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The effect of caffeine and stress on auditory hallucinations in a non-clinical sample

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ABSTRACT

Both the diathesis-stress model and the continuum theory of schizophrenia attempt to explain the mechanism by which stress may facilitate the expression of the symptoms of schizophrenia in non-clinical samples. Caffeine has also recently been reported to increase proneness to hallucinate. In this study, 92 non-clinical participants were assigned to either a high or a low stress condition and a high or a low caffeine condition on the basis of self-report. After they had been primed, the participants were asked to listen to white noise and to report each time they heard the song "White Christmas" during the white noise. The song was never played. The results indicated that the interaction of stress and caffeine had a significant effect on the reported frequency of hearing "White Christmas". The results demonstrated that high caffeine levels in association with high levels of stressful life events interacted to produce higher levels of "hallucination" in non-clinical participants, indicating that further caution needs to be exercised with the use of this overtly "safe" drug.

1. Introduction

Caffeine is the most commonly used psychoactive drug (Nehlig, 1999). The primary mode of consumption of caffeine is in coffee and other caffeinated beverages, such as tea, soft-drinks and energy drinks (Damianopoulos & Carey, 1999). Past research has linked coffee drinking with numerous side-effects (e.g. James, 1997). In their critical review, Higdon and Frei (2006) found the positive effects of coffee consumption to include the prevention of type II diabetes, Parkinson's disease, certain types of cancer and even suicide. However, caffeine has also been shown to increase the risk of cardiovascular disease, certain types of cancer, osteoporosis, mineral deficiencies and pregnancy-related difficulties (Higdon & Frei, 2006). It is thus apparent that in addition to its primary effect as a central nervous system (CNS) stimulant (James, 1997), it also has a multisystem effect on other organs of the body.

Caffeine acts upon a number of neural systems. The stimulant effects of caffeine have been shown to require the blockade of adenosine receptors, specifically the 2A subtype (Fredholm, Chen, Masino, & Vaugeois, 2005). The adenosine 2A (A_{2A}) receptors play a role in striatal function, while adenosine receptors as a whole are key to neuromodulation (Fredholm et al., 2005). Ledent et al. (1997) and Chen et al. (1999) conducted studies which examined knockout mice that were missing A_{2A} receptors. The mice displayed increased anxiety-related behaviour, decreased despair-like behavior, and most importantly, reduced sensorimotor gating. The impairment of the sensorimotor gating is typically present in people diagnosed with schizophrenia, and manifests as a reduction in startle habituation and in prepulse inhibition (Fredholm et al., 2005). Appropriate sensorimotor gating "prevents excessive irrelevant sensory stimuli from disturbing integrative mental processes in the brain" (Fredholm et al., 2005, p. 398). It thus seems reasonable to postulate that when high doses of caffeine are consumed, blocking the A_{2A} receptors, information processing measures are disturbed. Perhaps the degree of the disturbance differs according to other factors present, but the possible connection between caffeine and sensorimotor gating via adenosine receptor antagonism is intriguing.

Considering the frequency of caffeine use and the numerous side effects associated with the drug, it is clear that the potential health risks of caffeine consumption in large quantities warrant further investigation. Recent reports (Jones & Fernyhough, 2009) have indicated that the consumption of caffeine as well as of high levels of stress, can lead to an increased proneness to psychosis-like experiences in non-clinical samples.

Stress has long been implicated in both the development and the expression of schizophrenia (see Gispen-de Wied, 2000; for review). However, the mechanism of action by which this process occurs remains unknown. The heuristic neural diathesis-stress model of schizophrenia suggests that stressful life events play a contributory role in the development of schizophrenia (Walker & Diforio, 1997). It has also often been assumed that the symptoms of schizophrenia occur along a continuum, suggesting that everyone has schizotypal

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traits at least to some degree (Johns & van Os, 2001). Emotion regulation could possibly shed some light on the connection between stress and the onset of psychosis. An individual's ability to regulate emotions, such as anxiety in response to stress, varies; for some it can be automatic while for others regulation can be difficult (Davidson, Jackson, & Kalin, 2000). Since emotion regulation can be both trait-like and state-like in nature, perhaps an impairment of emotion regulation is the means by which stress impacts the psychopathology of schizophrenia. These theories combined indicate that stress may cause exacerbation of the symptoms of schizophrenia such as hallucinations in non-clinically diagnosed individuals.

