Caffeine, Alcohol, and Youth: A Toxic Mix

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Dr. O'Brien: *Thank you all for participating in the inaugural roundtable discussion for Journal of Caffeine Research. Let us begin with the popular perception of caffeine as an "antidote" to alcohol intoxication. The neurochemical relationship between alcohol and caffeine appears to be complex. Alcohol influences the interaction of several neurotransmitters, and this has important implications in terms of the mixture of caffeine and alcohol, particularly with respect to activities that require sustained attention and executive function. I am interested in your comments, Jonathan. Your research speaks to the safe execution of activities that require sustained attention.*

Dr. Howland: We have just published a randomized trial of the acute effects of intoxication with caffeinated beer versus non-caffeinated beer on attention/reaction time and a simulated driving task.¹ We found main effects for alcohol on both outcomes, with alcohol impairing both attention/reaction time and driving, but no performance differences between the groups receiving caffeinated versus non-caffeinated beer.

Dr. O'Brien: *And so, in your report, there was more variability in speed and lateral movement and increased crashes with alcohol, but there did not appear to be a protective benefit from the addition of caffeine. Am I right?*

Dr. Howland: Correct.

Dr. O'Brien: *Cecile, you studied dual task interference and psychological refractory periods. Tell us what your results suggest.*

Dr. Marczynski: Similar to the study that Jonathan just described, I have also found that caffeine does not counteract

some of the impairing effects of alcohol on some cognitive tasks.² For example, in the lab you can ask participants to do two tasks at once, called the dual-task paradigm, which is difficult even when sober. In the real world, driving in heavy traffic while talking on the cell phone is an example of a dual-task situation. The acute effects of alcohol make dual-task interference worse. When we mixed alcohol and caffeine, we found a small benefit of caffeine in counteracting the deleterious effects of alcohol on reaction time. However, accuracy was still impaired by alcohol, and caffeine administration did not change this. More importantly, we found that caffeine counteracted the subjective perception of intoxication. When you mix caffeine with alcohol, you feel less intoxicated and yet you are still impaired. There is dissociation between your subjective impression of how you are functioning and what happens objectively on your task performance.

This is a very dangerous scenario for a drinker. And as far as the popular perception of caffeine as an antidote, I think people are pretty aware that a cup of coffee after drinking will not make you sober up. I think that message has gotten out, but there are other messages such as "mixing an energy drink with alcohol is not a good idea." That message has not gotten out there, especially among young people. They just think that they can drink the energy drink with alcohol, like a Red Bull® and vodka, and therefore drink more and party longer. That is risky, and I do not know if that message has reached the general public.

Dr. Howland: I agree with you. I am not sure of the extent to which young adults and adolescents think about the energy drinks as caffeine. There is this old message that has been around since I was a kid, which is that if you give coffee to a drunk, you get a wide awake drunk. But I think, first of all, these energy drinks have other ingredients, such as guarana and taurine. Second, as I said, I do not know if the young

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people think of this as being like a cup of coffee or more of some kind of magical brew that gives you energy.

Dr. Marczynski: I totally agree.

Dr. Arria: I think that there definitely is a need for more real-world research in this area to assess the beliefs of young adults and adolescents regarding the combined effects of caffeine and alcohol. Part of the challenge of experimental research is to assess the effects of the intentional addition of caffeine to experimental drinks that mimic what is actually going on in the real world.

To my knowledge, researchers cannot induce a state of intoxication as high as what a college student might experience, just because it would be dangerous. So I think that it is very hard to do experimental studies that assess the effect of the doses of alcohol and the doses of caffeine that are consumed in the real world.

We do need more research, not only on the attitudes and beliefs but also to understand the real-world consequences and experiences of combining alcohol with high levels of caffeine.

Dr. James: A lot of interesting and important points have been raised. I just wanted to ask for a point of clarification in relation to the study Cecile mentioned. You indicated that you attained some effects in relation to improved reaction time for the people who received caffeine as well as alcohol. I just wonder in that context whether you included controls for withdrawal reversal.

Dr. Marczynski: No, we did not, and I agree that this is an important point. In my study, we had our subjects refrain from caffeine use for 8 hours. This ensured that the amount of caffeine that subjects received was controlled. However, it is possible that withdrawal reversal was involved in the results we obtained. However, we had to ensure that subjects did not consume lots of caffeine right before arriving in the lab, where they would receive a large dose of caffeine, for safety reasons.

