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Association Splitting: A randomized controlled trial of a new method to reduce craving among inpatients with alcohol dependence

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ABSTRACT

Association Splitting, a novel cognitive intervention, was tested in patients with alcohol dependence as an add-on intervention in an initial randomized controlled trial. Preliminary support for Association Splitting has been found in patients with obsessive-compulsive disorder, as well as in an online pilot study of patients with alcohol use disorders. The present variant sought to reduce craving by strengthening neutral associations with alcohol-related stimuli, thus, altering cognitive networks. Eighty-four inpatients with verified diagnoses of alcohol dependence, who were currently undergoing inpatient treatment, were randomly assigned to Association Splitting or Exercise Therapy. Craving was measured at baseline, 4-week follow-up, and six months later with the Obsessive-Compulsive Drinking Scale (primary outcome) and the Alcohol Craving Questionnaire. There was no advantage for Association Splitting after three treatment sessions relative to Exercise Therapy. Among Association Splitting participants, 51.9% endorsed a subjective decline in craving and 88.9% indicated that they would use Association Splitting in the future. Despite high acceptance, an additional benefit of Association Splitting beyond standard inpatient treatment was not found. Given that participants were concurrently undergoing inpatient treatment and Association Splitting has previously shown moderate effects, modification of the study design may improve the potential to detect significant effects in future trials.

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1. Introduction

Alcohol use disorders (AUDs) are characterized by a problematic pattern of alcohol consumption that leads to severe somatic, psychological, and social problems. Characteristics of AUDs include increased alcohol use in order to obtain the same effects, withdrawal symptoms (e.g., morning shakes, seizures), a strong inner desire to drink, difficulties limiting drinking, neglecting relationships, work or other activities to the exclusion of those involving drinking, and persistent alcohol use despite clear evidence of harmful consequences (e.g., health problems, drunk driving; APA, 2013). AUDs are among the most common psychological disorders worldwide, with a lifetime prevalence among the general adult population from developed countries (e.g., Germany, United States, Japan) at 5.5% (Glantz et al., 2014). Substance abuse disorders contribute to cognitive dysfunction (Naim-Feil et al., 2014) and diverse psychosocial problems, including depression and anxiety (Grant et al., 2009), relationship problems (Boden et al., 2013), and unemployment (Compton et al., 2014).

Craving, defined as the strong urge to drink alcohol, is of particular interest for treatment as it is a subjective and persistent experience, which even those who are "recovered" continue to experience (Lindenmeyer, 2009). The impact of craving on treatment outcome remains unclear as it has been shown to predict alcohol use, relapse and outcome of treatment in some studies (Bottlender and Soyka, 2004; Lindenmeyer, 2009; Higley et al., 2012; Fazzino et al., 2013), although craving does not contribute to outcome in other studies (Junghanns et al., 2005; Kiefer et al., 2005). Cognitive models of addiction suggest that in the course of the addiction process, previously neutral stimuli, such as an empty beer glass or the smell of alcohol, become strongly associated with reinforcing properties of alcohol through associative learning (Tiffany, 1990; Robinson and Berridge, 1993). With repeated opportunities for associative learning due to alcohol-seeking behavior, an attentional bias toward these alcohol-related stimuli develops, such that these cues become detected automatically (without conscious awareness). Thus, craving can be triggered by a variety of stimuli, including positive expectations (e.g., relaxation), specific situations (e.g., being in a bar, social atmosphere), thoughts (e.g., "Drinking is not my real problem," "I can stop at any time"), emotions (e.g., anger or happiness), and sensory experiences (e.g., withdrawal symptoms, normal restlessness; Fazzino

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et al., 2013). Such responses to alcohol-related stimuli, called cue reactivity, create measurable arousal (e.g., changes in pulse, breathing and skin resistance), and are related to activation of neural stress and reward circuits, as well as relapse mechanisms (Sinha et al., 2011; Vollstädt-Klein et al., 2011; Schacht et al., 2013).

The present study sought to examine a novel cognitive technique, called Association Splitting, which aims to disrupt automatic cognitive associations, with the ultimate goal among patients with AUDs of reducing craving. The intervention has already demonstrated success among patients with obsessive-compulsive disorder (OCD; Moritz et al., 2007; Jelinek et al., 2011), and eating disorders (Musiat et al., 2014), as well as in a non-clinical sample with unwanted intrusive thoughts (Rodríguez-Martín et al., 2013). With regard to AUDs, we conducted an online pilot study with individuals with (self-reported) alcohol addiction who were sent a digital Association Splitting self-help manual (Hottenrott and Moritz, 2009). In this study, we found a significant decrease in craving over four weeks with a large effect ($d=0.88$) for pre-post differences on the Obsessive Compulsive Drinking Scale (OCDS).