While the relationship between mood and caffeine intake varies widely across the population, a link has been established between caffeine consumption and stress. Ratliff-Crain and Kane (1995) have found that 50% of people who are stressed will increase their caffeine consumption. Steptoe and Wardle (1999) have found that men who reported high job demands drank more coffee on days when they felt more anxious, and women who reported high levels of job support drank more tea when they felt relaxed. However, these findings do not speak on the causal relationship between mood and caffeine consumption. In other words, it is not known whether the mood determined consumption or vice versa. There is also the possibility that another factor is influencing both mood and caffeine intake (Steptoe & Wardle, 1999). In the study conducted by Alsene, Deckert, Sand, and de Wit (2003) individuals who reported greater anxiety after caffeine administration were found to have two polymorphisms on the A_{2A} receptor gene. In the study by Rihs, Müller, and Baumann (1996), caffeine consumption was examined among psychiatric patients; caffeine consumption was found to be highest among patients with schizophrenia and lowest among those diagnosed with depression or anxiety disorders. Thus, it seems possible that caffeine may also promote the occurrence of psychosis-like experiences. A recent study by Jones and Fernyhough (2009) surveyed participants with regard to their caffeine consumption, stress levels and their proneness to psychosis-like experiences (including the presence of persecutory beliefs and hallucination proneness). They found a significant correlation between caffeine consumption and hallucination proneness. However they found no significant correlation between caffeine consumption and proneness to delusional beliefs.

Merckelbach and van de Ven (2001) conducted a study investigating whether the frequency of creative experiences is related to hallucinatory reports using the White Christmas Paradigm (WCP). The WCP involves participants listening to an audio track of white noise. They are then asked to indicate each time they hear the song "White Christmas", which they are told may or may not be embedded in the white noise. White Christmas is never played however. Signal detection theory provides an explanation as to how people interpret ambiguous stimuli. If a signal is present, either a hit or a miss will occur. If there is no signal (as in the WCP) either a false alarm or a correct rejection will occur (Wickens, 2002). Thus every time a participant reports hearing the song they are experiencing a false alarm.

As indicated above, there is a link between high levels of stress and psychosis, and caffeine was found to correlate with hallucination proneness. It was thus anticipated that the combination of caffeine and stress would affect the likelihood of an individual experiencing psychosis-like symptoms, specifically increasing the false alarm rate. It was thus hypothesised that individuals who reported consuming high levels of caffeine and who had high levels of self-reported stress would be more likely to report hearing the song. Also, we hypothesized that people who consumed high levels of caffeine *or* experienced high levels of stress would be more likely to experience false alarms than would participants who did not experience high levels of stress or who consumed little or no caffeine. The current study also measured creative experiences, mental imagery ability and social desirability factors in the participants. These factors may also be implicated with an individual's proneness to hallucinate (Merckelbach & van de Ven, 2001). However it was hypothesised that these factors would not be found to have a significant correlation with the occurrence or frequency of false alarms. Hallucination proneness was also measured, and it was hypothesised that this measure would be strongly correlated with the actual occurrence of false alarms.

2. Material and methods

2.1. Participants

Ninety-two, non-clinical volunteer individuals (35 males and 57 females) participated in the study. None of the participants reported having a known auditory impairment, or any past history of psychiatric disorder, psychotropic medication use or of neurological injury. Participants were recruited from the local community. Participants were not aware of the true nature of the study prior to their participation.

2.2. Materials

All questionnaires used in the study had a Cronbach's alpha of $\geqslant 0.7$ which was considered adequate. The two predictor variables, caffeine and stress were measured using self-report questionnaires. Assessment of caffeine intake was measured using the Durham Caffeine Inventory (DCI). The DCI is a self-report measure on which participants indicate their average daily intake of caffeine by reporting which drinks and food they have consumed which contain caffeine. Ratings of how often they consume the items ranged from "less than once a week" to "8+ per day" (Jones & Fernyhough, 2009). The DCI was used to classify participants as either high or low caffeine users. Participants were considered high caffeine users if they reported consuming more than five standard caffeinated drinks per day, approximately 200 mg (Giovannucci, 1998). All participants below this threshold were included in the low caffeine users group.

