Using a drug-word Stroop task to differentiate recreational from dependent drug use

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Abstract

Distinguishing dependent from recreational drug use can be a surprisingly difficult task, and the current means for identifying substance abuse can be inadequate or even misleading. In subjective self-reports, those who are most at risk may downplay their consumption, not admitting to the full extent of their habit, and measures purely of quantity of use rarely capture the true nature of an individual's relationship to the drug, such as a psychological dependence on the substance. This trend is particularly true for heavy stimulant use, which is absent the physical withdrawal symptoms that can help identify opiate or alcohol dependence. As such, a simple objective measure to help identify substance abuse, particularly in individuals who might not otherwise raise suspicion, would be a valuable tool in both clinical and experimental settings. We propose that the drug-word Stroop task, an objective assessment of attentional bias and distraction to salient drug-related stimuli, would be a valuable tool in helping to make these categorizations. This measure has been shown to correlate with drug craving, as well as successfully distinguish dependent from recreational stimulant users and help to predict outcomes in treatment-seeking individuals. Here, we survey prior literature on the drug-word Stroop task and provide a perspective on using the assessment as a potential diagnostic for drug use severity.

Introduction

In the recently released DSM-5 (http://www.dsm5.org), the diagnostic criteria for addiction were altered, doing away with the distinction between abuse and dependence [1]. Now, the disorder is viewed along a continuum, with a minimum of two symptoms being required to meet diagnosis. However, these evaluations, like the vast majority of psychiatric classifications, can be largely subjective in nature, lacking in empirical diagnostic tools. This is particularly the case for the dependence on stimulant drugs, which is absent any physical withdrawal symptoms and thus can be harder to identify than opiate or alcohol addiction. Additionally, little attention has been paid to individuals who use stimulant drugs like cocaine recreationally and without a pattern of abuse; an estimated 14.2 million people worldwide [2]. Methods for identifying these individuals and distinguishing them from those who are dependent, both for clinical purposes and empirical research, is wildly inconsistent, with some researchers relying on subjective self-reports while others make their classifications based solely on the quantity of drugs used. Furthermore, there are few evaluations that provide any insight into the possible trajectory of individuals who use drugs – i.e. whether recreational use will develop into dependence, and whether those who are seeking help for their addiction will be successful in their efforts at abstinence.

Currently, quantity rather than the quality of substance use is employed as the standard means for identifying harmful or abusive drug behavior [3]. However, a single approach for assessing dependence can be imprecise and even misleading, as important qualitative information such as drug craving, attitudes towards the substance, and significant life harm caused by the drug are lost when measuring only the quantity of use. Alternatively, self-report questionnaires like the Obsessive-Compulsive Drug Use Scale (OCDUS) [4] have been developed in an attempt to more objectively identify those who display symptoms of compulsive use or dependence. In addition to these methods, we propose using a relevant

cognitive-behavioral assessment that focuses on known impairments associated with addiction and that can help distinguish between casual or more severe drug-use behaviors. Tests of substance users' reactions to drug-related stimuli can be particularly helpful in this regard, measuring levels of craving or attentional bias to drug cues [5]. These tests have been used in the past to successfully distinguish recreational from dependent stimulant users [6], as well as predict treatment outcomes and relapse rates for those seeking help for their addiction [7,8].

The current perspective will review the recent literature and investigate the possibility of assessing drug-use severity with tests of attentional bias, particularly the drug-word Stroop task, a valid, objective, empirical measure that can be employed behaviorally and during functional neuroimaging to assess emotional salience to drug cues and their effect on cognitive functioning. Assessing unintentional attentional bias to drug-related stimuli can thus be used as a means for measuring distraction and preoccupation with these cues, serving as a proxy for drug-use severity.

