

**Background of question to be addressed:**

It has been shown that people discount the value of a reward when it is coupled with a time delay. Delay discounting is a neurological mechanism that has been extensively studied but is not completely understood. Social-behavioral research has demonstrated that in humans this process is involved in deciding the value of waiting for certain items or benefits. Previous research has asked questions such as “would you rather have 10 dollars now, or 100 dollars next week?” The amounts of monetary reward and time delay that have been investigated vary widely, but the results are almost always congruous: every person delay-discounts, but the rate of delay discounting (how long an individual is willing to wait for a certain reward) varies by person. To what can these differences be attributed?

There have been a few correlational studies conducted which measure the rate of delay discounting and cigarette smoking status. Bickel et al. (1999) conducted a study using smokers, never-smokers, and ex-smokers, and found that “cigarette smoking...is characterized by rapid loss of subjective value for delayed outcomes”, meaning that cigarette smokers would rather have small, immediate rewards than larger, delayed rewards. This conclusion is congruent with other studies with similar findings (Baker et al., 2003; Mitchell, 1999). Interestingly, it was also found that never-smokers and ex-smokers had similar rates of delay discounting (Bickel et al., 1999). This finding suggests that steeper rates of delay discounting may be a *consequence*, rather than a *precursor*, to nicotine dependence, and that cessation from smoking will lead to lower rates of discounting by delay. Conversely, it has been suggested that “ex-smokers may have been more likely to quit smoking because of their comparatively low delay-discounting rates” (Reynolds, 2006).

In addition, multiple studies have examined the relationship between substance abuse, or drug dependence, and rates of delay-discounting. Opioid-dependent individuals in treatment and receiving buprenorphine have been studied by Madden et al. (1997), Kirby et al. (1999), and Madden et al. (1999). Buprenorphine is an opioid substitute for illegal street opiates (drugs of abuse) such as heroin and morphine, and is an accepted treatment for opioid-dependent individuals. Similar to the cigarette smoking study mentioned above, it was found that opioid-dependent participants delay discount at greater rates than controls (Kirby et al., 1999).

Other studies also asked opioid-dependent patients questions such as “would you rather have .5 grams of heroin now, or 1 gram of heroin in one week” (Madden et al., 1997).

It was found that opioid-dependent participants delay discount heroin at a steeper rate than monetary rewards.

One study compared rates of delay discounting between individuals who were actively using heroin, non-substance abusers, and abstinent heroin users (Kirby et al., 2003). In that study, abstinent heroin users were found to have significantly lower discounting rates than those actively using heroin, but higher rates than non-substance abusers. As with the findings correlating cigarette smoking and delay discounting, it remains to be concluded whether steeper rates of delay discounting for monetary rewards are a *precursor* or a *consequence* of opioid drug abuse. It can be argued that the comparatively lower rates of delay-discounting in abstinent heroin users made them more likely to abstain from drug use; or that the act of cessation itself might have led to lower rates of discounting by delay.

A closer analysis of the studies on opioid-dependence and delay discounting reveals that the rules for classifying a person as “abstinent” or “opioid-dependent” varied from study to study. For example, Kirby et al. (2003) classified those individuals who had no heroin use in the past 14 days as abstinent; additionally, four of the seven participants in this heroin-abstinent group were maintained on methadone (a opioid-replacement and accepted form of treatment, similar to buprenorphine mentioned above). Controversially, those four would have been classified as opioid-dependent in studies such as Madden et al. (1997). Because of these discrepancies, a comprehensive study is needed comparing participants whom are actively using heroin; abstinent heroin and maintained on methadone or buprenorphine; or abstinent both heroin and buprenorphine/methadone. Though all opioids (both heroin and methadone, for example) have similar neurological effects, participants need to be grouped into different categories depending on which drug they use. This is important because there may be differences in delay discounting rates between opiate abusers (taking heroin) and those seeking treatment (taking methadone) (Kirby et al., 2003).