The self-reported level of stress during the past year was measured using the perceived stress questionnaire (PSQ) which has been previously demonstrated to have high test–retest reliability (Levenstein et al., 1993). The PSQ is a Likert-scale measure that asks participants to rate various aspects relating to the perceived level of stress they have been under over the past year. Example statements include "you feel that too many demands are being made on you" and "you feel you are doing things because you have to not because you want to" (Levenstein et al., 1993). Similar to the DCI, participants were divided into high stress and low stress groups based on their PSQ scores. Participants were considered highly stressed if they scored above .40 on the PSQ, as previously suggested by Bergdahl and Bergdahl (2002). Those with a score below .40 were included in the low stress group.

Creative experiences, mental imagery ability and social desirability seeking were also measured using self-report scales. The creative experiences questionnaire (CEQ) is a self-report index of fantasy proneness. Participants responded with a "yes/no" answer to questions such as "many of my fantasies have a realistic intensity". A high score on the CEQ implies that the individual is highly prone to creative and fantastical experiences. The CEQ has demonstrated high test–retest reliability and internal consistency (Merckelbach, Horselenberg, & Muris, 2001).

The questionnaire of mental imagery (QMI) has demonstrated validity (Sheehan, 1967) as a measure of individual differences in imagery ability. The self-report questionnaire includes items such

as "How vividly and lively can you imagine the taste of salt" and "how vividly and lively can you imagine the sound of the honk of a car horn". A low score on the QMI suggests excellent imagery ability of participants.

The tendency of participants to provide socially desirable responses was measured using the Marlowe–Crowne Social Desirability Scale (M–C SDS). Crowne and Marlowe (1960) have demonstrated the validity of this measure. The scale consists of statements such as "I am always careful about my manner of dress" and "I have never deliberately said something that hurt someone's feelings". A higher score on the M-C SDS indicates the extent to which the participant's responses are motivated by the attempt to appear socially desirable.

Hallucination proneness was also measured using a self-report scale. The Launay Slade Hallucination Scale (LSHS) is commonly used to measure an individual's predisposition to experience hallucinations. The scale considers aspects relating to both pathological and subclinical forms of hallucinatory experiences. Participants scored 12 items on a five-point Likert-scale ranging from zero (certainly does not apply to me) to four (certainly applies to me). Example items include "Sometimes my thoughts seem as real as actual events in my life" and "I have been troubled by hearing voices in my head". High scores on the LSHS indicate that an individual has a strong predisposition to hallucinate (Launay & Slade, 1981).

The song used in the study was "White Christmas" performed by Bing Crosby, as employed by Merckelbach and van de Ven (2001). White noise was played from a white noise generator. A dB meter was used to control the volume at which the audio was played. The audio was played at 85 dB, as this is regarded as loud enough to be heard but insufficient to induce physiological arousal (Crowe et al., 2001). Participants were supplied with a hand held, behavioural event recorder and headphones. The experimenter used a computer to deliver the audio tracks via a media player

2.3. Procedure

Participants were informed that the study was about auditory perception, thereby reducing selection bias and the possibility that participants held any special interest in hallucinatory experiences. When a participant entered the study room, the song White Christmas was playing through the external computer speakers. The participant's attention was directed to the music to ensure that they heard and were familiar with the song.

Participants were then given the behavioural event recorder and headphones, and the White Christmas song was stopped.

Based upon the prompt used by Merckelbach and van de Ven (2001), the experimenter then told the participant that:

> The White Christmas song you just heard might be embedded in the white noise, below the auditory threshold. If you think or believe that you hear the song, or a fragment of the song clearly, please indicate so by pressing the hand counter. Of course, you may press the counter several times if you think that you heard several fragments of the song (p. 140).

White noise was then played through the computer's headphones for a period of three minutes. Upon completion of the task, the frequency with which the participants pressed the hand counter was recorded by the experimenter. The song White Christmas was never played during the three minute period of white noise. Thus each time the participant recorded hearing the song they were recorded as having had a false alarm. To conclude the study, participants were asked to complete the questionnaires outlined earlier. Once all data was collected, the participants were given a copy of the debriefing form which informed them of the deception to which they had been subjected.