Dr. James: Fair enough. I just thought that point was worth making, that those kinds of specific results are quite ambiguous. We do not know whether the fact that the caffeine they are receiving is actually just reversing withdrawal effects or whether it is a net effect of caffeine.

Dr. Marczynski: That is an excellent point; something I can test next.

Dr. O'Brien: *Moving on, my concern is not just the misconception that caffeine ameliorates the drunkenness that comes with excessive alcohol consumption, but also that the addition of the caffeine might permit the drinker to stay awake longer in order to drink more. Your comments on this?*

Dr. Howland: In our study, we actually asked the various groups to estimate their level of intoxication in terms of blood alcohol, and we did not find a difference between the caffeinated versus non-caffeinated alcohol groups with respect to where they rated their blood alcohol levels.

Amelia makes a good point, which is that you can experimentally dose people just so high before you run into

human subjects problems. We were up at 0.12% with this trial, which is fairly buzzed, but I am sure the kids go much further than that. So it may be that the inability to perceive your level of intoxication does not really kick in until you are more intoxicated with your caffeinated alcoholic beverages (CABs).

Dr. Arria: There is still the issue of people mixing drinks on their own and not knowing how much caffeine is in the beverages that they are mixing with the alcohol. Mary Claire and I have worked together to limit the availability of premixed caffeinated alcoholic beverages.

Dr. Howland: I think this is a huge issue. And it is one of the points that we tried to make in a little essay we wrote.³ Part of that was driven by a survey done by one of our colleagues, James MacKillop, at the University of Georgia, where he asked some caffeinated alcohol beverage questions.

It looked as if the vast majority of students were not buying premixed drinks but were mixing energy drinks and alcohol by themselves, so these policy interventions of taking these premixed products off the shelves are probably not going to slow down the consumption of alcohol and caffeine in conjunction.

Dr. O'Brien: *Although I would argue that it affects availability. The primary venue for the sale of those premixed caffeinated alcoholic beverages was convenience stores; the packaging was so similar to non-alcoholic products that sometimes even store clerks were unable to tell the difference between the alcoholic and non-alcoholic versions. That does not mean you cannot go out and buy a case of non-caffeinated energy drinks at Wal-Mart and then get one person who is of legal age (or who can pass for legal age) to go and buy a jug of Everclear®. We all agree, though, that feeling more awake or, more accurately, feeling less sleepy as a result of caffeine ingestion is not the same as not being impaired. And we all have concerns about the combined ingestion of caffeine and alcohol.*

Moving on to genetic factors, we know that genetic factors influence alcohol absorption and metabolism and are estimated to account for about 50% of the risk for alcohol abuse. The vulnerability to alcohol dependence is genetically influenced through a variety of mechanisms, but genetic factors also appear to influence caffeine tolerance, caffeine intoxication, and caffeine withdrawal. Are we aware of any research that supports the genetic influence regarding the interactive effects of caffeine and alcohol?

Dr. Howland: I am not, but I have not been looking for it either.

Dr. James: I am not aware of any either. But to make a minor point, if you consider some of the research, for example, the work of Ken Kendler, his studies seem to be showing that familial and environmental factors are more important in determining drug usage patterns, whether they be illicit drugs or legal, at younger ages, and genetic factors are more important in mid-adulthood and later.⁴

I am just wondering whether that transformation is something of relevance in this context, given that we are generally

talking about younger people and their combined use of caffeine and alcohol, which may invoke more environmental, peer, and familial influences than genetic ones.

Dr. Arria: One major issue is that research on energy drinks alone or in combination with alcohol is scarce. Given the prevalence of use, I see it as a real knowledge gap and something that needs to be rectified with more resources and more investigators becoming aware of this issue.

Dr. O'Brien: *It is my impression as well; there is a dearth of research on this particular subject. But let's talk about the relationship between genetic factors and the use of psychoactive substances. As Jack mentioned, psychoactive substance use seems to be more strongly correlated with genetic factors as individuals age; in other words, genetics become more important through early and middle adulthood. But initiation and early patterns of use are strongly influenced by social and environmental factors.*

Regarding the popularity of mixing caffeine and alcohol among youths, the reported prevalence among U.S. college students is as high as 28% (Wake Forest University Survey, O'Brien et al., 2008, unpublished data). What might that mean in terms of risk for substance abuse and dependence as these young people age?

