Effects of Methadone Maintenance Treatment on Decision-Making Processes in Heroin-Abusers: A Cognitive Modeling Analysis

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A B S T R A C T

Background & Objective: Although decision-making processes have become a principal target of study among addiction researchers, few researches are published according to effects of different treatment methods on the cognitive processes underlying decision making up to now. Utilizing cognitive modeling method, in this paper we examine the effects of Methadone maintenance treatment (MMT) on cognitive processes underlying decision-making disorders in heroin-abusers.

Materials & Methods: For this purpose, for the first time, we use the balloon analog risk task (BART) to assess the decision-making ability of heroin-abusers before and after treatment and compare it to the non heroin-dependent subjects.
Results: Results demonstrate that heroin-abusers show more risky behavior than other groups. But, there is no difference between the performance of heroin-abusers after 6 months of MMT and control group. Modeling subjects' behavior in BART reveals that poor performance in heroin-abusers is due to reward-dependency and insensitivity to evaluation.

Conclusion: Results show that 6 months of MMT decreases reward-dependency and increases sensitivity to evaluation.

Introduction

Addiction is characterized as compulsive drug use, despite awareness of the deleterious future consequences (Hyman, & Malenka, 2001). The transition from regulated to compulsive drug use is rooted in actions of drugs of abuse on a vulnerable brain. Changing motivational circuitry is followed by associated alterations in several psychological functions, such as decision making. Such drug-induced decision making malfunctions are evidenced to be generalized to real-life circumstances. This provides researchers to investigate addicts brain disorders via tasks called Cognitive Assessment Tasks, which simulate real-life decision making situations. Subjects' performance in these tasks provides a mean for assessing their decision-making abilities. For instant, Iowa Gambling Task (IGT) de-

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signed by Bechara et al. (Bechara, Damasio, Damasio & Anderson, 1994), has become very influential for studying decision-making deficits in drug abusers. The Balloon Analog Risk Task (BART) is another example which is developed by Lejuez, C.W. et al. (Lejuez, Read, Kahler, Richards, Ramsey, Stuart, Strong & Brown, 2002) to examine risky behaviors. This computer-controlled task involves sequential risk taking with feedback. Several studies have confirmed that subjects' performance in this task, have significant correlation with their real-life risky behavior indices (Lejuez et al., 2002; Lejuez, Aklin, , Jones, Richards, Strong, Kahler, & Read, 2003).

However, merely analyzing subjects' performance, says little about cognitive processes underlying overt behaviors. Indeed, because of the complexity of decision tasks and their large number of unobservable components, it's difficult to identify the causes of disorders. For example, poor performance in gambling task may be due to weakness in contingency learning, difference in evaluation of wins or losses and even impulsive or erratic behavior (Stout, Busemeyer, Lin, Grant & Bonson, 2004). One method to decompose an observed behavior to its underlying cognitive processes is using cognitive modeling approach introduced by Busemeyer and Stout (Busemeyer & Stout, 2002). In their pioneer work, they contrasted various cognitive models of the decision maker (DM) in IGT and used them to describe the causes of poor performance of patients with Huntington's disease. They also used their models to analyse the decision making processes in cocaine-abusers (Stout et al., 2004).

In another work Wallsten et al. developed cognitive models to explain individuals' behavior in BART (Wallsten, Pleskac & Lejuez, 2005). Fitting the models to the individuals' data, they demonstrated that the estimated parameters of the best fit model correlate significantly with measures of real-world risk taking behaviors. In this paper, we employ cognitive modeling approach to investigate the effects of the Methadone maintenance treatment (MMT) on the decision-making disorders in heroin-abusers. Several studies indicate that MMT decreases risky behaviors such as needle sharing and risky sexual behaviors (Qian, Hao, Ruan, Cassell, Chen, Qin, Yin, Schumacher, Liang & Shao, 2008). Probably, this effect is due to the changes in the activity of prefrontal cortex after MMT (Ersche, Fletcher, Roiser, Fryer, London, Robbins & Sahakian, 2006). However, the cognitive processes underlying these alterations in risky behavior, remains mostly unknown. Here, to identify effects of MMT, we fit several models to the data of 4 groups of participants, including control male subjects, control female subjects, heroin-abusers before treatment and heroin-abusers after 6 months of MMT. Comparing the parameters of the best fit model, we investigate the causes of alteration in subjects' behavior after MMT.