3. Results

The sample consisted of 35 male and 57 female participants. There was no significant differences in false alarm scores for males ($M = 1.49$, $SD = .507$) and females ($M = 1.58$, $SD = .50$), $t(90) = -.371$, $p = .712$ *(two-tailed)*. The magnitude of differences in the means (mean difference = −.148, 95% CI: −.942 to .646) was very small ($eta^2 = .002$).

Participants were divided into four groups: Low Caffeine–Low Stress, High Caffeine–Low Stress, Low Caffeine–High Stress and High Caffeine–High Stress. Descriptive statistics of each group are presented in Table 1.

A two-way between-groups analysis of variance was conducted to explore the impact of the independent variables (caffeine and stress) on the dependent variable (the frequency of false alarms), as measured by the White Christmas Paradigm. The interaction effect between stress and caffeine was statistically significant, $F(1, 88) = 4.09$, $p = .046$. There was also a statistically significant main effect for stress, $F(1, 88) = 4.18$, $p = .044$, with a small effect size *(partial* $eta^2 = .04$). There was a statistically significant main effect for caffeine, $F(1, 88) = 9.35$, $p = .003$, for which the effect size was also small *(partial* $eta^2 = .10$). Fig. 1 presents these data.

An independent samples, post hoc *t*-test was conducted to compare the frequency of false alarms for the groups. Significant

Table 1
Descriptive statistics of variables according to group conditions.

Group name	Group 1 Low Caffeine–Low Stress	Group 2 High Caffeine–Low Stress	Group 3 Low Caffeine–High Stress	Group 4 High Caffeine–High Stress
n	35	14	27	16
Mean hallucination	1.03	1.43	1.04	3.0
SD hallucination	1.64	1.34	1.16	2.76
Mean caffeine	71.11	476.25	93.37	385.40
SD caffeine	57.07	93.37	56.69	131.96
Mean stress	.24	.25	.50	.63
SD stress	.10	.10	.08	.19
Mean SDS	15.49	14.57	15.22	15.63
SD SDS	5.67	5.33	4.01	3.88
Mean CEQ	5.89	9.71	9.22	9.44
SD CEQ	2.92	3.05	5.42	4.93
Mean QMI	173.66	195.79	185.26	192.44
SD QMI	26.96	21.41	28.59	30.76
Mean LSHS	11.80	15.93	21.15	26.06
SD LSHS	6.42	10.45	11.73	13.73
Mean age	23.31	22.57	26.74	27.81
SD age	7.23	4.20	10.32	9.30

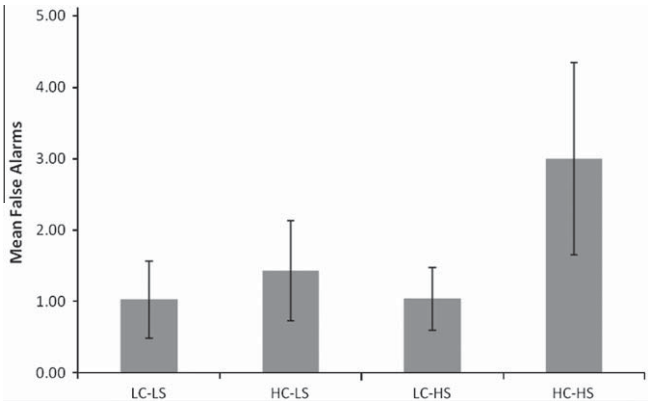

Figure 1. Mean false alarm occurrences of LC–LS (Low Caffeine–Low Stress), HC–LS (High Caffeine–Low Stress), LC–HS (Low Caffeine–High Stress) and HC–HS (High Caffeine–High Stress) groups, with 95% confidence intervals.

differences were found between Group 1 (i.e. Low Caffeine–Low Stress: $M = 1.03$, $SD = 1.64$) and Group 4 (i.e. High Caffeine–High Stress; $M = 3$, $SD = 2.76$); $t(92) = 2.65$, $p = .01$ (two-tailed). The magnitude of the differences in the means (mean difference = −1.97, 95% CI: −3.52 to −0.42) was large ($eta^2 = 0.125$). Fig. 2 illustrates the interaction effect of caffeine and stress on false alarms.