Cognitive Deficits and Attentional Bias in Stimulant Dependence

Several decades of work have reported on a wide-range of cognitive deficits observed in stimulant-dependent individuals [9–11]. This includes crucial difficulties with response inhibition and self-control [12,13], as well as detriments in working memory [14,15], decision-making [16,17], sustained attention [18,19], task-switching [20], and affective responding and emotion regulation [21]. These impairments often correlate with years of substance use and are not seen in the first-degree relatives of drug-dependent individuals [22], implicating prolonged exposure to stimulant drugs in more severe dysfunction. Additionally, stimulant-dependent individuals typically exhibit a significant decrease in prefrontal cortex activation on executive function

tasks, often accompanying these behavioral impairments in self-control, inhibition and working memory [9,14,23,24].

In addition to the cognitive dysfunction present in dependent stimulant users, there is profound evidence of a disruption in affective system processing, thought to stem from abnormalities in the fronto-striatal reward circuitry. This is particularly evident in the face of salient drug stimuli, where the associated drug cues are thought to "hijack" the reward system, emphasizing drug rewards over other priorities. This can lead to significant drug craving, which can in turn cause unplanned or undesired use.

Attentional bias to drug-related cues can elicit these feelings of craving and, coupled with the poor decision-making and inhibitory control characteristic of stimulant-dependent individuals, can precipitate relapse [25–28]. These experiences are thought to be subserved by dysfunction in the prefrontal cortex [29,30], where dependent stimulant users have been shown to have decreased gray matter volume compared with healthy control individuals [31,32]. Exposure to drug-related cues or even a weakening in self-control may result in heightened attentional bias, the drug cue being flagged in the brain as having special salience [33]. This can then trigger rumination over the stimulus in drug users, potentially resulting in relapse [33]. Corroborating this theory, recent research has shown that attentional bias is most elevated after encounters with drug-related cues [34,35].

Drug-Word Stroop Task

While there are several measures that can be employed to assess attentional bias or salience attributed to drug-related words (eye-tracking, visual-probe), in the current review we have chosen to focus on the drug-word Stroop task due to its easy administration, extensive prior use in a wide variety of drug-using populations, and respectable internal reliability scores compared with other tests of attentional bias [36]. The drug-word Stroop is a derivative of the

classic cognitive control test, the color-word Stroop, where participants must name the font color of a target word that spells out either the same or a different color-word as the font (Figure 1) [37,38]. Responses to incongruent color-word combinations present a greater cognitive demand than congruent pairings because of interference from the prepotent tendency to read a word rather than determine its color. The interference score indexes how well a person exerts cognitive control over this automatic behavior (word-reading) in favor of a more unusual behavior (color-naming).

The adapted version of the task measures affective interference causing attentional bias in the face of salient compared to neutral cues. In the drug-word version, substance-relevant cue words are presented in different colors; again the participant must ignore the content of the word, responding only to its font color. In human drug users, heightened drug-related salience can result in undesired distraction and cognitive interference caused by the word content, rendering them slower to respond. Reaction times to the cocaine cue words are compared with times to neutral cue words matched for length and familiarity. The interference score is the resulting difference between these two task conditions. This measure thus enables each individual to serve as their own control, as their reactions to the drug words are compared against their own response latencies to the neutral cues. A significant increase in reaction time to the salient stimuli compared with the neutral ones is then indicative of impairment on the task.

This paradigm has been used in a variety of substance-dependent populations, consistently showing significant distraction to drug-related cues in individuals with high use of cocaine [39,40], heroin [41,42], alcohol [5,43], cannabis [44] and nicotine [45–47]. In the brain, this attentional bias relates to abnormal responding in the medial orbitofrontal cortex (OFC) and anterior cingulate cortex (ACC), areas implicated in craving, reward and attention [48–50]. Elevated activation in limbic regions, including the striatum, amygdala, ACC and OFC, is also

associated with increased craving in response to drug-related cues [46,51–53], and high scores on the drug-word Stroop commonly correlate with feelings of craving [5,49,54]. Additionally, areas involved in inhibitory control – such as the dorsal ACC, superior parietal lobe, dorsolateral prefrontal cortex and superior temporal gyrus – were activated during performance of another attentional bias task in heavy smokers, potentially reflecting the greater effort required to inhibit responses to these salient smoking-related stimuli in these individuals [55,56]. These findings have been reliably replicated in a number of studies, and these neural correlates may be used as an objective tool for determining the degree of drug use severity.

