Addiction and Rehabilitation: A Non-monotonic Computational Process

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Drug addiction is a worldwide epidemic. To reduce its spread, understanding the nature of addiction is crucial and possible treatments have to be developed. Current models of drug addiction only explain why addiction is overwhelming and cannot be overcome. Instead we focus on the dynamic of addiction, which includes rehabilitation and relapse. The model identifies the combination of factors that may defeat addiction. Thus, our model can provide not only a more complete description of addiction as a process but will also be useful for studying and evaluating possible treatments.

Introduction

Compulsive drug seeking and use, despite the negative consequences of drugs, characterize drug addiction. Furthermore, drug addicts are consciously aware of the negative consequences [1, 2]. A way to advance our understanding of addiction and thus of possible treatments is to introduce a computational model that describes the main properties of addiction as well as the

process of recovery.

Current computational models describe the process of becoming an addict as monotonic with positive feedback, which locks the system and prevents a way out [3]. Luckily, reality is not as one-directional as current modeling. Drug addicts can stop using drugs voluntarily [4]. Factors that influence voluntary behavior, such as economic and social costs can persuade many addicts to quit. Others require traumatic experience or life-threatening situations before seeking help. The most enduring problem of addiction is that even after prolonged withdrawal periods the sense of craving does not significantly dissipate; in some cases it may even increase [2]. Continued craving may lead to relapse [5]. Indeed most addicts do relapse [6]. Few succeed in staying abstinentit is their paths that are of particular interest. We propose a computational model of addiction that recognizes withdrawal and relapsing. This model may serve as a tool for investigating addiction and suggest and evaluate treatment strategies.

The main treatment, according to our model, is involvement of a ”recovery power.” The recovery power is a system parameter that has a strong positive and long-lasting influence on the cognitive rationality factor of the subject. The cognitive rationality factor mediates low and high level control of behavior, such as compulsion versus inhibition, and thus plays a crucial role in addiction. This paper introduces computational study of the recovery power concept in the context of drug addiction and provides predictions based on the model. A mathematical analysis of its effect and a software kit for further research are attached.

Previous Computational Work

There have been previous computational explanations of addictive behavior. In the rational addiction theory, the user is assumed to maximize utility over time. Since rewards are assumed to be discounted over time, the rational addiction theory explains that the addict selects the drug for the immediate enjoyment over late negative rewards e.g., losing a job and family. It was

lately proposed that since addicts suffer general lack of hedonism [7] they select (in the hedonic sense) drugs over other activities [8].

A more recent view of addiction places the rational addict into the framework of the ”temporal-difference reinforcement learning” (TDRL) process. This process describes how an animal in its current state acts in a probabilistic manner in order to reach one of the possible next states that bear the highest ”value” to the animal, while not paying too much for the action itself. The value of a state is the sum of future expected rewards (from now till end-of-life) in which the longer the animal moves into the future the more value is discounted. An agent that is new to the world cannot make a good estimate of future rewards, or the value function. As the agent learns from experience it is able to better estimate the ultimate value. This approach was elaborated by experiments demonstrating neural correlations for rewards in learning, approach behavior, and decision-making (for a review see [9]). However, addicts continue to consume drugs although they do not enjoy them [10]. Thus, in some cases the value of the reward and the state values are actually negative. Hence, the addiction does not seem very rational.

Redish proposed in a beautiful paper that TDRL can describe addiction, if the addicts ability to calculate the value of a state has been corrupted [3]. Instead of including the value of the future rewards only, the value function considers the maximum between the sum of reward (that may be negative) and dopamine, and the dopamine itself. The amount of dopamine in drug related states is always positive because of the supra-physiological increase in dopamine transmission caused by taking drugs such as cocaine [11], ethanol [12], heroin [13], cannabis [14] and others. As a result, states leading to dopamine production always increase their value and hence are more and more attractive. We agree that in order for drug states to dominate others their values should indeed exceed the other states, but we propose to calculate these values in a more biologically based manner. In this way, the values of the dopamine states need not increase in each step, but rather can go up and down according to various affecting factors.