Materials & Methods

The Balloon Analog Risk Task (BART)

In BART, participants sit in front of a computer screen on which a circle (as a balloon) is shown. The participants can click on a button on the screen to inflate the balloon. Each successful click that does not result in the balloon explosion, yields a gain of x$ in a temporary bank. If the participant stops before the balloon explodes, the money is transferred to a permanent bank. But, if the balloon explodes, all the money in the temporary bank will be lost and a new balloon will appear on the screen. Each participant has 30 balloons.

The participants are not aware of the probability structure governs the balloon's exploding. In fact, the computer allows a maximum number of n pumps for each balloon. The probability of explosion on the i'th pump is:

$$S_i = \frac{1}{n-i+1} \qquad (1)$$

Where in the original version, n is equal to 128 and each successful pump yields 5 cents. We used the Persian version of BART which is developed in the Iranian National Center for Addiction Studies (INCAS). This version has no difference with the original one except that each successful pump yields 50 Tomans.

Models

We used the developed models (Wallsten et al., 2005) to describe the participants' behavior in BART. Here we briefly describe these models. Each model yields the probability of pumping in each pump opportunity.

The simplest model is the baseline model. It merely provides a statistical baseline against which we measure fitness of other models. It assumes that DM assigns equal probability of pumping on each pump opportunity for each balloon.

Next in complexity is the model named the target model which assumes that the DM selects a target number of pumps prior to start pumping each balloon. The probability of pumping in each pump opportunity is determined with respect to the distance of current number of pumps from the target number.

Unlike the two previous models, all other models postulate learning and option evaluation. These models assume that the DM has a mental representation of the stochastic process that controls balloon's exploding. DM evaluates the outcomes of stopping or pumping based on this representation, and selects actions among alternative choices using its evaluation. Here we considered two potential DM mental representations, two methods of evaluation and two forms of translating those evaluations to choice probabilities. Combination of these submodels yields a total of 8 full models. Here, we only describe the model that best fit to our data (we call it model B) and the reader can refer to (Wallsten et al., 2005) for the description of other models.

In Model B, DM believes that the stochastic process of balloon's behavior is stationary. That is, probability of balloon explosion remains constant over all pump opportunity. Hence, we can assume that DM has a prior beta distribution with parameters a0 and m0, over this constant probability. This probability is updated using past experience at the start of pumping a new balloon in a Bayesian fashion. Having the probability of balloon explosion, DM evaluates outcomes of pumping and stopping actions. In (Wallsten et al., 2005), prospect theory (PT) is used to model how DM evaluates these options. In general the expected PT gain for i pumps on balloon h is:

$$E_i\,(pump)=\pi_{h,i}\,(ix)^{\gamma^+} \tag{2}$$

where $\pi_{h,i}$ is the probability of pumping the balloon h, i times without explosion and γ^+ is a free parameter. DM selects a target number of pumping that maximizes the expected gains. It can be shown that the optimal number of pumping, g_h, is:

$$g_h=\frac{-\gamma^+}{\ln(q_h)} \tag{3}$$

In Equation 3 q_h is DM's estimation of the probability that balloon will not explode in each pump. The probabilities of pumping are given by:

