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Attentional bias in opioid users: A systematic review and meta-analysis

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ABSTRACT

Background: Opioid use in the United States is a national public health emergency. The primary treatment for opioid use disorder (OUD) is medication assisted treatment (MAT). Although effective in improving treatment outcomes in OUD, there is a need to develop behavioral treatments adjunctive to MAT. The current study investigates attentional bias in OUD as a possible target for adjunctive behavioral treatments.

Methods: Comprehensive literature searches of psychological, medical, and educational databases were conducted through October 2017. Eligible peer-reviewed studies evaluated attentional bias in opioid users, used a task to evaluate attentional bias that included active response to study stimuli, calculated attention bias by comparing response to drug and neutral stimuli, and could isolate attentional bias specific to opioid versus neutral stimuli from bias to other salient stimuli.

Conclusions: The results of our systematic review and meta-analysis suggest that individuals with OUD exhibit robust attentional bias to opioid cues, even when engaged in MAT. Interventions that reduce attentional bias may be a useful adjunct to MAT.

1. Introduction

The United States is experiencing an epidemic of drug overdose deaths that is driven largely by opioid use. Since 2000, the rate of deaths attributed to opioid (i.e., prescription opioids and heroin) overdose has increased by 200% (Rudd et al., 2016). A total of 42,249 people died from opioid overdose in 2016, up 28% from 2015, and the rate of overdose attributed to synthetic opioids (excluding methadone) doubled from 3.1 per 100,000 in 2015 to 6.2 in 2016 (Hedegaard et al., 2017). Opioid overdose deaths closely correlate with the number of opioid prescriptions in the United States, which have been steadily rising since early 1990s (Centers for Disease Control and Prevention (CDC, 2011). The initiation of opioid use typically starts with prescription opioids followed by heroin, as the latter is cheaper and more widely available than prescription opioids (Cicero et al., 2014). Many prevention and treatment approaches have been proposed to curb the opioid epidemic including the development of more effective pharmacological and behavioral treatments for opioid use disorder (OUD).

The primary treatment for OUD is Medication Assisted Treatment (MAT), comprising methadone, buprenorphine and naltrexone. Compared to no treatment or rapid taper from opioids, MAT significantly reduces opioid use and improves health and psychosocial functioning and prevents overdose deaths (Schwartz et al., 2013); however, for buprenorphine and methadone treatment, the retention rates at one year are typically less than 50% (Carroll and Weiss, 2017; Proctor et al., 2015). Oral naltrexone maintenance is associated with high drop-out rates and has been suggested to be no better than placebo (Minozzi et al., 2011). Even with the injectable sustained release formulations, transition from opioid use to naltrexone treatment has been challenging with less than 50% retained at six months (Comer et al., 2006; Lee et al., 2017; Lobmaier et al., 2008). As indicated by these studies, there is room for improvement for MAT of OUD.

The efficacy of behavioral treatments as adjuncts to MAT remains inconclusive. Several clinical trials have shown that cognitive behavioral treatment (CBT) or drug counseling may not enhance the efficacy of MAT in reducing heroin or prescription opioid use (Fiellin et al., 2013, 2006; Ling et al., 2013; Weiss et al., 2011). Similar to its efficacy for other drugs of abuse, contingency management may improve the efficacy of MAT and reduces opioid use and improve retention (Christensen et al., 2014; Schottenfeld et al., 2005), but effects weaken once contingencies are removed. As suggested in recent reviews, appropriate comparisons between behavioral treatments are confounded

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by the dose of MAT, selection of control condition, and variation in the frequency and length of behavioral treatments (Carroll and Weiss, 2017; Sokol et al., 2018). With these caveats in mind, there is a need to develop innovative behavioral treatments adjunctive to MAT that can enhance treatment engagement and reduce relapse.

Recent research has examined cognitive targets for intervention in substance use disorders (SUD) (e.g., Robinson et al., 2017; Sofuoglu et al., 2013). Treatments that target deficits in executive functions and/or changes in automatic processing in individuals with SUD are promising (Sofuoglu et al., 2013). Most pertinent here, individuals with a SUD may develop an attentional bias towards drug-related cues. In addiction research, attentional bias refers to the tendency to attend to, and maintain attention on, drug-related cues, rather than neutral cues. Studies have reported that attentional bias is associated with drug use behavior and treatment outcomes across various drugs of abuse (Carpenter et al., 2006; Cox et al., 2002; Field and Cox, 2008; Field et al., 2014; Marissen et al., 2006; Waters and Leventhal, 2006; Waters et al., 2003). Attentional bias for drug cues is a potential target for behavioral and pharmacological treatments of SUD (Sofuoglu et al., 2013). For example, pharmacological treatments, including atomoxetine (Passamonti et al., 2017), n-acetylcysteine (Levi Bolin et al., 2017), and haloperidol (Franken et al., 2004) have also been shown to reduce attentional bias towards drug cues.