Dr. Arria: Some of our research has shown in a longitudinal context that energy-drink users, not necessarily in combination with alcohol, are more likely to initiate use of prescription drugs non-medically than non-energy-drink users, even after controlling for some risk-taking characteristics that might confound that association. So we are concerned that there is a possible link between the exposure of highly caffeinated energy drinks and later propensity for addiction, although we are not clear at all on the possible mechanism.

Dr. Howland: I think this raises a really interesting sort of causal arrow. A question for Amelia: what were you controlling for in terms of personality, impulsivity, and other characteristics that might drive both energy-drink use and addictive behaviors later?

Dr. Arria: We have self-report measures of sensation-seeking and early conduct problems. Impulsive sensation-seeking was used in the longitudinal analysis. More recently, we were able to look at the risk of alcohol dependence among energy-drink users and non-users. The same sort of relationship seemed to exist in a cross-sectional way.

But certainly, we are not controlling for genetic predisposition. There are other things that we would need to control for in order to really understand the direction of the arrow, as you said.

Dr. O'Brien: *I would add that my own research, still in progress now, showed that the consumption of caffeinated alcohol was associated with more frequent binge drinking and more drunken days in a typical week, even after adjusting for sensation-seeking personality, as measured with a brief sensation-seeking scale. And even when you account for the brief sensation-seeking score and the amount of alcohol consumed, students who drank caffeinated alcohol were still more likely to be taken advantage of sexually, drive under the*

influence of alcohol, and ride with a driver under the influence of alcohol.

The prevalence of injury requiring medical treatment was significantly higher among students who drank caffeinated alcohol, but that was moderated by the risk-taking score after adjustment for typical drinking levels.

I would like to talk for a minute about the developing adolescent brain. This is a subject that concerns me in that the adolescent brain may be particularly sensitive to the combined effects of caffeine and alcohol. The planning of complex cognitive behaviors, decision making, and social control are regulated by the prefrontal cortical executive function. The maturation of the prefrontal structure progresses into the third decade of life. My question is: if one's brain is not fully "hardwired" until one is in one's mid-20s, what happens if the receptors and the neurotransmitters that are responsible for things like arousal and learning and motivation and aggression and social inhibition are chronically stimulated or blocked by psychoactive substances like caffeine and alcohol? What could that mean, long term?

Dr. Marcinski: You are talking about the age range when college-aged individuals, whose brains have not fully completed development, are binge drinking to very excessive levels. You wonder what that is doing to their brains. If you add caffeine into the mix and they drink even more than they would have before, that would suggest that perhaps the damage that might be occurring is going to be worse than if they had just been drinking beer.

I do not know if there is much research on the actual damage to the brain, but I know there are a couple of studies that have examined binge drinking and brain dysfunction in people in their late adolescence and early 20s. So that would suggest that this area needs to be looked at much more closely, especially by people who have expertise in brain imaging.

Dr. O'Brien: *Perhaps a little bit more is known about the long-term cardiovascular consequences of both excessive alcohol intake and the development of hypertension. Among adolescents, caffeine consumption has been linked to high blood pressure. We know that excessive alcohol is associated with the development of hypertension, although it seems that moderate alcohol intake may have some cardioprotective effect. Jack, you have written extensively about the cardiovascular effects of caffeine. Could you hypothesize about the possible long-term risks of consuming both caffeine and alcohol?*

Dr. James: In relation to caffeine, I guess the major risk would be the fact that patterns of usage early in life are likely to lay down the foundation for continued patterns later in life. So if it is the case, as we know experimentally it is the case, that caffeine elevates blood pressure moderately but to levels that are of concern when we consider that caffeine is so widely consumed, then we might expect that we would see increased levels of hypertension and cardiovascular disease as a consequence of early exposure to caffeine continuing throughout the remainder of life.

In terms of the possible interaction between that and usage of alcohol, it is an area that I could not specifically comment on in terms of having any direct experience research wise, and I am not sure that it is being researched extensively

anyway. As you say, there seems to be a bimodal effect of alcohol on blood-pressure level. Moderate amounts may be protective; larger amounts may be damaging. It is hard to know how that process is going to interact with lifelong exposure to caffeine, but I think it is an area that is crying out for additional research.

