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The role of social stimuli content in neuroimaging studies investigating alcohol cue-reactivity

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HIGHLIGHTS

- Stimuli content of 26 alcohol cue-reactivity neuroimaging studies was systematically reviewed.
- More social interaction was found in alcoholic compared to non-alcoholic beverage stimuli.
- Brain areas associated with processing of social and reward-related information overlap.
- Matching stimuli on social content improves the reliability of alcohol cue-reactivity studies.

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ABSTRACT

Introduction: Cue-reactivity is thought to play a fundamental role in the maintenance of addiction. The incentive sensitization theory proposes that conditioned responses are related to increased sensitivity of the reward-related dopaminergic pathways in the brain. However, neuroimaging studies on alcohol cue-reactivity show inconsistent results.
Methods: Stimuli content of 26 alcohol cue-reactivity studies was systematically reviewed.
Results: No differences were found between alcoholic beverage stimuli and non-alcoholic beverage stimuli in human display and brand factors; however, alcoholic beverage stimuli were more likely to display social interaction compared to non-alcoholic beverage stimuli.
Conclusions: Given that processing of social information activates brain areas that partly overlap with reward-related brain areas associated with cue-reactivity, such differences between conditions can introduce noise in the findings. We therefore suggest matching stimuli sets on the reviewed factors carefully to improve reliability of neuroimaging studies investigating alcohol-related cue-reactivity.

Contents

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1. Introduction

Reactivity to substance-related cues has been extensively investigated during the last decade, as it is perceived to be a key factor in the development and maintenance of addiction (Carter & Tiffany, 1999; Chase, Eickhoff, Laird, & Hogarth, 2011). The incentive sensitization theory (Robinson & Berridge, 1993, 2001) proposes that addiction is related to dopamine sensitization to substance-related cues, making these cues more attractive, attention grabbing and able to elicit drug-taking behaviour. These conditioned responses include physiological and subjective responses to alcohol-related cues in substance dependent patients (O'Brien, Childress, Ehrman, & Robbins, 1998; Powell et al., 1990). Conditioned responses to alcohol-related cues have been found to be associated with treatment outcome and the risk of relapse (Heinz, Beck, Grusser, Grace, & Wrase, 2009; Hogarth, Dickinson, & Duka, 2010; Ray, Mackillop, & Monti, 2010). For these reasons, many studies investigated reactivity to substance-related cues.

Neuroimaging techniques provide exciting opportunities to investigate the underlying neural processes of substance-related cue-reactivity. Yet, when studying neural responses to substance-related cues, stimuli content in both substance-related and control pictures largely determine neuroimaging findings. While in most studies attention has been given to adequate match alcohol and control stimuli for characteristics such as complexity and brightness (Pulido, Brown, Cummins, Paulus, & Tapert, 2010), the importance of stimuli content has received less attention. Stimuli content may be important, as it can evoke different reactions in both brain activation and behaviour. Given this gap in the literature, the aim of this commentary was to draw attention to the importance of stimuli content in alcohol-related cue-reactivity paradigms by systematically reviewing social stimuli content in neuroimaging studies on alcohol-related cue-reactivity.

A recent meta-analysis conducted by Schacht, Anton, and Myrick (2012) showed increased activation in the ventral striatum (VS), the ventral anterior cingulate cortex (vACC) and the ventro-medial prefrontal cortex (vmPFC) in heavy drinkers or individuals with alcohol dependence in response to alcohol-related stimuli relative to control stimuli. Alcohol-cue related brain activation in the ACC and VS was also reported in an earlier meta-analysis (Kuhn & Gallinat, 2011). This activation in areas of the reward-related dopaminergic pathway in response to alcohol-related stimuli is in line with the incentive sensitization theory. However, no significant group differences were found or reported in these brain areas when alcohol dependent individuals were compared with social drinking controls (Kuhn & Gallinat, 2011; Schacht et al., 2012). Moreover, when examining all twenty-eight studies included in this meta-analysis, only one study reported increased VS activity in heavy drinkers compared to controls (Ihssen, Cox, Wiggett, Fadardi, & Linden, 2011). The lack of group differences between individuals with alcohol dependence and social drinkers in reward-related brain areas is in contrast with the incentive-sensitization theory. Recently, Jasinska, Stein, Kaiser, Naumer, and Yalachkov (2014) proposed several individual-and-study specific factors, which modulate neural reactivity to drug cues that may introduce inconsistencies, for instance sensory modality, length of stimuli presentation as well as addiction severity and drug availability. In addition to these factors, we suggest that stimuli *content* in alcohol-related and control pictures during alcohol cue-reactivity tasks is pivotal for the generalization, validity and reliability of neuroimaging findings, especially since stimuli content is related to social information processing.

The emerging field of social neuroscience revealed that brain regions show specific activation patterns when processing social information, such as the amygdala, the vmPFC (Adolphs, 1999; Amodio & Frith, 2006) and the superior temporal sulcus (STS) (Allison, Puce, & McCarthy, 2000). Stimuli with social content can also be associated with feelings or thoughts of such a social context, which can then trigger (emotional) reactions reflected in brain responses (Adolphs, 2009; Nees, Diener, Smolka, & Flor, 2012). In nicotine dependence, stimuli with social content are found to elicited greater psychophysiological responses, such as skin conductance and electromyography, compared to stimuli displaying pure nicotine related objects (Choi et al., 2011). Importantly, individuals with different drinking patterns may differ in reactivity to social stimuli content in combination with alcohol-cues, as social content in alcohol stimuli may be more important to social and light drinkers compared to heavy drinkers or individuals with alcohol dependence (Larsen, Engels, Granic, & Overbeek, 2009). Lastly, misinterpretation of results can occur when imbalances exist between alcohol-related and control stimuli in terms of social content, e.g., when more stimuli with social content are displayed in the alcohol-related condition compared to the control condition.

Given that neuroimaging studies investigating alcohol related cue-reactivity have paid less attention to (social) stimuli content, the purpose of this commentary is to review the social content of stimuli used in visual alcohol cue-reactivity paradigms by focussing on three factors; 1) human display, since the perception of humans may require greater and different activation in brain areas such as the amygdala, vmPFC and STS (Bentin, Allison, Puce, Perez, & McCarthy, 1996), 2) social interaction, as alcohol use is a form of social behaviour (Larsen et al., 2009) and social alcohol contents can trigger emotional reactions or associations (Nees et al., 2012), and 3) brands, since familiarity and perception of a brand can be reflected in different brain activation in the ventral striatum, vmPFC, DLPFC, or amygdala (Pravettoni & Lucchiari, 2012; Schaefer & Rotte, 2007). The current commentary provides an overview of the included studies and their stimuli sets, followed by a description of the three factors of interest. We further discuss how these factors could have affected the current knowledge of the neurobiological basis of cue-reactivity. Finally, some recommendations for future studies are provided.

2. Materials and methods

2.1. Literature search and selection

A literature search was conducted in PubMed, using the keywords 'alcohol', 'cues' and 'fMRI' or 'PET'. Inspection of the 124 initially identified studies (end-date of search is June 2014) revealed that 95 studies were excluded because they 1. did not focus on alcohol (i.e., studies on other substance uses or disorders (n = 24), 2. did not use visual cues (i.e., taste and odour cues, n = 26), 3. did not use a passive viewing paradigm (n = 43), 4. did not use human subjects (n = 2), and 5. did not use of fRMI or PET techniques (n = 0). One study was added based on reference sections, resulting in 30 studies that were included in this review. All authors of the selected studies were contacted and asked to provide their stimuli set.