It is important to note that a block design should be used during neuroimaging assessments of the drug-word Stroop task, ensuring that salience-related activity prompted by the drug cues does not "spill over" into the neutral trials, contaminating them with heightened arousal due to a too short recovery period during event-related designs. It has also been shown that using a block design significantly increases the internal reliability of the task [36].

Franken [49] posits that this biased attention network in drug users stems from dysfunctional involuntary reactions to drug-related cues. Due to the limited nature of the brain's attentional capacity, attention is typically allocated to only a subset of external stimuli to avoid overstimulation. However, when a stimulus is particularly potent it can "hijack" this system and assume a greater proportion of the attentional resources. Modeled in the drug-word Stroop task, this results in higher response latencies for salient words, as too much attention is paid to the content of the word rather than the color of the font, distracting the individual from the task at-hand [27,40].

Despite its widely established use, the drug-word Stroop task is not infallible, and recent reviews have raised concerns about internal reliability and consistency with the test [36]. Reviewing six different studies employing an alcohol or nicotine Stroop task, Ataya and

colleagues used Cronbach alpha scores to assess internal reliability rates on the test. Reliability coefficients ranged from 0.53-0.98 in the different studies (a score of 0.70 is considered acceptable). However, as stated above, employing a block design can help to improve reliability scores, as can using picture rather than word stimuli and increasing the number of trials in the task. Notably, the drug-word Stroop task was significantly more reliable than using a visual probe assessment to measure attentional bias. To help address concerns over consistency, Field and Christiansen [57] have suggested modifying the task for each individual based on their personal drug preference (i.e. type of alcohol, cocaine administration route) to ensure maximum salience, and thus improved reliability.

Recreational Versus Dependent Stimulant Use

As noted in the introduction, it is important to remember that although these cognitive impairments can be serious, they do not afflict all drug users. In fact, the vast majority of individuals who try stimulant drugs do not become addicted to them [2]. Moreover, there seems to be a select subset of the population who are able to use cocaine recreationally in a controlled manner without developing dependence [58]. These individuals report consistent, occasional, social use of cocaine without experiencing a loss of control or exhibiting symptoms of dependence or abuse [58]. They also do not self-report feeling cravings for cocaine, and their use is planned rather than impulsive. These individuals who have used cocaine in a stable manner for an extended period of time without developing a dependency could be an intermediary group that can be used to assess potential cocaine-induced abnormalities and distinguish them from traits involved in underlying risk for addiction or current compulsive use and dependence.

Recreational users would be expected to show similar, though not as severe, changes in structure and function attributed to prolonged stimulant use, but not the abnormalities

associated with increased premorbid risk for dependence. Furthermore, there may be additional differences in the brains of recreational stimulant users that serve as protective factors against addiction [58]. However, it should be noted that inherent differences in cocaine exposure between the dependent and recreational users may create potential confounds when comparing cognitive function and attentional bias to drug cues – though greater use does not always correspond to greater impairment [59].

There are currently no established means for identifying recreational use and distinguishing it from abuse or dependence, and previous investigations into this population have reported somewhat conflicting results. Some studies have shown similar cognitive impairments in recreational users as in dependent individual [3,60], while others have reported varying difference between recreational users and healthy control volunteers [61–63]. One possible reason for these discrepancies may be the criteria used to define "recreational use". Some investigations have relied solely on quantity of use to make these determinations [3,60,61], while our own lab has deemed to focus more on the pattern and quality of use when making these distinctions. We now believe that attentional bias to drug-related stimuli may also be a more objective means for making this identification.

