Drug Addiction as a Non-monotonic Process: a Multiscale Computational Model

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Abstract — Addiction is considered a "bio-psycho-social-spiritual disorder" [1] for which complete recovery cannot be assured. Although addiction was computationally characterized as a non-reversible process [2,3], behavioral evidences support the possibility of recovery [4, 5, 6,7]. We thus propose to consider addiction as a non-monotonic dynamical disease. Previously, we presented a multiscale computational model that combines three scales of observations: behavior, cognition, and neuropsychology. This model evaluates the drug-seeking behavior in virtual subjects. We use our model to analyze dynamical properties of two typical virtual subjects. One has become an addict at the age of 17 and has since expressed a severe multi relapse pattern. The other was exposed to addictive behavior at age 36 but managed to cease drug seeking. The results are encouraging for further explorations into the individual dynamics in addicts.

Keywords — Addiction, Multiscale Modeling, Behavioral Processes, Cognition, Neurophysiological Processes.

I. INTRODUCTION

Drug use estimates presented in the United Nations World Drug Report 2008 claim that in 2006/07 about 24.7 million people used amphetamines, 16 million used cocaine, and 12 million used heroin at least once. In an effort to investigate the dynamics of addiction, we propose a computational model that considers addiction as a non-monotonic reversible process [8].

This mathematical framework combines three different scales of observations - social, cognitive and neuropsychological – and is hypothesized to predict the outcome of a virtual subject’s behavior with respect to drug-seeking behaviors. We analyze two case studies in terms of their tendency to relapse and ability to rehabilitate.

II. MATERIALS AND METHODS

The multiscale computational model combining neuropsychological (NepS), cognitive (CogS), and behavioral (BehS) scales is shown in Figure 1.

The output G(t) is the severity of the behavioral condition which that we propose to equate with the likelihood of drug-seeking behavior, generated at the BehS. The value G(t) lies in the interval [-1, 1], and we consider the range [-1,0] to correspond to a subject with maladaptive behavior and the range [0,1] to a subject with healthy behavior, both in the probabilistic sense.

The BehS is simply suggested to include the inhibition I(t) and compulsion C(t) functions. This is along the line of the I-RISA model that describes addiction as impaired inhibition (to stop sensory-driven behavior) and salience attribution (with larger interest in drugs than in other possible rewards) [9]. On the one hand, the function G(t) is positively influenced by the inhibition I(t), which by itself combines the inhibition stemming at the subject's neural development of the frontal lobes of the cortex [10, 11, 12] together with the inhibition coming from social rules of this individual. On the other hand, the function G(t) is negatively influenced by the compulsion C(t), which is calculated according to the incentive-sensitization theory of addiction [13,14]. In computing G(t), the balance between I(t) and C(t) is weighted by r(t), the cognitive process, as described in equation (1).

\[ G(t) = |I - r(t)| \cdot I(t) + r(t) \cdot (-C(t)) \]

The cognitive process r(t) is a combination of its previous value r(t-1) and the input to the cognitive process f(t), as described in equation (2). Both functions r(t) and f(t) are computed at the CogS.

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\[ r(t) = \frac{1}{2} \cdot \tanh[\alpha \cdot r(t-1) + \beta \cdot f(t) + \gamma] + \frac{1}{2} \] (2)

The input to the cognitive process \( f(t) \) is a weighted sum of the internal and external processes. While the exact realistic structure of \( f \) is hard to guess, we propose a reasonable model:

\[
f(t) = \left[ -\omega_S S(t) + \omega_P P(t) - \omega_D D(t) \right] + \left\{ \omega_A [ -A_S(t) + A_P(t) - A_D(t)] - \omega_Q Q(t) \right\} \] (3)

The internal processes are \( P(t) \), representing the level of pain or negative consequences in areas such as health or social relations; \( S(t) \), representing the level of stress or negative emotional state of the virtual patient; \( D(t) \), representing the craving level, based on the dopamine transmission in the Nucleus Accumbens (NAac); and \( q(t) \), representing the saliency of drug-associated cues. Intakes of drugs can increase \( P(t) \) [15]. The level of \( S(t) \) increases during withdrawal periods [16, 17, 18] and may trigger craving [19]. These intakes were shown to affect the level of dopamine in the NAac and the addicted behavior in rats [20, 21] and in humans [22, 23]. The value \( q(t) \) increases with repeated drug consumption [24, 25] and weights the affects of drug related cues \( Q(t) \) when encountered.

External processes in this model are \( A_P(t) \), representing a painful trauma that may cause a virtual patient to stop taking drugs [26, 27]; \( A_S(t) \), representing a stressful episode that may lead into instantaneous drug-use [28, 29]; \( A_D(t) \), representing drug priming that may cause drug-use [30, 31]; and \( Q(t) \), representing a drug-associated cue [32]. Relevant mathematical details are presented in [8].