Robinson and Berridge [15, 16] in their incentive sensitization theory explain how two different processes may explain the discrepancy between rational and non-rational behavior. They distinguish between liking the drugs effect, i.e. the reward value, and wanting to consume the drug, i.e., the craving. While the consumption of drugs may first start with the hedonic liking, with repeated consumption another process takes over–the process of wanting. That is, the hedonic liking effect undergoes tolerance while the wanting-craving effect undergoes sensitization. The addict may continue to crave for the drug and eventually consume it although it lacks hedonic enjoyment.

The Dual Process of Decision Making

The prediction of all the above computational models is that addiction is monotonic and so is the behavior. Our alternative computational theory of drug addiction takes into account additional dynamics. It includes withdrawal phases and relapse, which are caused by several known triggers such as drug cues [17], stress [18] and priming [19]. Most importantly, our model does not doom addicts to a bad end but rather includes the possibility that addicts can cease using drugs if their internal state enables it.

The key idea is to separate between internal processes such as craving (or wanting) and the actual decision-making (or action taking). The decision-making is based on a more global procedure including dual parallel computational process of compulsivity in one hand and of inhibitory control in the other. These two forces are mediated by the cognitive rationality into one global value, which is the basis for the decision-making. This is summarized by the formula:

$$G(t) = (1 - r(t))(-C) + r(t)I \tag{1}$$

Here C is the level of compulsivity, I is the level of inhibitory control, G is the global value, and r ($0 \leq r \leq 1$) is the cognitive rationality. When $G < 0$ the individual is likely to take

drugs (equivalent to value of drug states dominating); the individual is likely not to take drugs for positive values of G. Eq. (1) provides the simplest possible and linear formulation of combining and balancing two contradicting forces.

One can think of C and I as determined by genetic factors combined with past experience or education prior to the onset of our time in the model. If C is high, then the individual demonstrates a more compulsive nature and will have a stronger predisposition for addictive behavior. There are genetic [20] and social [21] risk factors that increase the probability to become an addict –only about 17% of people who consume drugs become addicted [22]. On the other hand, the higher the I value is the higher the inhibitory control is, which helps to prevent addiction (see Figure 1).

The value of $r(t)$ is an ongoing changing activity (of the neuronal patterns). Low levels of the cognitive rationality cause compulsiveness (C) to dominate which will decrease the global value function. On the other hand, high levels of rationality will cause I to dominate exerting a strong inhibitory control over behaviors that might otherwise have negative consequences to the agent in the long run. If $r = 1$ (a highly unlikely case) our model falls into the rational theories. If $r = 0$ our model is similar to the theory by Redish or the one by Robinson and Berridge which emphasize the monotonic growing of drug consumption.

Physiological Justification of Dual System The physiological basis underlying our model is the existence of two different strategies of behavior. One that uses high cognitive resources which calculates the long term benefits of a set of consecutive actions and one that is more cue-based habitual. There is plenty of data suggesting that the cognitive action planning is associated with loops [23, 24] between cortical (frontal and medial temporal) areas and the dorsomedial striatum, whereas habitual behavior is more associated with loops between frontal cortical areas and the dorsolateral striatum [25, 26]. Recently, a very interesting computational

model described the possible properties of these two systems [27]. This paper included a call for future work which would not need to assume that these systems are separated, since the anatomical and behavioral data shows that they are interconnected [28]. Our model can be considered to provide answer to this call.

Our model recognizes that the two systems, which are based on striato-thalmo-cortical loops, work in parallel and compete for dominance in selecting the strategy for action [26]. These systems are highly dependent on dopaminergic and glutamatergic transmission [28], and it is indeed well established that the pathophysiology of addiction is heavily mediated by alterations in these neurotransmitter systems and in these loops. For example, the activity of the orbitofrontal cortex (OFC) and the anterior cingulate gyrus (aCG) is altered dramatically in drug addicts [29]. In addition, electrophysiological and cellular studies [30] demonstrate altered neuronal structure and function in these striato-thalamo-cortical loops after repeated drug taking. Therefore, if one of the main problems of addiction is the altered function of these pathways, this will result in a shift from a balanced compulsive-inhibition system to a system which is biased towards a dominant habitual behavior. Our model thus takes an additional step forward by defining that the decision-making is based on these two systems working in concert and in relevance to addictive behavior.

