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Review article

Decision-making ability in current and past users of opiates: A meta-analysis

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ABSTRACT

Opiate use is associated with deficits in decision-making. However, the impact of abstinence and co-morbid factors, like head injury and poly-substance abuse, on this ability, is currently unclear. This meta-analysis aimed to assess 1) the magnitude of decision-making deficits in opiate users; 2) whether co-morbid factors moderate the severity of these deficits; 3) whether ex-opiate users demonstrate smaller decision-making deficits than current users; and 4) whether the length of abstinence is related to the magnitude of decision-making deficits. We analysed 22 studies that compared the performance of current and ex-opiate users to healthy controls on decision-making measures such as the Iowa Gambling Task. Current users demonstrated a moderately strong impairment in decision-making relative to controls, which was not significantly moderated by co-morbid factors. The magnitude of the impairment did not significantly differ between studies assessing current or ex-users, and this impairment was not related to length of abstinence. Thus, it appears that opiate users have relatively severe decision-making deficits that persist at least 1.5 years after cessation of use.

Contents

1. Introduction

Long term opiate use is associated with a range of problems in everyday life, including poor physical and mental health, impaired social functioning, and high unemployment rates (De Maeyer et al., 2010, 2011; Meulenbeek, 2000). These difficulties may be linked

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to deficits in cognitive functioning, with a number of cognitive processes including attention, verbal memory, and executive functions shown to be impaired in both heroin and prescribed opiate users (see Baldacchino et al., 2012; and Wang et al., 2013 for reviews). Of the cognitive processes negatively impacted by opiate use, decision-making ability appears to be one of the most consistently and severely affected (Baldacchino et al., 2012).

While it is relatively well-established that decision-making is compromised in opiate users (Baldacchino et al., 2012), little is known about which individuals within this heterogeneous population are most at risk. Similarly, the trajectory of the decision-making impairment following treatment is currently unclear. In particular, it is not known whether decision-making deficits abate during periods of abstinence. Such information has the potential to improve understanding of the difficulties that opiate users face and to assist policy makers and service providers to develop effective support services.

A more detailed understanding of the relationship between opiate use and decision-making ability has been limited by the fact that most available studies in this field have relatively small sample sizes, and findings have been inconsistent, making it difficult to draw reliable conclusions. Therefore, the current study used a meta-analysis to pool and re-examine available data to investigate the temporal trajectory of decision-making deficits in opiate users, and examine the potential influence of individual factors on the severity of these deficits.

In the current context, effective decision-making refers to the ability to avoid making choices that result only in small or short-term benefits, and/or choices that carry a high risk of adverse outcomes. Studies of decision-making have shown that, compared to non-drug-using controls, opiate users tend to select options with short-terms gains but long term losses (e.g., Lemenager et al., 2011; Mintzer et al., 2005; Mintzer and Stitzer, 2002; Verdejo-Garcia et al., 2007; Verdejo-Garcia and Perez-Garcia, 2007) as well as smaller immediate rewards over larger delayed rewards (i.e. delay discounting, Kirby and Petry, 2004; Kirby et al., 1999). In addition, opiate users generally choose riskier options, such as choosing a large but unlikely reward, over a smaller, but likely reward (Brand et al., 2008; Ersche et al., 2006, 2005b). The magnitude of these decision-making difficulties is substantial, with medium to large effect sizes (Cohen's $d = 0.70$) reported in studies that compare opiate users to non-drug-using controls (Baldacchino et al., 2012). These decision making difficulties have the potential to impact on real life choices about money, housing, and health related behaviours (e.g. Wilson and Vassileva, 2016).

