A Precise Computational Measure of Impulsivity that Signals Relevant Outcomes in Opioid Addiction Treatment

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Abstract

Computational models of impulsive decision-making, like temporal discounting, are widely used to study addiction. However, clinically validating a marker supposes developing methods that provide high accuracy and reliability. We first show that a modified model of temporal discounting incorporating individual-specific risk sensitivity - provides a more precise, unbiased, and reliable measure of impulsivity than the standard approach. Using this tool, and given the current opioid epidemic, we set out to investigate longitudinally whether discounting would signal relevant negative outcomes like drug use, relapse and dropout in patients undergoing treatment for opioid addiction. We found that changes in discount rates were related to increased drug use in patients, indicating a vulnerability to full relapse and treatment failure.

Keywords: impulsivity; opioid addiction; computational psychiatry; decision making; risky decision-making; delay discounting

Introduction

Computational psychiatry promises to deliver answers to clinically relevant questions by applying model-informed approaches rooted in cognitive neuroscience. What will it take for this burgeoning field to deliver on that promise? We present here a body of work to develop a precise computational measure of impulsive decision making and apply it to monitor clinical outcomes in a population of patients with opioid addiction receiving treatment in a local clinic.

Overwhelming evidence indicates that impulsive decision-making is altered in addiction (Amlung, Vedelago, Acker, Balodis, & MacKillop, 2017). Temporal discounting, or the tendency to discount the value of rewards that will be delivered in the future, is a widely-used algorithm that provides a measure of an individuals level of impulsivity, their discount rate. Interestingly, reports have suggested that in patients addicted to opioids, the discount rate appears to be affected by treatment (Landes, Christensen, & Bickel, 2012). This contrasts with the widely held belief that discount rates are stable and unchanging over long periods of time (Ohmura, Takahashi, Kitamura, & Wehr, 2006).

We assessed individual patients discount rates repeatedly over the course of seven months of treatment for opioid addiction and tested whether increases or decreases in this behavioral marker signal changes in primary clinical outcomes: heroin use, treatment plan adherence, and treatment dropout.

Critical to this endeavor was to ensure that we could achieve a highly precise and reliable measure of their impulsivity. Although the literature that focuses on individual differences in discount rates and their relation to different behavioral disorders is extensive, most studies employ the same hyperbolic discounting model (Mazur, 1987). This functional form of temporal discounting assumes subjects have a linear utility function, that is, a linear relation between an objective amount of money and the individual's subjective value of this amount. However, an extensive literature on this topic shows that this is often not the case, even in healthy volunteers(Holt & Laury, 2002). This relationship may be supralinear - often referred to as risk-seeking preferences-, or infralinear - equivalently referred to as risk-averse preferences.

We show here that a modified model of temporal discounting incorporating individual-specific risk sensitivity - provides a precise, unbiased, and reliable measure of impulsivity. This individual discount rate, when measured longitudinally in our patients, achieved a high level of test-retest reliability and was correlated to increases in drug use, signaling when a patient might be at risk of relapse and treatment failure.

Methods

We recruited a cohort of 30 patients with opioid use disorder (OUD) starting standard-of-care treatment in a local clinic. We also recruited a cohort of 41 controls from the same community (CC) matched demographically to the OUD sample. On

each visit subjects completed both a risk attitude task (RA) and an intertemporal choice task (ITC). For the RA task, subjects chose between a certain gain of $5 versus a variable lottery. For the ITC task, participants chose between an smaller immediate reward and a larger delayed reward.

For OUD patients, information about their clinical state was also collected at each visit including drug use (by self-report and toxicology). We estimated participants' discount rates with two different models of temporal discounting: 1) a standard" hyperbolic model which assumes a linear utility function and 2) a modified hyperbolic model which incorporates a parameter that accounts for risk preferences. Note both models have the same number of parameters.

Results

We found that the model that includes a risk sensitivity parameter outperformed the "standard" hyperbolic discounting model - accounting for significantly more variance in the data (Figure 1A). Furthermore, we found that assuming linear utility (risk neutrality) introduces a pattern of systematic bias that could lead to spurious interpretations on both control and patient data: with the standard approach, impulsivity appears higher in risk-averse individuals and lower in risk seeking individuals (Figure 1B).

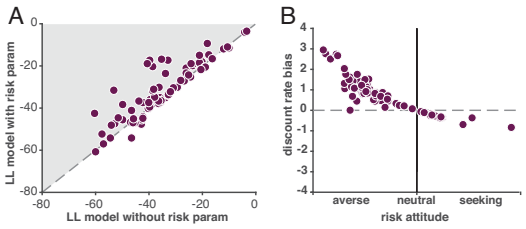

Figure 1: A) Cross-validated log likelihood comparisons of both models; B) discount rate bias (difference in natural logarithm of discount rates from model without risk parameter and with risk parameter.

Using our winning model, we observed high test-retest reliability of the discount rates in both groups (Figure 2A). Our results indicate that while stationary in our control group, in OUD patients discount rates change dynamically through time in treatment. The steepness of these trajectories relates to the patients level of illicit drug use (Figure 2B), while their baseline level of discount rate does not, suggesting its the change in time and not the stationary impulsivity which may be predictive of treatment failure. A finer analysis showed that in a shorter time scale, discount rates tend to peak around the time that drug use occurs, suggesting that this change may be predictive of these events and may potentially indicate imminent full-blown relapse events and dropout.

Conclusions

A central aspect to the endeavor of applying cognitive models to clinically-motivated questions is that the estimated parameters must have high precision and reliability. We find that using the standard temporal discounting model introduces a major bias in the estimates has important implications for the interpretation of differences in impulsivity levels across individuals and groups. It is particularly relevant to the ever-growing number of studies concerned with impulsivity in disorders with diverse risk preferences like addiction, ADHD, anxiety and PTSD. In our patients, we find that discount rates are strongly tied to an individuals clinical state and could be predictive of relapse, a major shortcoming of treatment for this disorder. This might be key in developing precision medicine approaches informed by cognitive computational markers and aimed at achieving better outcomes by tailoring treatment to the individual.

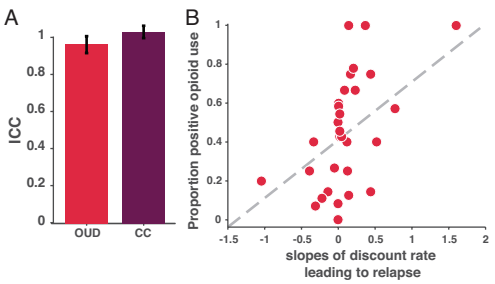

Figure 2: A) Intraclass correlation coefficient for OUD and CC; B) correlation between slope of discount rate and proportion of positive opioid use, Spearman's $rho = 0.32$, $p < 0.05$.

Acknowledgments

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