The purpose of this study was to conduct a systematic review and meta-analysis of attentional bias studies for OUD. There are several systematic and narrative reviews for attentional bias in cocaine (Leeman et al., 2014) as well as alcohol and tobacco use disorders (Field et al., 2009; Sinclair et al., 2010), but we are not aware of a systematic review of attentional bias specific for OUD. We sought to address the following questions: 1) Do individuals with OUD have greater attentional bias for opioid cues than healthy controls? 2) Do individuals with OUD have greater attentional bias for opioid cues than nondependent prescription opioid users? 3) Are there task differences in OUD? 4) Does MAT reduce attentional bias for opioid cues? We first briefly review the theoretical background and assessment of attentional bias.

1.1. Review of attentional bias

Research suggests that “automatic” (or implicit) cognitive processes play an important role in the maintenance of drug addiction (Waters and Leventhal, 2006; Wiers and Stacy, 2006). Automatic processes are fast, parallel, and often outside of one’s conscious awareness. As noted above, attentional bias refers to the cognitive processes in which attention is automatically captured by drug cues, and maintained on drug cues (Field and Cox, 2008). A drug user may find that his or her attention is drawn to drug cues without having insight into the cognitive processes underlying the shift in attention.

Theoretically, attentional bias to drug cues may reflect sensitized incentive salience of drug cues, reflecting changes in neural circuitry underlying attribution of incentive salience (Goldstein and Volkow, 2002; Robinson and Berridge, 1993). Excessive attention to drug cues can promote maintenance of addiction in part because drug cues trigger craving (Franken, 2003). Attentional bias can also be induced in healthy controls when arbitrary stimuli are associated with a non-drug reward (usually money), meaning that attentional bias may also in part reflect normal reward learning (Anderson, 2016).

Attentional bias to drug cues can be assessed using reaction time tasks such as the drug Stroop task and the visual probe task. In the drug Stroop task, participants are instructed to identify as rapidly and as accurately as possible the ink color of words while ignoring the meaning of the word (Cox et al., 2006). For the opioid Stroop task, participants identify the colors of opiate (e.g., “heroin”) and neutral (e.g., “chair”) words. A slower response to identify the color of opioid (versus neutral) words indicates that attention has been captured by the drug-related words. The difference in reaction times is termed attentional bias, with higher values indicating greater attentional bias.

In the visual probe task (also referred to as the dot probe task) a picture (or word) pair is presented for a brief duration on a computer screen. One member of the pair is located on the left side of the screen and the other is located on the right side. For the opioid visual probe task, one picture is opioid-related (e.g., a needle) and the other is motivationally neutral (e.g., a telephone). When the picture pair disappears, a probe is presented in a position that had been occupied by one of the two pictures (or words). Participants are required to make a decision about the probe (e.g., indicate its location) as quickly and as accurately as possible. Individuals are typically faster to respond to probes that replace motivationally salient stimuli than neutral stimuli as individuals’ attention is automatically shifted in space to the location of the picture, thereby facilitating the probe location task (Mogg and Bradley, 1998). Attentional bias is calculated from the difference in reaction times to indicate the location of the probe, with higher values indicating greater attentional bias.

Other tasks used include eye movement tasks, the flicker change blindness task, and the attentional blink. For eye movement tasks, a participant’s eyes are monitored while they view drug-related and neutral stimuli; this can be done during the visual probe task (Mogg et al., 2003). Attentional bias is calculated by subtracting gaze durations for neutral pictures from gaze durations for drug-related pictures (Frankland et al., 2016). Higher values of attentional bias reflect more processing of drug-related (versus neutral) stimuli. The flicker change blindness task rapidly presents two pictures that are different in one specific feature separated by a mask. Attentional bias is evident from a faster time to detect differences when the feature is drug-related (versus neutral) (e.g., Jones et al., 2006, 2003). Attentional blink tasks require participants to identify two target stimuli (T1 and T2) presented in rapid succession. When T2 rapidly follows a neutral T1, attentional bias can be assessed as increased accuracy to identify drug-related target stimuli (T2) compared to neutral stimuli (T2) (e.g., Waters et al., 2007).

2. Method

A systematic review and meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards (Moher et al., 2009).

2.1. Search strategy and selection criteria

Database searches in Google Scholar, PubMed, PsychINFO, and Web of Knowledge were constructed using a Boolean strategy for terms related to attentional bias and opioid use. Search strings included the following terms: (“attentional bias” OR “attentional bias modification”) AND (“opioid” OR “opiate” OR “heroin”). Follow up searches included commonly used tasks to measure attentional bias such as (“drug Stroop” OR “dot probe”). The search terms were modified as needed to meet individual database search guidelines. Manually searching reference lists of included articles, reviews, and relevant meta-analyses were used to identify additional relevant studies. All literature searches were performed in October 2017 with no restrictions on publication date. After deletion of duplicate search results, titles and abstracts of remaining manuscripts were evaluated for possible inclusion. Lead author (RRM) performed an initial screening and then potentially relevant manuscripts were discussed and evaluated with other authors (MS and AJW).

2.2. Inclusion criteria

Studies were included if they (a) evaluated attentional bias in opioid users, (b) used a task to evaluate attentional bias that included active response to study stimuli, (c) were peer-reviewed, (d) calculated attention bias by comparing response to drug and neutral stimuli, and (e) could isolate attentional bias specific to opioid versus neutral stimuli from bias to other salient stimuli.