caffeine has been shown to share similar addictive properties with other addictive substances, such as nicotine, when tested in a CTA model measuring pre-exposure effects (Kunin, Bloch, Smith & Amit, 2001). However, many studies investigating

withdrawal and tolerance in caffeine addiction have produced weak, inconsistent results (Satel, 2006). Inconsistencies are largely due to the variability of consumption and administration of caffeine, for example coffee versus soft drinks, and the degree to which individual differences may play a role. Animal studies measuring the aversive or palliative effects of caffeine alone have also displayed varying results based on conditions, timing of administration, and dosage (Fedorchak, Mesita, Plater & Brougham, 2002; Steigerwald, Rusiniak, Ekel, & O'Regan These variables pose a challenge in 1989). determining caffeine's role as an addictive substance, however in an animal study of conditioned flavor preferences Fredorchak et al. found that low doses of caffeine paired with unsweetened Kool-Aid® flavors increased flavor preferences. In addition to caffeine concentrations, hunger mediated enhanced caffeineflavor pair preference (Fredorchak et al.). These findings suggest that caffeine may strengthen or mediate a preference for soft drinks. For example, while investigating the role of caffeine addiction in soft drinks, we (Schmidt et al.) found a strong preference for caffeinated soft drink compared to non-caffeinated soft drink, but the presence of sweeteners in the soft drinks could not be excluded from consideration when interpreting results.

Sugar and Sweeteners

The presence of sugars and sweeteners in caffeinated soft drinks may also be involved in mediating the addictiveness of these beverages. Unlike caffeine, the sweetener content of soft drinks are thought to be involved in the development of negative health outcomes associated with chronic soft consumption. drink including metabolism dysfunction thought to contribute to obesity (Bray et al., 2004; Jurgens, Haass, Castaneda, Schurmann & Koebnick, Dombrowski, et al., 2005; Wolff and Dasinger, 2008; Vartanian et al., 2007). Under certain conditions, such as intermittent feeding schedules, sugar consumption has been found to produce physical, behavioral, and neuronal symptoms that mimic those of drugs of abuse including withdrawal, craving, binging, and neurochemical fluctuations of dopamine and acetylcholine (Aveena, 2007; Aveena, Rada & Hobel, 2008). This evidence presents support for the investigation of addictive properties of soft drinks, specifically comparing preferences for caffeine and sweetener contents.

The purpose of the current study was twofold. First, to replicate the findings of Schmidt et al. and, second, extended the Schmidt et al. investigation of the role of caffeine vs. sugar addiction in soft

Group	Soft drink + 10% apple juice	Alternative soft drink
С	Coke	Caffeine Free Diet Coke
DC	Diet Coke	Caffeine Free Coke
CFD	Caffeine Free Diet Coke	Coke
CF	Caffeine Free Coke	Diet Coke

Table 1. Day 16 scheme for post-CTA test.

drinks consumption based on the APA's seventh criteria of continued drug use despite known adverse consequences. Given the widespread use of soft drinks by consumers of all ages, it is important to determine if caffeine and/or sugar content play a role in mediating an addiction to soft drinks. This study used the same behavioral model developed by our lab and described above, and aims to differentiate caffeine and sugar preference by testing Coca-Cola®, Caffeine-free Coca-Cola®, Diet Coca-Cola®, and Caffeine-free Diet Coca-Cola®. Results were expected to replicate Schmidt et al. to an extent lending support for the reliability of the new behavioral model; Results were also expected to further the soft drink investigation and possibly provide an explanation behind the propensity for continued use of soft drinks despite strong evidence for negative health outcomes of consumers. Findings may ultimately provide support for a critical examination of soft drink products and their contents.

Methods

Subjects

The study used 40 Long-Evans (Harlan) rats 135 days old. There were four different groups with 10 rats assigned to each group. Group C received Coke® while group DC received Diet Coke®. Group CFD was given Caffeine Free Diet Coke® and group CF received Caffeine Free Coke®; all groups received their treatments daily via test tubes with drinking spouts for 14 days. The animals were housed in the animal vivarium where the lights were kept on a 15:9 light/dark cycle starting at 7am. The rats were housed in Plexiglas cages and were given free access to food with water restricted as noted below for 23 hours every day. This experiment had full IACUC approval before the start.

Procedure

All four groups received a 15-min exposure of 20 mls of their drinking mediums for 2 weeks in graduated drinking tubes (An Care). The

amounts of the solutions ingested were recorded daily. After day 14, the rats were water deprived for 23 hours. On the 15th day, all animals were given a 15-minute exposure to a 10% solution of no-sugar added apple juice (Wal-Mart), mixed with tap water. Immediately following, the rats were given a 0.15 M lithium chloride intraperitoneal (IP) injection at 2.0% of their body weight (Carolina Biological Supply). The IP injection was used to provide a conditioned taste aversion. On day 16 of the study, the four groups were given simultaneous 15-minute access to both 10% apple juice mixed with soft drink vs. control soda (See Table 1). Therefore, Group C was given a choice between apple juice/Coke® mixtures vs. Caffeine Free Diet Coke®, Group DC given apple juice/Diet Coke® mixtures vs. Caffeine Free Coke®, Group CFD given apple juice/Caffeine Free Diet Coke® vs. Coke®, and Group CF given apple juice/Caffeine Free Coke® vs. Diet Coke®.