$$r_{h,i}=\frac{1}{1+e^{\beta.\delta_{h,i}}} \tag{4}$$

Where $\delta_{h\,i}= i- g_h$ and β is the response sensitivity parameter. This model has 4 free parameters: a_0, m_0, γ^+ and β. Let q_1 be the DM's subjective probability that the first balloon does not explode in the first pump. The greater the DM thinks q_1 is, the greater is a_0 and the more certain the DM is about his opinion, the greater is m_0. β determines the sensitivity of DM's response to his evaluation. Greater values of β shows that DM gives more attention to his evaluation of outcomes of pumping. Lower values of this parameter show that DM has more erratic behavior. As we can see in Equation 3, γ^+ determines how DM values gains. Individuals that have higher values of γ^+ give more value to gains. It is clear also from Equation 3 that this parameter determines the optimal number of pumping. Higher values of it, shows that DM pumps more.

Participants

Data used in this paper consists of 4 groups of participants: control male subjects, control female subjects, heroin-abusers before treatment and heroin-abusers after 6 months of MMT. All heroin-abuser participants are male treatment seeking heroin dependents (based on DMS-IV (Pirastu, Fais, Messina, Bini, Spiga, Falconieri & Diana, 2006). The demographical properties of these groups are shown in Table 1.

Group	Control (men)	Control (women)	Pre	P6
Number of participants	27	23	25	19
Age	26.37 ± 5.50	28.04 ± 6.02	27.69 ± 5.45	30.37 ± 5.58

Table 1. demographical characteristics of participants NEUROSCIENCE

(Pre: heroin-abusers before treat- ment,P6: heroin-abusers after 6 months of MMT)

Results

BART scores

In Table 2 subjects' performance in BART are presented. Typically, riskiness in BART is indexed in terms of adjusted BART score, i.e. the average number of pumps on balloons that did not explode (Lejuez et al., 2002). Results show that adjusted BART score (AV) and maximum number of pumps in heroin-abusers before treatment is higher than those of control male subjects and heroin-abusers after 6 months of MMT ($p < .05$). This demonstrates that heroin-abusers before treatment show more risky behavior than two other groups. However, there is no meaningful difference between the scores of heroin-abusers after 6 months of MMT and control male subjects.

BART score	Control (men)	Control (women)	Pre	P6
AV	27.54 ± 11.52	22.38 ± 12	38.59 ± 13.79	25.14 ± 11.32
SUC	22.55 ± 3.55	23.80 ± 4.02	19.72 ± 5.27	23.58 ± 3.83
MAX	51.88 ± 24.22	45 ± 20.77	69.56 ± 22.64	50.16 ± 25.40

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Table 2. performance indices in BART for different groups. (AV: Adjusted Value, SUC: Number of successful pumps, MAX: Maximum number of pumping)

Parameter Estimation

We use maximum likelihood (ML) to estimate the parameters of each model. Then, we compare the models with respect to the number of participants best fit by each model according to Akaike Information Criterion (AIC). Results show that among all models, two of them fit majority of the participants (we call them model A and B). Parameters of model A had no significant difference among the groups. They also have little correlation with the BART scores. Additionally, in (Wallsten et al., 2005) it is shown that parameters of this model are not correlated with external risk indices. Therefore, model A is not a descriptive model for our data. Unlike model A, parameters of model B can discriminate individuals that had different BART scores. Based on this, we focus on model B for analyzing behavior of subjects. Table 3 shows the estimated parameter for this model and Table 4 presents correlation between model B parameters and BART scores.

Regarding to these results, these points can be inferred:

1. γ^+ in heroin-abusers before treatment is significantly higher than γ^+ in control male subjects ($p < .01$). This means that heroin-abusers before treatment give more value to gains and hence are more likely to show reward dependence behavior than other groups. Additionally, in heroin-abusers after 6 months of MMT, γ^+ is lower than heroin-abusers before treatment ($p < .05$) and has no significant difference with that of control male subjects. This proves that MMT decreased reward dependency in heroin-abusers and brought it back to the normal level.

2. As it appears from Eq 3, γ^+ is directly proportional to the optimal number of pumping. Significant correlation of γ^+ with maximum number of pumping is consistent with this fact.