For the measures of hallucination proneness (LSHS), creative experiences (CEQ), mental imagery ability (QMI), and social desirability (MC-SDS) a correlational analysis was conducted (See Table 2). A significant correlation was only found between the CEQ and the LSHS ($r = .70$, $p < .01$). A hierarchical multiple regression analysis was performed to assess the ability of the two control measures (Stress; Caffeine) to predict false alarms after controlling for the influence of social desirability, mental imagery type, hallucination proneness and creativity. QMI, SDS, LSHS and CEQ were entered at step 1, explaining 4.2% of the variance in recorded false alarms. After entry of age at step 2 the total variance explained by the model was 6.5%. After entry of caffeine and stress at step 3 the total variance explained by the model as a whole was 24.7%, $F(7, 84) = 3.938$, $p = .001$. The two independent variables explained an additional 18.2% of the variance in reported false alarms after controlling for the inventories and age. R square change = .182, F change $(2, 84) = 10.14$, $p < .0005$. In the final model, stress level and age were statistically significant, with PSQ scale recording a higher beta value (beta = .486, $p < .0005$), than age (beta = −.303, $p = .004$). Caffeine was not statistically significant, (beta = .169, $p = .088$).

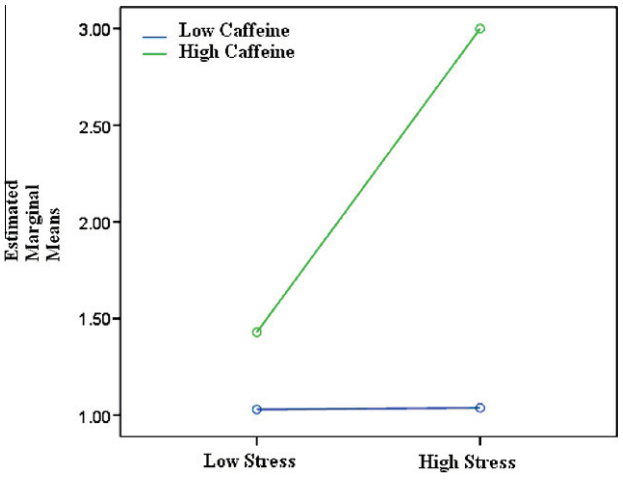

Figure 2. Estimated marginal means of false alarms for each of the groups.

Table 2
Zero order correlations among questionnaire/measures.

Variables	MC-SDS	CEQ	QMI	LSHS
Social desirability (MC-SDS)	1.00	.01	−.05	.07
Creative experiences (CEQ)	.01	1.00	.20	**.70****
Mental imagery ability (QMI)	−.05	.20	1.00	.14
Hallucination proneness (LSHS)	.07	**.70****	.14	1.00

** $p < .01$.

4. Discussion

The effects of caffeine and stress on the occurrence of false alarms in the general population were investigated in the current study. It was hypothesised that people who consumed high levels of caffeine and who also reported high levels of stress would be more likely to experience false alarms. The interaction effect of caffeine and stress significantly predicted the occurrence of false alarms in the participants, thus supporting this hypothesis. It was also hypothesised that people who consumed high levels of caffeine *or* experienced high levels of stress would be more likely to report false alarms than would people who did not experience much stress and who consumed little or no caffeine. Both caffeine and stress as individual factors had a significant ability to predict the occurrence of false alarms, providing support for this hypothesis. Thus the main hypotheses of the current study were supported. The results also support the heuristic neural diathesis-stress model and the continuum theory of schizophrenia. That is, that stress plays a role in the symptoms of schizophrenia and that everyone, to some degree, can experience these symptoms. This was demonstrated by a significant effect of stress on the occurrence of hallucinatory experiences or false alarms. However these findings are not entirely in accordance with previous research.