**Proposed research and methodologies:**

Abstinent users of both cigarettes and heroin were found to have lower rates of discounting by delay than active users in multiple studies. However, because of the varying methods used to classify individual participants as either abstinent or active, it is unclear how these results can be incorporated in further addiction research. In order to clarify and solidify previous findings, and to possibly solve the question of whether a higher rate of

delay discounting is a *precursor* or a *consequence* of drug abuse, the following research is proposed:

Participants will be recruited to the study using advertisements at gas stations, group homes, halfway houses, around campus, and in free counseling agencies. The consenting participants will be classified into one of four categories: 1) current heroin user 2) past heroin user maintained on methadone 3) past heroin user not maintained on methadone 4) users of both heroin and methadone 5) non-substance abuser. Participants will fill out questionnaires that include demographics, a delay discounting task (Robles and Vargas, 2007; 2008), and the Severity of Dependence Scale (Gossop et al., 1992). Importantly, past heroin users (those maintained on methadone and those not in substitution treatment) will report how long they have been abstinent from heroin. Those not currently maintained on methadone will also report how long they have been abstinent from methadone, or report if they never received methadone treatment. This is an important component so that during statistical analysis data can be indexed by length of current abstinence, and delay-discounting rates can be evaluated as a function of each individual's phase of recovery.

After the initial screening, participants will provide a urine sample. This is necessary to check for the presence of opiates and other drugs, so that participants can be correctly classified. Because different rates of delay-discounting have been observed depending on the drug of abuse, participants who test negative for heroin, but positive for other drugs (cocaine, etc.) will not be included in the data. Participants will then complete a computerized delay-discounting task (Robles and Vargas, 2007; 2008). In total, assessments will take approximately one hour to complete. After completion, participants will be compensated for their time.

**Benefits:**

This study will benefit addiction research by providing more comprehensive data on delay discounting within opioid-dependent subjects. Understanding the mental processes of opioid-dependent peoples is necessary for furthering the prevention and treatment of substance abuse disorders, including drug addiction. Opiate addiction (heroin, morphine) is a serious and life-threatening illness. A better understanding of opioid-dependence is needed to further the advancement of drug addiction treatment and prevention.

I will receive personal benefits from this research as well. I aspire to obtain admittance into a dual MD/PhD program upon graduation from Arizona State University,

with my PhD being in neuroscience. I want to be a medical scientist and research treatments for addiction, schizophrenia, multiple sclerosis, and other neurological and psychiatric diseases. Being involved in research as an undergraduate, and especially receiving a grant to conduct research, will help increase my chances of acceptance into one of the prestigious Medical Scientist Training Programs.

**Feasibility:**

A great deal of time will need to be invested into the recruiting aspect of this study. Based on other studies, it is estimated 100 participants will need to be recruited to be able to rely on the data and findings from the proposed research. I am currently consulting with a statistician to determine the exact number of participants. Finding this number of participants is possible, and Dr. Robles and I have spent time discussing our plan for reaching this goal. We feel confident we will be able to recruit as many participants as needed.

The assessments (SDS, Computerized Delay-Discounting Model) have already been developed and tested in numerous studies. Both Dr. Robles and I have used the Computerized Delay-Discounting Model in previous studies, and are confident in our ability to give the assessment and process the data.

AccuSign Urine-Analysis kits can easily be obtained from an online source, and both Dr. Robles and I have previous experience handling specimens from these types of tests. The validity and reliability of AccuSign tests are well-documented.

**Expected outcomes:**

Based on the previous findings, it is difficult to hypothesize what the outcome for this study will be. Research on opioid-dependence is divided on whether or not abstinence from opioids decreases the rate of discounting by delay.

We expect two possible outcomes. First, that there will be no difference between current and past heroin users, no matter how long the user has been abstinent from heroin or how long they have been maintained on methadone. This would support the hypothesis that the higher rate of delay discounting observed in heroin users is a *precursor* to heroin use, not a *consequence*. The second possible outcome is finding differences in delay discounting rate between current and past heroin users. We expect discounting rates will negatively correlate with amount of time abstinent from heroin. That is, past heroin users will gradually discount less by delay as they remain abstinent from heroin use. This would support the hypothesis that high rates of delay discounting are a *consequence* of heroin use.

In both cases, it is expected that heroin use – current and past – will predict higher rates of delay discounting compared to controls.

**Timeline and budget:**

AccuSign tests - *Approximately \$1,000*

Participant compensation - *Approximately \$1,000*

Advertising materials – *Approximately \$50*

Recruit and conduct trials January through May 2011. At least 70 participants should be completed by March 12, 2011. Sufficient data should be collected by May 30, 2011.

Researchers will begin analyzing the collected data in early August. If it is found that a larger sample size is needed, recruitment will take place August through the end of October 2011. November and December will be used for analyzing the final dataset, creating graphs, charts, and tables, and writing the final report. A publication-quality manuscript will be produced within six months.

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