Dr. O'Brien: *I would agree. There appears to be little research on this subject. Additionally, one wonders about the long-term implications of mixing alcohol and caffeine on other health issues such as sleep disturbance. We know that poor sleep quality in adolescents is associated with a number of problems, including mood disorders, exacerbation of asthma, and poor school performance. Alcohol, of course, has a number of effects in the brain. It is just not clear what the long-term effects on the neurotransmitters are and how that will affect cognitive function, sleep, and cardiovascular function. I would add that I am concerned that both caffeine and alcohol may reduce the retention of dietary calcium, and there perhaps may be an increased risk for osteoporosis, especially in young women. There is little if any research on this. Does anyone want to comment?*

Dr. James: I was just about to say that the way you have articulated the problems – namely, the problems regarding the things we do not know – is itself a very clear statement of the kind of research that needs to be done. The fact that we might be floundering, trying to work out what we know and do not know, is itself testimony of how much more work needs to be done, and it is important that that point be made. I think you have done that eloquently.

Dr. O'Brien: *Regarding gender, there are a few studies about the direct effects of caffeine in relation to the menstrual cycle phase, including an article by Kamimori et al.⁵ There is conflicting evidence about ovarian hormones and caffeine, particularly in humans. On the other hand, we know that gender does influence the bioavailability and metabolism of alcohol, and may also modify the metabolic responses to alcohol. I believe there is no research as of yet that supports a gender influence regarding the interactive effects of caffeine and alcohol. That may be an additional avenue for inquiry.*

Dr. Marcziński: I am not aware of any published research addressing this question. However, I think one can hypothesize that there would be interesting gender effects on the interaction of the two substances, just based on the reports that there are differences between men and women in their subjective response to alcohol. For instance, studies suggest that if you give young women a dose of alcohol, they tend to report more sedation, whereas men tend to report more stimulation.

There are also studies that have reported more disinhibiting effects of alcohol for males than females. So if caffeine is a stimulant and women tend to feel sedated when they drink, that might suggest that women might be more at risk in these substances permitting them to drink more and longer than men because it is counteracting some of the sleepy feelings that they get when they drink. If they do not want to feel sleepy and they want to party, then having that source of energy with their alcohol may be very appealing.

While this is just my hypothesis, I would think that gender differences are something that needs to be looked at when consuming alcohol and caffeine.

Dr. O'Brien: *What do each of you see as the biggest limitation of the current research? We have mentioned a few areas that beg for additional inquiry. But what do you see as the biggest limitation of the current research on the subject of caffeine and alcohol?*

Dr. Howland: I think that cross-sectional studies have raised some very interesting hypotheses. I think there is plenty of reason to suspect that the addition of caffeine to alcohol increases the demand and distorts perceptions of sedation and capacity and perceptions of impairment.

On the other hand, you know, these are all questions that can be asked experimentally. It seems to me we should be doing that.

To me, the most fundamental question is whether or not this relationship between caffeinated alcoholic beverages and behavior is confounded by personality. I have heard from two of you today that you have controlled for this in your cross-sectional studies. I think that still remains a really pivotal question.

On the other hand, I would certainly be interested experimentally in seeing how the two beverages or the addition of caffeine distorts perceptions of impairment and capacity to perform functions, and I think all three of those issues really need to be looked at.

Dr. Arria: I agree. I think that one of the most important areas, at least for epidemiologists like myself, would be to understand the mechanisms behind the consistent findings that energy-drink use or highly caffeinated beverage use is associated with alcohol problems, risky behavior, and possibly later addiction problems. I think clarifying that mechanism and really understanding the temporal association is critical and has policy implications.

Dr. Howland: We do a lot of alcohol dosing experiments. Our participants are almost always college juniors and seniors, so I have seen a lot of them go through the lab. One of the impressions I get is that these kids make a conscious decision to get drunk. They decide, "Okay, on Friday night I am going out and getting wasted." They may not drink a lot during the week, but they make this decision.

The question is whether or not they see the caffeinated alcoholic beverages as a way of partying longer, which I think they probably do. But in that decision to go out and get crazy, that entails a certain amount of risk taking that you are going to take on as well. Even if it is not a personality thing, it may be a sort of state decision. You know, "I am going to drink a lot and I am going to hook up. If I get in a fight, I am going to get in a fight." All of this is part of the same premeditated decision.