3. β in control male subjects is higher than that of heroin-abusers before treatment ($p < .05$). Thus, heroin-

	Control (male)	Control (female)	Pre	P6
A_0	9220 ± 35033	3123 ± 4883	4305 ± 4529	2351 ± 4343
M_0	9281 ± 35052	3163 ± 4918	4365 ± 4560	2428 ± 4447
β	0.14 ± .09	.15 ± .11	.10 ± .08	.15 ± .1
γ^+	.93 ± .64	.75 ± .59	1.14 ± 1.25	.93 ± .92

Table 2. Estimated parameters of model B

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	AV	SUC	MAX
A_0	-0.00	-0.01	-0.03
M_0	-0.00	-0.01	-0.03
γ^+	0.45	-0.43	0.52
β	-0.46	0.41	-0.66

Table 4. correlation between model B parameters and BART scores (AV: Adjusted Value, SUC: Number of successful pumps, MAX: Maximum number of pumping)

abusers before treatment disregard their evaluation of outcomes of pumping or stopping. The value of this parameter is higher for heroin-abusers after 6 months of MMT than heroin-abusers before treatment ($p < .05$) but has no significant difference with control male subjects. Thus, MMT was effective in increasing the sensitivity of response tevaluation in heroin-abusers.

4. a_0 and m_0 have no difference between groups. Hence, the ability of learning the balloons' stochastic process is similar among groups.

5. None of the parameters have meaningful difference between control male subjects and control female subjects, as well their BART scores. Therefore, there is no difference in the risky behavior on BART for male and female subjects.

Discussion & Conclusion

In this study we used cognitive modeling to assess effectiveness of MMT on decision-making disorders in heroin-abusers. We fit different models on subject's behavior in BART. Results demonstrated that heroin-abusers before treatment show more risky behavior in comparison to the control group. This disorder in decision making is due to imbalance in reward dependency and insensitivity to evaluation. This group has no deficit in learning the balloons' stochastic process. Also, as there is no meaningful difference between performance of control group and heroin-abusers after 6 months of treatment, we can infer that MMT was effective in improving these disorders in heroin-abusers. Previously, Stout et al, (Stout et al., 2004) utilized cognitive modeling to study decision- making deficits in cocaine-abusers. Their study shows that cocaine-abusers have poor performance in IGT. Moreover, the result of cognitive modeling revealed that this poor performance is due to motivational and choice consistency factors. In their study, the parameter which determines the relative attention of DM to the loss vs the win was biased in favor of wins. Moreover, deficits in choice consistency indicate that choices of addicts were highly insensitive to their evaluation of different options. From these aspects, pattern of results in our study is consistent with their study.

As current study investigates effect of MMT on cognitive functions using BART for the first time, our results cannot be compared with previous works directly. However, several studies indicate that MMT reduces risky behavior in drug dependent individuals (Qian et al., 2008; Ersche et al., 2006; Lollis, Strothers, Chitwood & McGhee2000). But, in general there is no consensus on the effect of MMT on cognitive functions. For example (Gruber, et al., 2006) has shown that after 2 months of MMT, subjects demonstrated significant improvements from base- line (before treatment) on measures of verbal learning and memory, visuospatial memory, and psychomotor speed and reduced frequency of drug use. In contrast, (Pirastu, Fais, Messina, Bini, Spiga, Falconieri & Diana, 2006) reported that subjects under methadone treatment had more errors on the Wisconsin card sorting task (WCST) and performed worse relative to control subjects in IGT.

Regarding this reports, more investigations is needed to identify effects of MMT on cognitive functions involved in decision-making, especially in risky situations. One important limitation of our work is that all heroin-abusers were male subjects. For future works effects of MMT on female heroin-abusers can be investigated. Also, effect of MMT on cognitive abilities can be studied using other cognitive assessment tasks such as IGT. If done so, the effects of MMT can be better understood by comparing performance of subjects among different tasks.

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