



## Full length article

## The impact of co-occurring opioid misuse and PTSD on response inhibition

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## ABSTRACT

**Background:** Posttraumatic Stress Disorder (PTSD) and opioid misuse are commonly co-occurring disorders. Both disorders are associated with deficits in response inhibition; however, these associations have not considered their comorbidity. Response inhibition has not been examined in a sample with comorbid PTSD and opioid misuse. The present study examined the effect of PTSD symptom severity on response inhibition in current and past opioid misusers.

**Methods:** Participants were currently (used within the last month) misusing opioids (56.6%) or in recovery (43.4%). All participants met DSM 5 criteria for PTSD. Response inhibition was measured with the stop signal task.

**Results:** Response inhibition was associated with increased PTSD symptom severity for those in recovery but not among current users. Additionally, across both groups, there were deficits in response inhibition when withholding automatic responses for a threatening stimulus compared to a neutral stimulus.

**Conclusions:** PTSD Symptoms may exert a stronger effect on response inhibition among those in recovery as opposed to those who are actively using opioids.

## 1. Introduction

Individuals who misuse opioids experience potentially traumatic events (PTEs) at a markedly high rate (Dore et al., 2012; Mills et al., 2012). Exposure to such events is associated with increased risk for psychopathology including posttraumatic stress disorder (PTSD) (Kilpatrick et al., 2013). Indeed, studies examining psychopathology across samples of individuals who report using multiple substances have reported PTSD as the most prevalent disorder (Cottler et al., 1992; Mills et al., 2006a), and similar findings have found that opioid misuse is elevated in trauma-exposed samples (McCauley et al., 2009; McCauley et al., 2010; Seal et al., 2012). Mills et al. (2006b) reported that 92% of individuals with an opioid use disorder had experienced a traumatic event, and 41% had comorbid PTSD. Those with co-occurring PTSD and substance use disorder in general, and opioid misuse in particular, present with more severe PTSD symptomology, greater levels of functional impairment, and respond less well to treatment (Gros et al., 2013; Mills et al., 2006a; Ouimette et al., 2006). This increased impairment suggests the mechanisms that underlie these disorders may be further affected in those with both conditions. Understanding how such mechanisms are affected by this prevalent comorbidity is necessary to improve understanding of both conditions and identify potential treatment targets.

Separate literatures have suggested that those who misuse opioids (for review see Gruber et al., 2007) and those who have PTSD (for review see Aupperle et al., 2012) have deficits in inhibitory functions. Inhibitory functions allow an individual to withhold an automatic or prepotent response during a goal-directed task (Norrholm et al., 2015). An element of inhibitory functioning that has received considerable attention is response inhibition, defined as the ability to withhold a prepotent response in light of an inhibitory signal (Verbruggen and Logan, 2008). Within substance use, an inability to withhold responding is posited to reflect an increased willingness to misuse substances despite available information to abstain (de Wit, 2009). Within PTSD, response inhibition is thought to correspond to a deficit in emotion regulation such that it is difficult to withhold fearful responses to potentially threatening stimuli (Norrholm et al., 2015).

Prior work with those who misuse opioids suggests this population performs poorly on tasks of inhibition. Relative to healthy controls, methadone-maintained individuals had poorer overall performance on tasks of impulsivity, which are related to response inhibition (Bracken et al., 2012). Interestingly, there was a moderating effect of time on methadone such that those who had begun methadone treatment within the last 12 months performed significantly worse than those who were on methadone for more than 12 months. A related study examined response inhibition between those who were in methadone

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maintenance treatment, those with a history of opioid misuse but who were currently abstinent, and healthy controls (Constantinou et al., 2010). There were no significant differences among the groups with regards to inhibition errors. However, those who were in methadone maintenance treatment had slower overall reaction times relative to the other groups. A final study showed that individuals who were heroin-dependent had poorer response inhibition compared to healthy controls (Fu et al., 2008). These findings suggest that the impairment in response inhibition may be related to the active misuse of opioids. Among those who are in treatment, however, variability in response inhibition is thought to be attributed to other factors.

Others have hypothesized that PTSD symptom severity affects response inhibition among those using opioids. PTSD has been conceptualized as a deficit in the inhibition of responses to aversive stimuli (Norholm et al., 2015). That is, those with PTSD display a deficit in their ability to withhold a fear reaction when exposed to stimuli associated with the adverse event (Jovanovic et al., 2009, 2010; Norholm et al., 2011). The severity of this deficit is positively correlated with the severity of PTSD symptoms. This deficit is also posited to maintain the disorder in that it perpetuates a fear and avoidance of trauma-related stimuli. Several studies have also shown that PTSD is associated with deficits in inhibition more broadly. Casada and Roache (2005) compared performance in individuals with a trauma history for those with PTSD and without PTSD on a task of response inhibition using neutral stimuli. Individuals with PTSD made more commission errors. In a larger sample of combat veterans, those with PTSD had more commission errors on a response inhibition task than veterans without PTSD (Swick et al., 2012). Furthermore, PTSD symptoms and re-experiencing symptoms specifically were positively correlated with commission errors. In another study, those with PTSD had more inhibition-related errors than healthy, non-trauma exposed controls (Falconer et al., 2008). Taken together, these data suggest that PTSD is associated with poorer inhibition overall, and the extent of the impairment is associated with more severe PTSD symptoms.