Dr. O'Brien: *Although I would suggest—not in disagreement—that when presented with the argument that "the only people drinking caffeinated alcoholic beverages are people who have already demonstrated by virtue of their behavior that they are extreme risk takers," I like to point out that 28% of college students are not bungee jumpers.*

The behavior seems to me to be so prevalent that it goes beyond what we would anticipate for that portion of students who are particularly prone to risk taking by virtue of their personality.

Dr. Arria: Nonetheless, Mary Claire has definitely demonstrated that no matter what the mechanism, the consequences have costs. There is significant morbidity associated with this combination, including the possibility of alcohol poisoning. So no matter what leads them to that state, there is still a significant cost, no matter if they were a risk taker or not or what their personality was. If they end up engaging in more risky behavior because of the combined consumption, we have a problem.

Dr. Howland: Sure. And you know, I do not want to sound skeptical about this at all. I actually think that these sorts of hypotheses about these beverages are probably right, but I also think that they are testable and need thorough investigation.

Dr. Arria: One alternative hypothesis that we are trying to investigate with our longitudinal data is that alcohol-dependent individuals might be using energy drinks to counteract hangover-like effects. That hypothesis can be tested using longitudinal data. Maybe both mechanisms exist and each would call for a different policy response. If it is true that energy-drink use is a way of ameliorating hangover-like effects, then people who use energy drinks regularly might be screened for alcohol dependence, either in the general population or in a college campus.

On the other hand, if energy-drink use increases the risk for alcohol dependence prospectively, then putting more warning labels on the products and limiting their availability to young people might be warranted.

Dr. O'Brien: *So Amelia, is it your impression that there are a certain number of young people who drink caffeinated alcoholic beverages with the belief that even though they consume extreme amounts of alcohol, having consumed caffeinated alcohol, that they will not get hangovers?*

Dr. Arria: No. Actually, our anecdotal data show that the hangovers are worse. When we ask students about the positive and negative effects of combining energy drinks with alcohol, some say that the hangover-like effects are worse when you combine energy drinks with alcohol.

Dr. O'Brien: *Even when you control for the amount of alcohol?*

Dr. Arria: That is an interesting question, but we have not been able to answer it yet. But what I am talking about is that using energy drinks after having a hangover might be a way of getting through the day. Maybe that is one of the reasons for the co-occurrence of energy-drink use and alcohol dependence.

Dr. O'Brien: *Perhaps this involves adenosine receptors? Chronic caffeine consumption upregulates the number of adenosine receptors. So what happens to people who consume high doses of caffeine on a regular basis and then have an oversupply of adenosine receptors? It is these indi-*

viduals who seem to suffer the most unpleasant effects of caffeine withdrawal (the dysphoric effects). One wonders when you put alcohol into the mix with its effects on several different receptors, not just adenosine receptors...perhaps that has something to do with why the hangovers are worse? I am not sure. Your comments?

Dr. Howland: Interestingly, the people in our study who were randomized to the caffeinated alcoholic beverage drove better in the morning than the people who were randomized to straight alcohol. That is probably because the alcohol is gone but the caffeine is still active.

Dr. James: That sounds like a very interesting result. Can I just ask, have they had a further dose of caffeine in the meantime though? They probably have not had any more alcohol, but might they not have had caffeine?

Dr. Howland: They had caffeine in the morning. Now I did find that the period before the experimental trials when they could not have caffeine was 8 hours. So those who were randomized to no caffeine then by the morning had not had caffeine for another 8 hours—16 hours.

Dr. James: They are approaching the peak point at which withdrawal symptoms will kick in.

Dr. Howland: Right. But then we did allow them to have caffeine for breakfast.

Dr. O'Brien: *I would suggest that in the clinical setting, the opposite is true. We are seeing individuals with extreme amounts of alcohol consumption, and it is, in fact, the caffeine that wears off first; that is a particular problem. For example, a young person who consumes alcohol to a 0.35 or even a 0.40 percent level, which is sufficient to induce coma in a majority of individuals and sufficient to cause death in a number of individuals, by the time the caffeine wears off in that person, the alcohol is still metabolizing at 15 or 20 mg percent per hour. That is the clinical scenario, the exact opposite of what is happening in the lab.*

Dr. Howland: So that is simply a function of how much alcohol we can give them, so that is a good point.