In an investigation of dependent and recreational stimulant users, we showed that recreational users of cocaine performed no differently from controls on a test of the cocaine-word Stroop task [6]. Conversely, dependent stimulant users were significantly more impaired, with longer response latencies, higher interference scores and more errors committed on the task. Additionally, there were significantly different patterns of brain activation between the two stimulant-using groups, with dependent users showing a heightened functional magnetic resonance imaging (fMRI) blood oxygen level dependent (BOLD) response to the cocaine cues compared with the recreational users, particularly in the OFC and ACC, regions known to be involved in attentional bias and feelings of craving (Figure 2). The recreational users

also showed an overall decrease in activation in the inferior frontal gyrus (IFG), an area crucial for inhibitory control and one in which dependent individuals often show impairments. Interestingly, there were no differences in activity between the dependent users and control participants in the OFC or ACC, and in some instances the dependent individuals actually showed greater activation in the IFG during attempts to inhibit their response to the cocaine-related words. These measures of attentional bias and emotional salience are often used as a proxy for drug-related craving. However, unfortunately no direct tests of cocaine craving were administered in the current study, nor is there evidence of a craving comparison in prior research with these populations. An empirical examination of this measure would be an important addition for future research as an extension and corroboration of these findings.

The lack of attentional bias to the cocaine cues in the recreational users, demonstrated through an absence of interference scores and no significant slowing on those trials, indicates that these stimuli did not carry any increased salience in these individuals. This is in stark contrast with the dependent individuals, who were significantly impaired in the face of the cocaine cues. Thus, there appears to be an inherent difference between the two groups in their automatic processing of cocaine-related stimuli, reflecting an important distinction in their attitudes towards the drug. This is further supported by the underlying difference in neural activation between the two groups, with recreational users showing a relative decrease in IFG/OFC activation in response to the cocaine words. This suggests that the stimuli do not hold the same salience for these individuals as they do for the dependent users. Drug-related attentional bias has been linked to increased motivation to obtain the substance, as well as heightened emotional salience for these cues [27,64]. The increased activation of the OFC in the dependent individuals could be due to heightened arousal caused by the cocaine cues, resulting in elevated activation in this reward-processing region [65]. Similarly, the dependent individuals' increased IFG activity may be reflective of greater effort required to resist the

content of the distracting cocaine words. In the recreational users this area was not equivalently recruited, as the need to inhibit attentional bias to the salient words was not present.

These results are in line with research into attentional bias among users of differing severity in other substance-using groups, including alcohol and cannabis. For example, dependent cannabis users, as determined by frequency of use and self-report questionnaire, demonstrated increased attentional bias on a cannabis-word Stroop task than occasional smokers [44]. Interference scores were positively correlated with both number of joints smoked per month and level of cannabis craving [44]. Additionally, in a comparison of light and heavy social drinkers, less alcohol consumption was related to diminished attentional bias to alcohol cues, as well as decreased craving for the substance [66,67]. Thus, we believe that both the differing quantity and quality of drug consumption may be captured with the drug-word Stroop task, reflected in the different reactions to drug cue words between recreational and regular users of the substance. To the best of our knowledge, the studies mentioned here constitute an exhaustive list of prior research into drug-related attentional bias in non-dependent individuals, and there are no studies showing equal levels of attentional bias between recreational or occasional substance users and addicted individuals.

Treatment Success Prediction

Attentional bias tasks have also been used to help better determine the potential trajectory of drug treatment and to better predict rehabilitation outcomes in drug users [59]. By and large, the better a patient's initial cognitive abilities and resistance to drug-related distraction, the higher their potential success rates for abstinence. This is true across a range of substances, including nicotine [68], alcohol , cocaine [7,8,69,70] and heroin [71]. This is unsurprising given the

association stated above between an individual's attentional bias or interference on the task and their craving for drugs, which is associated with a greater risk for relapse.

In the brain, these impairments manifest as abnormal activation in the insula, ACC and prefrontal cortex, thought to correspond with the increased cognitive demand required to override the initial emotional reaction to the words [48,50,70,72]. Those with greater activation in these relevant regions – signifying greater effort required to resist distraction to the words or increased salience to the cues – consistently showed higher rates of relapse. Thus, higher levels of craving, greater interference on the drug-word Stroop task, or increased neural activity in response to drug cues can help to better predict relapse rates and treatment success among those entering rehabilitation programs.