The literature discussed thus far suggests that impaired response inhibition is present in those who misuse opioids and those diagnosed with PTSD. These literatures, however, were developed separately with no studies examining the extent that co-occurring PTSD symptoms influence response inhibition among those who misuse opioids. It is unclear if impaired response inhibition is comparable in those with co-occurring PTSD and opioid misuse or if the impairment is greater relative to those with a single condition. It is hypothesized that those who are currently misusing opioids and have elevated PTSD symptoms have more impaired response inhibition than those who do not have elevated PTSD symptoms. This hypothesized reduction in response inhibition is a potential explanation for the diminished response to SUD treatment and greater functional impairment in these individuals. Furthermore, prior work suggests there are differences when comparing both those who are actively using opioids and those who are in recovery relative to individuals who are not current or past opioids users. It is unclear, however, how response inhibition varies among those who are actively using opioids and those in recovery. Poorer response inhibition among those who are actively using opioids may reflect their difficulty in abstaining as well as emotion regulation impairment. Given how emotion is proposed to affect response inhibition in those with PTSD, it is hypothesized that response inhibition will be more impaired when reacting to emotionally threatening stimuli than neutral stimuli. Examining such differences is necessary to determine how response inhibition changes as a function of an individual's opioid use and their emotional state. Understanding how emotion influences response inhibition would help determine appropriate treatment targets. That is, if deficits in response inhibition are enhanced by emotional state, then better treatment results may come from strategies that focus on emotion regulation. However, if emotional state does not play an important role in determining response inhibition, then treatment should target executive functioning.

## 1.1. Present study

The present study aimed to further evaluate the relation between inhibitory functioning, PTSD, and opioid misuse. The primary goal was to determine if response inhibition differed between those who were actively misusing opioids as opposed to individuals in recovery and if PTSD symptom severity moderated this relation. It was hypothesized that those who were actively using substances would have poorer response inhibition than those in recovery. It was also hypothesized that PTSD symptom severity would moderate this relation such that severity would be more strongly associated with response inhibition performance among those in recovery than those who were actively using opioids, and those who were actively using opioids would have poorer response inhibition regardless of severity. Such hypotheses are thought to reflect the greater impairment found among those with both conditions. Given that PTSD is associated with a deficit in inhibition towards aversive stimuli, the role of emotional valence of stimuli with regards to response inhibition was explored as well. It was hypothesized that threatening stimuli, defined as angry faces, would further impair response inhibition.

## 2. Methods

### 2.1. Participants

Participants were 53 individuals with a history of opioid use, defined as using heroin or misusing prescription opioids for more than 1 year (Heroin:  $M = 4.19$  years,  $SD = 4.63$ ; Prescription opioids:  $M = 7.98$  years,  $SD = 6.84$ ). Inclusion criteria for the study were: meeting DSM-IV criteria for substance abuse for opioids, identifying opioids as their drug of choice, and being between 18–65 years of age. Exclusion criteria included active psychosis and non-English speaking. Participants were eligible for the study if they used other substances. Historical use of substances (in years of regular use) were as follows: Alcohol:  $M = 11.55$ ,  $SD = 10.73$ ; Cocaine:  $M = 6.92$ ,  $SD = 7.55$ ; Cannabis:  $M = 14.64$ ,  $SD = 10.80$ . Participants were recruited through online advertisements, flyers posted in the area in which the study was conducted, and at methadone maintenance clinics. Recruitment procedures were approved by the University of Vermont IRB, and anonymity was maintained through a subject running numbering system that de-identified the collected data for each participant. The research team maintained a record of linking information to connect an identity with a participant's data if needed.

Participants' ages ranged from 20 to 54 ( $M = 35.2$ ,  $SD = 7.98$ ). The sample was split evenly across genders with 49.1% identifying as female. The majority identified as White (83%), 1.9% as African American, 3.8% as Asian American, 1.9% as Pacific Islander or Native Alaskan, 5.7% as American Indian, and 3.8% as Bi-Racial. The majority identified as not Hispanic or Latino (98%). 90.6% of participants reported an annual income of \$30,000 or less. 22.6% reported some high school as their highest education level, 28.3% completed high school, and 28.3% completed 1–2 years of college.

### 2.2. Measures

The following interviews and self-report measures were used.

#### 2.2.1. Addiction severity index lite (ASI-lite; McLellan et al., 1997)

The ASI-Lite is a 169-item structured interview that was adapted from the ASI-5. It is a shorter alternative to the ASI-5. It assesses the severity of an individual's drug or alcohol addiction as well as different domains that may be impacted (McLellan et al., 1992). The ASI-Lite has demonstrated excellent validity in identifying substance use and related problems in those with co-occurring psychopathology (Kosten et al., 1983). The ASI-Lite determined the history of substance use for individuals as well as if they were currently misusing opioids, defined as

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