III. RESULTS

In this section two different case studies of drug-seeking behavior are considered: The profile of GD outlines a continuous relapse pattern of a person who started using drugs at age 17 and has later been unsuccessfully trying to get away from drug-seeking behavior, whereas the profile of VR exhibits a person that has first used drugs close to age 36 and for which the drug-seeking behavior changes from healthy to maladaptive and back to healthy.

The \( G \) value of both cases, depicted in Figure 2, is averaged over 10 simulations, having a noise injected in the process. The constants used for both simulations are presented in Table 1. For the presented simulations, the inhibition \( I(t) \) of VR was set 33% higher than the one of GD, and the compulsion \( C(t) \) of VR was set 60% higher than the one of GD. The initial values of all the signals were chosen randomly in their defined intervals.

![Fig. 2: G(t) means, SEMs and G(t+1) versus G(t) for 10 simulations. At the top, GD’s evolution between ages 19 to 21, and at the middle, VR’s evolution between ages 36 to 38. At the bottom, G(t+1) against G(t). The diagonal line corresponds to G(t+1) = G(t).](image)

| \( \alpha \) | 0.15 | beta | 0.25 |
| \( \gamma \) | 0.2449 | \( \text{S decay for } G > 0 \) | 0.02 |
| \( S \) decay for \( G < 0 \) | 0.02 | \( \text{P decay for } G > 0 \) | 0.0002 |
| \( P \) decay for \( G < 0 \) | 0.1 | \( \text{D decay for } G > 0 \) | 0.00002 |
| \( A_S \) constant steps | 20 | \( \text{D decay for } G < 0 \) | 0.02 |
| \( A_S \) probability | 0.02 | \( A_S \) decay | 0.9 |
| \( A_D \) decrease steps | 20 | \( A_P \) decay | 0.4 |
| \( A_P \) probability | 0.04 | \( A_P \) constant steps | 10 |
| \( A_D \) decrease steps | 5 | \( A_0 \) decay | 0.2 |
| \( A_0 \) probability | 0.03 | \( A_0 \) constant steps | 3 |
| \( \text{q saliency constant steps} \) | 10 | \( \text{q decay for } G > 0 \) | 0.002 |
| \( Q \) constant steps | 20 | \( \text{q decay for } G < 0 \) | 0.005 |
| \( Q \) probability | 0.01 | \( \text{Q decay} \) | 0.9 |
| weight \( P \) | 1.1 | \( \text{Q decrease steps} \) | 40 |
| weight \( A \) | 0.4 | weight \( S \) | 0.3 |
| weight \( Q \) | 1 | weight \( D \) | 0.4 |
Next, we asked whether the dynamic behaviors of the individuals differ in fluctuations based on the severity of their addiction. For both simulations, we measured average and standard deviation, and then calculated the integral of the function from its average to measure the consistency of the fluctuations. The values of averages, standards deviation and integrals were (-0.0975, 0.0623, 24.5661) for the more severe case, GD, and were (0.4117, 0.1083, 41.4371) for the lighter case, VR. The addictive person has less fluctuations and flexibility in his drug-seeking behavior that the healthier one, seemingly due to the strong saliency to cues [9].

In Figures 3 and 4 the values of G(t) for GD and VR are plotted against the internal processes and the external processes, respectively. The internal processes affect G, and G affects these processes. The values of S(t) are higher during withdrawal than during use. The values of P(t), D(t) and q(t), on the other hand are higher during drug use. The effect on G by both internal and external events correlates with equations (1), (2), (3).

IV. CONCLUSIONS

The dynamical analysis in this paper provides analytical measures to behavioral facts pertaining to addiction. The underlying hypothesis that addiction is a non-monotonic dynamical disease differs from the current state-of-the-art. The effort here is to understand the individual fluctuations in drug seeking behaviors with the future goal of predicting stages of possible treatments and stages of need for extra cautiousness.

The typical case of the more compulsive, less inhibited individual will have an early onset to addiction. His behavior does not fully converge to addictive behavior due to internal and external events that cause him to try a way out; we stress in our model that none of the cases are monotonic. This virtual individual demonstrates numerous efforts to rehabilitate mainly due to pain, and may have short periods of withdrawal, but relapses are fast and overwhelming. The overall flexibility of this subject's behavior is far smaller than the flexibility in the behavioral variables of the less severe case, probably due to the growing saliency to drug cues.

The healthier person, with the stronger inhibition falls into addiction later in life. With similar internal and external events to the other virtual case, this individual rehabilitates. The total flexibility and change in the behavioral parameters is overall much greater than the severely addicted individual, and the actual behavior do not present a relapse pattern.

Both cases demonstrated a behavior that is affected by internal and external events, providing a hope for rehabilitation for people in either situation. A translational application of the model could be the identification of a treatment that given with the right timing will change the effect that the internal and external processes have on the drug-seeking behavior of the individual, and hence ease the process of recovery.

The analyses presented in this work are promising, and we will continue with deeper investigations into the individual dynamics of addiction.

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REFERENCES


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