Conclusion

The ability of the drug-word Stroop task to identify aberrant salience for drug-related words, signifying distraction, cognitive interference and potentially craving, makes it a key behavioral measure that could be used as a diagnostic for drug dependence, particularly in the difficult distinctions between dependent and recreational stimulant users. Evidence suggests that the task is not only helpful at the end-stage of addiction when the individual is seeking help, identifying those who may be more successful in their attempts at abstinence, but also in earlier junctures, which is a much more difficult period to define. This test could help to predict who at the beginning phases of drug use is at a greater risk for developing dependence based on their reaction to the drug-word cues, with greater interference potentially indicating a heightened susceptibility for addiction.

The drug-word Stroop could also potentially be used not only in specific addiction research or clinical environments, but in schools, general practice doctors' offices, and on control volunteers in any research setting to help identify those who may have problems with drugs

or alcohol. The task could be implemented to determine whether a person is deliberately downplaying their alcohol or drug use – potentially supplying misleading answers on self-report questionnaires to avoid identification as a problem user. However, given the research presented here, it is likely that they would still show signs of enhanced attentional bias to drug-related cues, thus the task could be used as a confirmation for subjective self-report measures. Additionally, the task's success at predicting relapse rates among treatment seeking drug users indicate that it could also be used as a means to help reliably predict rehabilitation outcomes, and thus could be a valuable measure to help determine the allocation of resources to those who may be most assisted by them.

However, further research is still needed to validate the drug Stroop task as a means for distinguishing recreational from dependent drug use. While our research mentioned here provides evidence of both behavioral and functional differences between the two groups [6], more studies are needed to confirm the task's potential as a diagnostic. Additionally, logistical concerns must be addressed, such as cut-off scores for differentiating dependent from recreational users. Furthermore, tests confirming the Stroop's correspondence to drug craving scores in recreational users need to be conducted. Also, given the concerns over consistency in the Stroop, tests of internal reliability should be carried out in recreational users as well. While the Stroop task is certainly not an infallible measure, evidence suggests that it is better than some other assessors of attentional bias, such as the visual probe task [36]. An alternative to using reaction time measures to assess attentional bias, which may be at the root of the problem with internal reliability, is employing an eye-tracking assessment [57]. However, while this type of task has been shown to be more reliable, they are more difficult to administer and analyze, requiring specialized equipment and software, and thus may not be as practical in non-research settings. We believe an advantage of the Stroop task is its relative ease and practicality, only requiring a standard laptop to administer.

Finally, there is a wide belief that it is not possible to use more typically addictive substances, like cocaine, recreationally without developing dependence. However, our research and the results from this objective measure suggest otherwise, showing that it is possible to have a similar relationship to substances like cocaine as to more socially acceptable drugs, like alcohol or tobacco. Instead of the potential for addiction residing solely in the addictive properties of the drug itself, we believe that there is an underlying heightened vulnerability in certain individuals and environments that make them more susceptible to the formation of dependence on drugs.

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Legends

Figure 1. Drug-word Stroop task. Participants are instructed to ignore the content of the word and instead focus on responding only to the color of the font. Greater distraction to the cocaine-related stimuli results in higher response times compared with the neutral words, indicating greater interference and impairment in the face of drug cues. Difficulty on the task has been associated with increased drug craving, higher quantity of use, and may be indicative of dependence on the drug.

Figure 2. Group contrast between recreational and dependent stimulant users and healthy control volunteers, comparing activation during cocaine versus neutral trials on the cocaine-word Stroop task. Significant differences emerged in two clusters: the right orbitofrontal cortex (OFC) and anterior cingulate cortex (ACC), and the right angular gyrus and posterior cingulate cortex. Recreational cocaine users significantly under-activated these two regions in comparison with the other two groups, while dependent stimulant users showed a relative increase in activation, though this was not significant when compared to control participants. Coordinates listed are in MNI standard space. Cluster significance set at $p<0.05$ family-wise error correction for multiple comparisons. Group comparisons made using ANCOVA models, controlling for age, gender, years of education, smoking status, BDI-II depression scores, and AUDIT alcohol scores, with Bonferroni post-hoc correction $p<0.05$.