A recent neurobiological theory based on human imaging studies [29] demonstrates that repeated drug-induced supraphysiological increase in dopamine transmission triggers a series of neuroadaptations in circuits that are involved in reward, cue saliency, motivation and memory. This results in an enhanced and long lasting saliency value for the drug and its associated cues at the expense of decreased sensitivity to salient events of everyday life including natural reinforcers such as food or sex.

Other studies suggest that it is not only the amount of dopamine that affects addiction but also the dopamines dynamic, whether the dopamine fired from the VTA to the nucleus accumbens

(NAac) follows a slow tonic manner or a phasic burst firing [31]. The NAac is considered a center of the reward system. It mediates goal-directed behavior by integrating hippocampus-dependent contextual information, amygdala-dependent affective information with prefrontal cortex cognitive functions to select behavioral responses [32, 33]. Goto and Grace recently found that tonic and phasic dopamine release selectively modulates PFC and hippocampus inputs to the NAac through D2 and D1 receptors respectively to affect goal directed behavior [32]. This means that the dynamics of the dopamine is what changes the balance between more cue-based behavior of the hippocampus and more cognitive-based behavior of the PFC.

The Cognitive Rationality Factor

The time-dependent factor $r(t)$ is affected by many variables and parameters, and can be written as:

$$r(t) = 1/2 \tanh\left(\alpha r(t-1) + \beta f(t,h) + \gamma\right) + 1/2 \tag{2}$$

With this formulation, r lies in $[0, 1]$. The letters α, β and γ are parameters, whereas f is a function including three parts. The first part consists of the feedback parameters that make addiction so difficult to overcome. The second part of f consists of the acute variables that when encountered have a strong but temporary affect on the cognitive rationality factor. The main novelty of our paper is the scientific recognition of the recovery power h as a crucial parameter of the cognitive rationality; this is the third part of f and will be discussed in the next section. The recovery power not only affects the rationality directly but it actually changes the predisposition within f to the other parameters and thus is able to lead to a permanent change. The general formula for f is:

$$\begin{aligned} f(t,h) &= \Big[\omega_P(h)P(t) - \omega_S(h)S(t) - \omega_D(h)D(t)\Big] + \\ &\quad \Big[\omega_A\Big(A_P(t) - A_S(t) - A_D(t)\Big) - \omega_{A_Q}Q(t)\Big] + \omega_h h(t) \end{aligned} \tag{3}$$

The Feedback Parameters There may be various feedback parameters, we include three main feedback parameters to affect r:

1. P - denoting the level of pain or negative consequences in areas such as health or social relations that can be increased by drug intake [34]. The increase of P leads to an increase of r.

2. S - denoting the level of stress or the negative emotional state of the agent. Stress increases during withdrawal periods [35, 36, 37] and may trigger craving [38]. The increase of S leads to a decrease of r.

3. D - denoting the level of current craving dependant on dopamine transmission in the NAac. There is ample of evidence demonstrating a close correlation between the level of dopamine in the NAac and addicted behavior in rats [39, 40] and in humans [29]. In rats repeated drug intake resulted in an increase in striatal extracellular dopamine [41] and a decrease during withdrawal [42]. In humans it has been shown that during intoxication there is increased activity in the OFC and aCG [43], which is associated with the availability of dopamine D2 receptors and the subjective perception of intoxication [44, 45]. On the other hand during long term withdrawal from repeated drug intake (more than a week) striatal dopamine response or D2 receptor availability was lower [46] and it was associated with lower metabolism in the OFC and aCG [44]. Craving for drugs is associated with increased availability of dopamine D2 receptors [46]. Therefore r increases when D decreases.