Dr. O'Brien: *I am not suggesting we exceed what our IRB would permit. I am only pointing out that students have not read the literature about the pharmacokinetics of the two substances on the majority of college campuses.*

Dr. James: We have identified a host of exciting and interesting questions to research, and certainly questions that are worth researching. I just wonder in relation to the funding bodies, do people have any views about the sexiness, if you like, of doing research involving caffeine given its ubiquity. There is a sense that with some people that perhaps the funding bodies do not take caffeine seriously, since they sit around the table drinking their cups of coffee deliberating over research that is going to look at the effects of caffeine.

Do we have any sense about that in the group, whether there might be some obstacle to attracting research funds?

Dr. O'Brien: *One particular problem that we have had in the United States is the fact that caffeine as a pharmacologic substance or drug has traditionally been under the purview of one institute, the National Institute on Drug Abuse, and that a parallel institute, the National Institute on Alcohol Abuse and Alcoholism (NIAAA), has traditionally investigated alcohol. At times, there does not seem to be enough cross-talk between the two institutes in terms of funding projects that would look at the simultaneous consumption of the two substances, both in cross-sectional and longitudinal analyses.*

Dr. Howland: But, you know, we have been developing and conducting research studies on the effects of caffeinated alcoholic beverages for probably about 6 years. So we have had a number of grants into NIAAA. When we started, we were getting reviews that we had just failed to make a compelling argument that this was a problem. I think that since then, people are over that and this is an issue that has much more saliency than it did 5 or 6 years ago.

Dr. O'Brien: *That brings me very nicely to our final topic of conversation, which is policy change. There has been growing international concern about the consumption of caffeinated alcohol, including statements from the Irish Food Safety Promotion Board, the Swedish National Food Administration, the Australian Drug and Alcohol Office, the French Ministry of Health, the Dutch National Foundation for Alcohol Prevention, and the European Centre for Monitoring Alcohol Marketing. Most recently in November, 2010, the United States Food and Drug Administration (FDA) ruled that caffeine is an unsafe food additive in manufactured alcoholic beverages, effectively making the premixed alcoholic energy drinks prohibited for sale in the United States.*

Amelia, you were one of several scientific experts who very strongly advocated that ban. But I know that you have concerns that those premixed alcoholic energy drinks are really only a fraction of the true public health risk. Your comments?

Dr. Arria: I think that the FDA regulations were a good first step, but I think that there is a lot more to be done with regard to advocating for better information for consumers, in terms of beverage labeling, such as adding the caffeine content to the label as a requirement. And we need a research-guided limit on caffeine levels in certain beverages. I think that with more research, perhaps we can get there.

Dr. O'Brien: *I have a couple of cans on my desk of a very popular energy drink that were purchased abroad. The can from France says, "Not recommended for children or pregnant women." The can from Switzerland adds, "or for persons sensitive to caffeine" and "do not mix with alcohol." The cans from Italy and Austria have no warnings. The editors of the Canadian Medical Association Journal have advocated for government-mandated restrictions on the labeling of caffeinated beverages. Do we have consensus on that?*

Dr. Marczynski: I am concerned about children and adolescents consuming a lot of these energy drinks. The doses of caffeine in them can be extremely high, and yet their body

weight is so small. So the doses that they are consuming are far beyond what we would recommend, and yet any 10-year-old child can walk into a variety store and buy these high-volume cans of energy drinks.

I think that the lack of laboratory studies that have examined the effects of these energy drinks alone is problematic. We cannot really inform people about the effects of these drinks in these high doses if we do not actually study them. I think warning labels for children or pregnant women not to consume them are appropriate. But we do not do that in the United States.

Dr. O'Brien: *Do we think that industry-imposed standards are enough? Does anyone else have an opinion about governmental regulation?*

Dr. Howland: I wish we knew more to make sure that our labels had strong scientific evidence behind them. I think probably the protection of children and pregnant women, fetuses, should err on the side of protecting those populations anyway. So I think the labeling that speaks to that is good.

But it seems to me that there are two issues: one is whether we have sufficient evidence of the harm of energy-drink consumption; the other is whether we have evidence that energy drinks provide little or no benefit. I think that we need to know more before we warn the public about the harm of energy-drink consumption. But I think that we know that much of the marketing of energy drinks is misleading with respect to benefit. I would certainly advocate for some public counter to the marketing of these drinks that suggests that they are some kind of tonic that provides benefits such as improved athletic performance or improved energy and attention. Our study shows that it is unlikely that mixing energy drinks with alcohol offsets alcohol-related impairment. Thus, in the absence of definitive data on harm, we can at least counter the marketing argument that energy drinks are good for you.