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Figure 1.

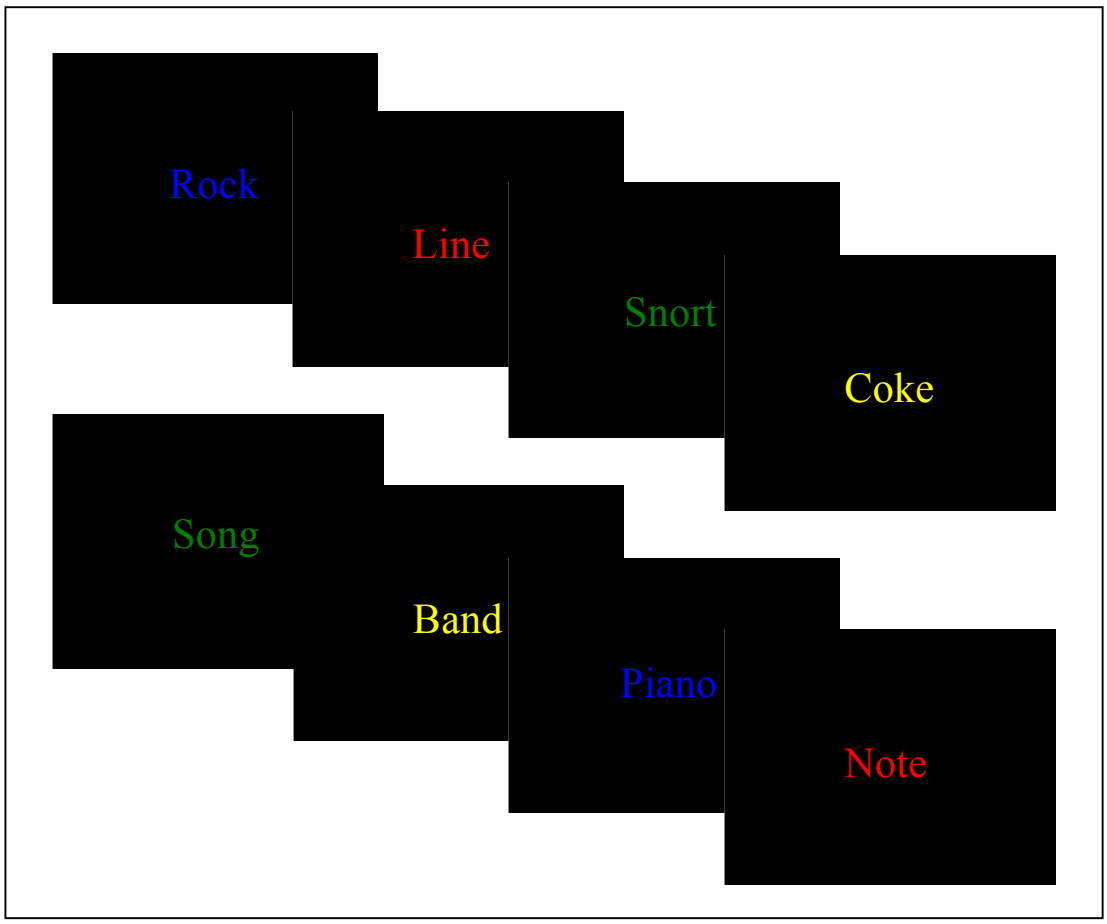
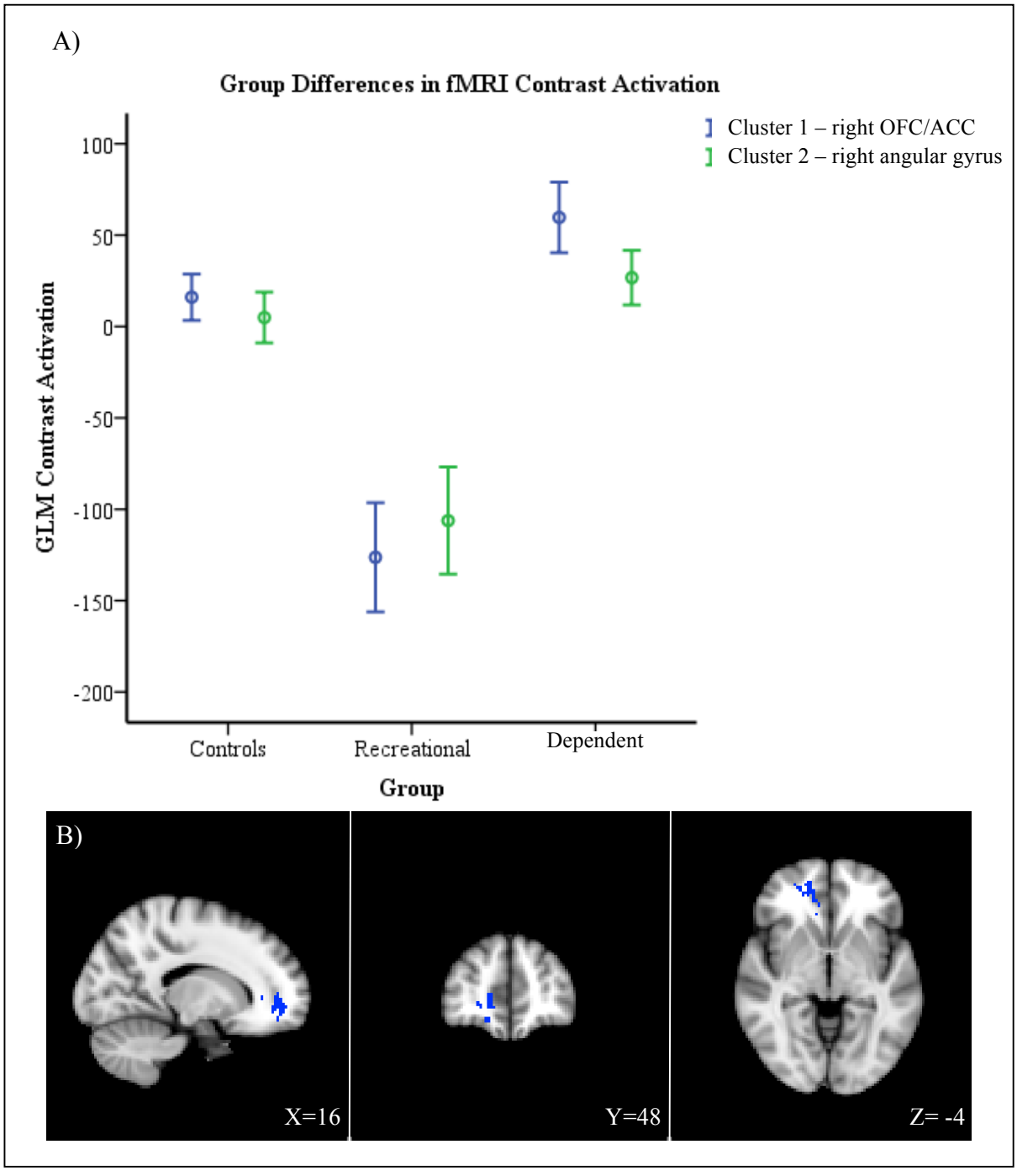


Figure 2.


A)
Group Differences in fMRI Contrast Activation
Cluster 1 – right OFC/ACC
Cluster 2 – right angular gyrus
GLM Contrast Activation
100
50
0
-50
-100
-150
-200
Controls
Recreational
Dependent
Group
B)
X=16
Y=48
Z= -4