Results

There was one independent variable with four levels for this study, namely soft drink given prior to CTA: either Coke®, Caffeine Free Diet Coke®, Diet Coke® or Caffeine Free Coke®. There were two dependent measures which were the Pre-CTA/Post-CTA difference score and what the preference was for the two different solutions Post CTA. The Pre-CTA/Post-CTA difference score was calculated by determining the difference between consumption of the 10% apple juice before CTA and subtracting the 10% apple juice/soft drink mixture at test. Two subjects from CFD group were excluded from analysis due to lack of consumption on day 15 (n=8). A one-way ANOVA of the pre-CTA apple juice consumption was significant (F(3,34)=5.37, p=.004). Further Tukey HSD post hoc tests discovered only one significant difference (p=.002), which was between the Coke® (M=7.8, SD=1.75) and Caffeinefree diet Coke® (M=11.25, SD=1.67). These groups were the lowest and highest consumptions, with the Diet Coke® (M=9.4, SD=2.17) and Caffeine Free Coke® (M=9.9, SD=1.73) falling in the middle. No other comparisons were significantly different.



Figure 1. Mean differences between pre-conditioned taste aversion consumption and post-conditioned taste aversion consumption. The error bars represent the standard deviation. The asterisks over the bar represent significant group differences.

The one-way ANOVA for the Pre/Post CTA data was significant F(3,34)=14.74, p=0.01. A subsequent Tukey HSD was performed and showed that the Coke® group (M=-2.7, SD=2.63) significantly increased their post-CTA apple juice mixture consumption (p < 0.001) than the Caffeine Free Diet Coke® (M=4.13 SD=2.53). Furthermore, the Caffeine Free Diet Coke® (no sugar/caffeine) (M=4.13 SD=2.53) significantly increased the Post-CTA apple juice mixture (p=0.006) than the Diet Coke® group (M=0.1, SD=2.38) over Pre-CTA apple juice. All other group comparisons were not significant (See Figure 1). However, the Coke® group (M=-2.7 SD=2.63) approached, but failed to demonstrate, a significant increase in the Post-CTA apple juice mixture (p=0.057) over the Diet Coke®. Finally, to test replication of Schmidt 2008, an independent t-test comparing Coke® to Diet Coke® was significant t(18) = -2.50, p = 0.01).

The preference for the two different solutions was measured by consumption of the 10.0% apple juice/soft drink Post-CTA mixture minus the other Coke® product. The one-way ANOVA was significant F(3,34)=3.59, p=0.023. A subsequent Tukey HSD test was performed and showed the Coke® group (M=3.7, SD=1.57) significantly preferred the apple juice mixture/soft drink (p=0.023) mixture over the novel Coke® product (p=0.023) than Caffeine Free Coke® (M=1.7, SD=1.64). All other group comparisons were non-significant (See Figure 2).

Discussion

This study employed a condition taste aversion model discovered in our lab (Schmidt et al.) to test the seventh criteria of dependency, as outlined by the American Psychiatric Association (2000) as continued use of the drug of abuse, despite known adverse consequences on the part of the user. In order to differentiate the addictiveness of caffeine and sugar, this study compared four levels of soft drinks: Coke®, Caffeine Free Coke®, Diet Coke®, and Caffeine Free Diet Coke®. The pre-test/post-test differences in this study were consistent with the previous study (Schmidt et al., 2008). However, by introducing four levels of caffeine-sugar content the results of this study suggest that sugar may be the more addictive property when compared to caffeine. The retention test also supports a preference for sugar, but differences in sweeteners used in soft drinks may account for the variability in the retention Coke® and Caffeine Free Coke® test results. contained high-fructose corn syrup sweetener, compared to Diet Coke® and Caffeine Free Diet Coke® which used an artificial sweetener (aspartame).

This study implicates sugar to be a potential substance of abuse according to the seventh behavioral criteria of addiction, lending support to previous studies of sugar addiction. Previous studies demonstrated that under certain conditions of abstinence-binging, sugar could produce behavioral



Figure 2. Comparisons of post-conditioned taste aversion preference index measured by the consumption of the 10.0% apple juice/soft drink post-conditioned taste aversion minus the alternative Coke© product. The error bars represent the standard deviation. The asterisks over the bar represent different group differences.

and neurochemical changes similar to those of other substances of abuse, such as amphetamines (Avena, 2007; Avena et al., 2008). Future investigation is necessary to differentiate the palatability of different sugars and sweeteners used in soft drinks.

This experiment provided two important findings. First, this study was able to reproduce the previous findings by Schmidt et al. Secondly, the use of our novel behavioral measure of addiction was able to demonstrate that sugar (namely high fructose corn syrup) appears to be more addictive to rats than caffeine. To strengthen the validity of this model, future testing should be conducted using other substances of abuse and sex-differences could also be accounted for. The use of this model provides the means for measuring the seventh criteria of addiction (American Psychiatric Association, 2000; Schmidt et al.) and may be used to measure additional motivational factors underlying substance abuse.

Author Note

The first four authors contributed equally and all deserve first authorship.

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