Numerous pharmacological (Addolorato et al., 2005) and psychological interventions for the treatment of AUDs have been developed. Teaching patients to cope with craving is a central goal of cognitive therapy for AUDs (Beck et al., 1993) and small to moderate effects have been found for cognitive behavioral strategies (McHugh et al., 2010). Mindfulness training has gained increasing attention and aims to help patients to objectively experience cravings without acting on them (Bowen et al., 2009; Garland et al., 2010; Murphy and Mackillop, 2014). Apart from traditional therapeutic approaches, attention-bias modification techniques aim to reduce attentional biases for alcohol-related stimuli; however, their effects on reducing alcohol use and craving are mixed (Wiers et al., 2011; Cox et al., 2014). Differing from attention-bias modification and cognitive behavioral approaches, Association Splitting aims to reduce craving by strengthening alcohol-neutral associations and thus serves to reduce attention to and the availability of alcohol-related cognitions that occur in response to alcohol-related stimuli. To this end, patients are neither taught to actively monitor craving and identify connections between thoughts and behaviors (as in cognitive therapy), nor to "ride the wave" of craving (as in mindfulness training).

As described in more detail elsewhere (Moritz et al., 2007), Association Splitting targets intrusive thoughts, characterized as unwanted, repetitive and stereotypical thoughts that are difficult to resist. Association Splitting is based on semantic network models (Reisberg, 2001), which assume that nodes (i.e., cognitions) are stored in the cortex according to their (semantic) relatedness. For example, a word like "happy" is strongly connected and located adjacent to a word like "love" and the image of a loved one's face (Albery et al., 2015). Once a node in a semantic network is activated, associations with other nodes are (automatically) activated and these associations are strengthened with increasing co-occurrence of cognitions.

Significant evidence exists for these semantic networks among individuals with semantic aphasia (e.g., Lambon et al., 2007; Zannino et al., 2006). Imaging studies have also demonstrated that semantically-related words activate neighboring cortical regions (e.g., Sachs et al., 2008). More recently, Ching et al. (2015) provided support for contamination-relevant association splitting and semantic networks among an unselected college sample. Semantic networks among individuals with AUDs have also been identified in studies utilizing modified Stroop tasks, such that longer response latencies for alcohol-related words in comparison to neutral words were found in individuals with problematic drinking behaviors (Bauer and Cox, 1998; Sharma et al., 2001). Because many individuals with AUDs associate positive situations and feelings (e.g., relaxation, friends, sporting events) strongly with alcohol use, just seeing a bottle of one's favorite liquor can evoke certain thoughts and feelings (i.e., good memories) that can "open the door" for craving, and possibly lead to use (for evidence of such biased semantic networks in OCD see Jelinek et al., 2014, 2009 and Ching et al., 2015). Therefore, the Stroop effect observed in individuals with AUDs may be accounted for by automatic activation of a semantic network related to alcohol (Cox et al., 2006; Field and Cox, 2008; Sharma et al., 2001).

Central to our approach is that reciprocal connections between cognitions are not necessarily equivalent in strength. Association Splitting capitalizes upon findings from cognitive studies showing that the strength of activation of a thought is limited and its sum activation is distributed across neighboring associations (Anderson, 1974; Reisberg, 2001). For example, the word "black" is strongly activated by the word "white" in most individuals. Priming studies have also demonstrated that the acquisition of new associations or the strengthening of existing ones automatically leads to a reduction or weakening of other associations (e.g., Moritz et al., 2001). Moreover, demonstrating the "fan effect", in memory studies, participants demonstrate delayed response times and decreased accuracy for items that have a high number of associations with other items (Schneider and Anderson, 2012). Therefore, when more associations are available for a given cognition, less weight remains for a single association. Applying this to AUDs and against the background of positive findings in other disorders, we hypothesized that for patients with AUDs, alcohol-related stimuli are associated solely (or very strongly) with positive expectations (cognitions), thus weakening neutral associations. When patients are taught to generate or strengthen neutral associations for alcohol-related stimuli (e.g., beer – Halle Berry [similar word], flask – mask [rhyme]), craving may be decreased. The new associations should not be in direct competition with the alcohol-related stimuli (e.g., wine – headache). Therefore, the goal is not to replace unhelpful associations (e.g., beer – buzz) that may increase craving, but rather to increase the availability of neutral associations. It is hypothesized that by creating new associations with alcohol-related stimuli, attention is diverted away from alcohol-related cognitions and toward neutral associations, thus leading to decreased craving and risk for relapse. The urge may not be abolished, but will be markedly decreased, so that the patient is empowered to resist the urge. Importantly, the technique is practiced in situations where the patient is not directly bothered by intrusive thoughts (for further details see Moritz et al., 2007).

In the present study, a randomized controlled trial of Association Splitting among individuals with AUDs was conducted to examine the feasibility and effectiveness of therapist-assisted Association Splitting in inpatients with a verified diagnosis of alcohol dependence. It was expected that patients in the Association Splitting group would experience a greater reduction in craving both four weeks and six months after completing the intervention compared to those in an active control group. Change on the Obsessive Compulsive Drinking Scale (OCDS) was the primary outcome of interest.

2. Methods

The study was a randomized, controlled, parallel-group, assessor-blind trial in which patients were randomized on a 1:1 ratio to one of two treatment conditions – Association Splitting or an Exercise Therapy group.

2.1. Recruitment

Patients from the inpatient unit of the Addictive Disorders

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