Compromised decision-making ability in this population is not surprising given that opiate use is associated with abnormalities in the orbitofrontal cortex (OFC) and associated neural networks. The OFC supports the integration of sensory and emotional inputs when calculating the value of rewards (Elliott et al., 2000; Krawczyk, 2002; Rolls, 2000; Wallis, 2007). The OFC is also part of a larger neural network involving the dorsolateral prefrontal cortex (dlPFC) and nucleus accumbens (Cohen et al., 2005; Ernst and Paulus, 2005; Krawczyk, 2002) which is particularly important for planning behaviour that leads to distant, as opposed to immediate, rewards (Bechara, 2004, 2005; Bechara et al., 2000a, 2000b; Gläscher et al., 2012; Wallis, 2007). Opiate users show evidence of reduced OFC and dlPFC grey matter density (Lyoo et al., 2006; Yuan et al., 2010) and damage to white matter (Li et al., 2016; Liu et al., 2008; Lyoo et al., 2004; Qiu et al., 2013). Abnormal functional connectivity in OFC networks has also been found in opiate users (Cheng et al., 2013; Liu et al., 2009; Ma et al., 2010), and this has been linked to poorer decision-making performance (Qiu et al., 2011). In addition, in comparison to controls, users of different types of opiates have demonstrated either hyper- or hypo-activation of the OFC while making risky decisions during a gambling task (Ersche et al., 2006). Furthermore, reductions in dopamine and serotonin transmission systems are also evident amongst opiate users (Liu et al., 2013; Shi et al., 2008; Yeh et al., 2012; Zaaijer et al., 2015). Although the relationship between neurotransmitters and decision-making has not been specifically investigated in opiate users, abnormalities, for example in dopamine transmission, have been linked to reduced performance in other aspects of cognitive functioning in opiate users (Liang et al., 2016). Taken together, the research reveals that there are abnormalities in relation to OFC and dlPFC structure, function, and neurotransmission in opiate users that might underpin, at least to some extent, their impaired decision-making ability. Although it should be noted that the extent to which neural pathology precedes opiate use is currently unclear, a recent longitudinal brain imaging study by Li et al. (2016) showed that opiate use was associated with white matter degeneration over the period of one year. This research has confirmed that at least some measurable degeneration occurs over a period of active opiate use.

If neural pathology does contribute to the decision-making deficit in opiate users, it may be anticipated that people with a longer history of opiate use will display more severe decision-making impairments, given that structural brain changes have been shown to be greater in people who have used opiates for longer periods of time (Yuan et al., 2010, 2009). However, findings from the five available studies directly addressing this relationship have been mixed. Some have reported a negative association between duration of opiate use and decision-making ability (Cheng et al., 2012; Yan et al., 2014), whereas others failed to detect such a relationship (Brand et al., 2008; Clark et al., 2006; Lemenager et al., 2011). The limited number of these studies however, makes it difficult to make firm conclusions regarding the relationship between decision-making and duration of opiate use. It is nevertheless possible to investigate this issue further by considering other studies of decision-making in opiate users that do not *directly* investigate this relationship. More specifically, because the mean duration of opiate use across such studies varies, we were able to collate the data from these studies in the current meta-analysis and use meta-regression to further examine whether the size of the decision-making deficit varies as a function of the duration of opiate use.

Over and above opiate use duration, co-morbid conditions may also affect the severity of decision-making deficits in opiate users. For example, a large proportion of people who use opiates are also dependent on other street drugs (Astals et al., 2008). In addition, many long term opiate users have experienced neurological damage, either as a result of overdose, or physical trauma (Darke et al., 2012b). To the best of our knowledge, the potential impact of poly-substance abuse and head injury on decision-making has not been examined in this group to date (Darke et al., 2000; Loeber et al., 2012). However, in opiate users, poly-substance abuse and head injury are both associated with greater levels of impairment in other cognitive domains including memory, information processing, verbal learning, and executive and general cognitive function (Darke et al., 2012b, 2000; Henry et al., 2012; Loeber et al., 2012). Thus, it is possible that poly-substance abuse and head injury may also detrimentally affect decision-making. In the current meta-analysis, we compared the size of the decision-making impairment reported in studies that included only opiate users who were free of co-morbid issues, to that reported in studies that included people with poly-substance abuse and head injuries.

A further issue that lacks clarity in relation to the decision-making ability of opiate users is whether deficits in this capacity abate when opiate-users enter a period of abstinence. There is evidence that there is some recovery of neurotransmitter receptor availability and function after opiate cessation (Shi et al., 2008; Yeh et al., 2012), and therefore some improvement in decision-making might be anticipated. However, abnormal neural connectivity has been observed in abstinent ex-users (Cheng et al., 2013; Liu et al.,