Dr. Marczynski: I just published a study that examined the acute effects of an energy drink, Red Bull®, on a reaction-time task in the lab.⁶ I found that my subjects actually had improved reaction times, but only for a very small dose of energy drink; half a can, which is approximately 125 ml of Red Bull® for the typical 70-kg subject. So I agree with the statement that we need more lab research to demonstrate where the benefits of energy drinks are and how small the effective doses really need to be. Then again, are these doses even beneficial for some people, like the people who experience caffeine withdrawal? Maybe a small amount of energy drinks is beneficial for some people but not for others.

More lab research is clearly needed so that we are saying the right thing if we want to influence policy. There is just not sufficient research to make a lot of good statements to people who want to make policy changes. I do not know if others agree with that.

Dr. Howland: Cecile, would you agree that it is safe to say that mixing caffeine with alcohol does not improve your driving performance?

Dr. Marczynski: Definitely.

Dr. Howland: So that is what I mean. We could probably speak fairly definitively to the argument that it is good for you. The argument that it is bad for you and exactly how it is bad for you is where we need more information.

Dr. Marczinski: Right. But I also think that we should examine a lot of these drinks alone. I do not think there is enough research on just energy drinks and the effects of energy drinks alone because lots of people are looking to the scientific literature. People in the general public want to know the answer to whether energy drinks are beneficial to work performance or sports performance. If you actually look at the number of existing studies about energy drinks and sports performance, it is fairly small.

Dr. James: I would like to respond to that point about a half a can of Red Bull® perhaps enhancing performance. Again, I would have to ask the question about whether or not there were adequate controls in that study to account for withdrawal reversal, because actually, withdrawal reversal has a fairly flat dose-response curve. So the finding that half a can has an effect but nothing above that amount has an additional effect fits nicely with what we know about the reversal of caffeine withdrawal effects. So without other information, I would be inclined to think that the observed improvement in reaction time was a withdrawal reversal effect rather than a net performance effect of caffeine.

Dr. Marczinski: Well, that is an excellent point. Now I have to go back and test that because I had my subjects 8 hours deprived, so that explanation seems feasible.

Dr. O'Brien: *It is my opinion that there should be specific warnings on these caffeinated beverages not to mix them with alcohol. The addition of caffeine to these beverages has not been demonstrated to be safe at any level. And because there is evidence that suggests the combination of caffeine and alcohol poses some health concern, a good bit of which, we would agree, is unresolved and bears significant further investigation, I think while the jury is still out, the burden is on the health professionals and educators and on the scientific community to recommend extreme caution about mixing any kind of caffeinated product with alcohol.*

Dr. Arria: It is important to inform the public that there has not been enough research on the health and safety effects of these drinks and that we need labeling to inform consumers about how much caffeine is in the drink. I think that is a point that we can all agree on.

Dr. Howland: Absolutely. You know, some of these drinks have no caffeine in them and some of them have incredible amounts.

Dr. Arria: Energy shots have a very high concentration of caffeine.

Dr. O'Brien: *Does anyone have anything else that they would like to add to our discussion—any closing points, concerns, conclusions?*

Dr. Howland: The only thing I would like to add is hats off to Mary Claire and to Amelia because your work has done an incredible amount to draw attention to this whole issue. I think that it has really paved the way and made it all that much easier for those of us who are following in your path to get the attention of funders and colleagues.

Dr. Arria: Thank you.

Dr. O'Brien: *Thank you. My advocacy for additional research and for public education was motivated by a clinical encounter. Current research is limited by a paucity of longitudinal data, by inconsistent control for withdrawal reversal, and by the challenges of assessing real-world usage patterns. Additional research is needed: to elucidate the neurochemical mechanisms of caffeine-alcohol interaction; to clarify the influence of personality, gender, and genetics; to explore the beliefs of adolescents and young adults regarding the combined effects of caffeine and alcohol; and to investigate the long-term health consequences of caffeine-alcohol consumption.*

We support product labeling regarding caffeine content, in addition to warnings about the potential risks of caffeine consumption in children, pregnant women, and sensitive individuals, and when combined with alcohol.

This concludes our inaugural roundtable, and I thank you all very much for your expertise and your participation. I will look forward to hearing great things from you in the future.

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