Jones and Fernyhough (2009) found a significant correlation between caffeine intake and hallucination proneness. Yet they found no significant effect for the interaction of caffeine and stress to predict hallucination proneness. This may be due to the unreliability of their use of the self-report measure regarding hallucination proneness. These main findings regarding caffeine, stress and false alarms are unique to the current literature as no other study has performed this kind of empirical analysis.

As hypothesised, creative experiences, mental imagery ability and social desirability were also found to be non-significant. Imagery ability factors were not significantly correlated with false alarm occurrence. This finding, which indicates that the performance on the White Christmas paradigm cannot be attributed to imagery ability, was also noted by Merckelbach and van de Ven (2001). Social desirability factors were not found to be significantly correlated with the occurrence of false alarms. This is consistent with the finding of Young, Bentall, Slade, and Dewey (1987), who claimed that the White Christmas paradigm cannot be explained by factors such as compliance. Merckelbach and van de Ven (2001) found that participants who reported hallucinatory experiences had higher scores on creative experiences. As hypothesized, we did not find a significant correlation between false alarm occurrences and creative experiences.

One of the hypotheses was not supported by the current findings however. Merckelbach and van de Ven (2001) found that participants who "hallucinated" had higher scores on hallucination proneness. Additionally, Jones and Fernyhough (2009) found that caffeine consumption predicted hallucination proneness. Yet, contrary to our hypothesis, we found no correlation between hallucination proneness and the actual occurrence of false alarms as measured by our procedure. However, it should be noted that

the hallucination proneness measure and creative experiences measure were significantly correlated. This finding suggests that perhaps the hallucination proneness measure does not directly measure hallucination proneness, but instead may be related to an individual's proneness to fantastical and creative experiences.

The findings of this study have further developed the findings of the Jones and Fernyhough (2009) study. Rather than simply finding a link between caffeine consumption and hallucination proneness, the current study found a link between caffeine consumption, perceived stress and the actual occurrence of false alarms as measured using the WCP. Other potential influences that may explain the occurrence of hallucinatory experiences (including creative experiences, imagery ability and social desirability seeking) were also ruled out in the current investigation, which is a strength of the study.

There are however a number of limitations that can be identified with the study. Concerning the effects of caffeine, it is important to note that we did not take into consideration all possibly influential factors that could affect an individual's ambient level of caffeine. There are a number of factors that are known to mediate the effects of caffeine. This includes factors such as age, gender, body mass, habitual user status, caffeine source, liver function, cigarette smoking, use of oral contraceptives and pregnancy (James, 1997). Future research should consider these factors before conclusively stating the influence of caffeine on hallucinatory occurrences. The current study had fewer participants in the high caffeine groups than in the low caffeine groups, which is another limitation. The number of participants in the study overall would not have been sufficient to study the effects that specific caffeine sources, or a combination of sources, has on hallucinatory occurrences.

The extensive use of self-report measures may have reduced the reliability of the current findings. The Durham Caffeine Inventory has yet to be independently validated, and no formal mental health assessment of participants was conducted. Future research should consider a number of options that may validate the current findings. It may be useful to induce stress in participants, for example, by having them perform an oral presentation to a group of people. For the control group, the participants may be asked to perform a neutral task or one that actually reduces stress, such as meditation. Additionally, future research may consider administering caffeine to participants in a double-blind study. As Jones and Fernyhough (2009) have suggested, this could more directly assess the causal effect of the relationship between caffeine and hallucinations. Such a study is currently underway in our laboratory. The caffeine dosage, time of administration, and absorption time are all being taken into consideration. Even though social desirability, mental imagery ability, creative experiences, and even hallucination proneness were found not to correlate with the actual occurrence of false alarms, it would be interesting to alter the WCP to better examine the effect of the song on performance. Future studies could omit playing the song for participants so close to study procedures or perhaps they could suggest that one of two possible songs might be played during the white noise session. Research efforts should also focus on determining the mechanisms of action by which caffeine and stress promote hallucinatory experiences.

5. Conclusion

The results from this study demonstrate that increased caffeine consumption, combined with high levels of stress, has the ability to increase the experience of psychotic symptoms, specifically auditory hallucinations. While these findings require further replication and support, it is apparent that the health risks of excessive caffeine use must be addressed and caution should be raised with regards to the exacerbating use of this stimulant.

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