The details of these parameters appear in the supplementary material.

The Acute Parameters The acute parameters may affect the cognitive rationality acutely but these changes are not persistent. While there may be various such acute parameters we include

only four of them:

1. A painful trauma that may cause an addict to stop taking drugs immediately by temporarily by increasing r, we call it A_P [47, 48].

2. A strong stressful episode A_S [18, 49] that lead into immediate drug-use,

3. Drug priming A_D such as social drinking [19, 50] brings into drug-use again,

4. Drug-associated cues Q such as visiting a particular friend [17]. The parameter Q is carefully crafted to fit biological findings. The saliency of drug-associated cues increases with repeated drug consumption. That is, when considering drug addiction as a disease of learning and memory mechanism [51], repeated learning results in a stronger association between the stimuli and the rewards, causing a sensitized saliency for drug associated cues [52]. When A_D, A_S, or Q are encountered during withdrawal, r is strongly decreased, shifting G to become negative and the agent undergoes a relapse episode.

The four acute parameters may in turn affect the feedback parameters via changing G for the duration of the relapse. Since their affect is temporary, they are detrimental in rare cases only when the person is a boarder line addict (see Figures 2 and 3). The details of these parameters appear in the supplementary material.

The Recovery Power: Enabling Rehabilitating from Addiction

The revolutionary and possibly long-term change of the cognitive rationality factor is modeled by the recovery power. A common aspect in many people who succeed to stop using drugs seems to be long term increased rationality that enables the control of inhibition over compulsion. Some of these factors are family or social support in the form of economic help, rehabilitation programs, anonymous meetings such as Alcoholics Anonymous, psychological

support and even religion [53]. In addition, there are some pharmacological substances that in some cases prevent addicts from relapsing such as methadone [6] or nicotine replacement therapy [4].

In our model, the recovery power represents these events or agents that have a long term increasing affect on r, both directly as well as indirectly by changing the weights of its constituting parameters. Each recovery power event has a set window of time during which it influences r the strongest. However, if a consecutive event occurs before the prior one ended then their joint influence on r is lengthened. Furthermore, if a consecutive event occurs not too long after the main affect of the former event ended then the duration of affecting r grows wider for the next event and the agent will stay rehabilitated for longer time. This "memory" of the events represents the notion that repeated recovery power events are more helpful than events occurring in a sporadic manner (see Figure 4). The effect of the recovery power is demonstrated in Figure 5: an addict encounters a series of recovery power events that lead to abstinence.

Discussion

Our model computationally demonstrates why addiction is so persistent (the feedback parameters that push to stability), as well as how it can be overcome (via the recovery power). Craving is hard to control and activates compulsive behaviors, which lead to drug seeking and taking. However, mammalian behavior is more complex and diverse than basic compulsion. In certain circumstances high cognitive processes may take over and dominate behavior. Usually, these circumstances involve planning and the postponing of immediate reward in order to receive a higher reward in the long run.

Thus, a healthy organism may inhibit craving by using his cognitive rationality mechanisms. The problem is that addiction is a brain disease that disrupts these mechanisms [45]. These disruptions allow a shift towards compulsive behaviors and a weakening of inhibitory high cog-

nitive control. In our model we introduced the rationality factor r that determines the balance between compulsive behavior and inhibitory control. The cognitive rationality factor is a basic principle for describing the neuronal pattern activity of the competition between higher cognitive control and basic adaptive evolutionary instincts that seek reward. We call for future research to evaluate the properties of r and propose clinical ways of how to increase r and keep it high.

The solution proposed for improving r was introduced in terms of the recovery power. This can be thought of as related to the term Higher Power, which its meaning vary depending on whether the subject is a member of an Alcoholics Anonymous, is being counseled by a clergymen, or under treatment by medical professionals. It also is related to motivation and emotions which this paper does not include implicitly.

Our model provides some testable hypotheses regarding addictive behavior. The fundamental hypothesis is that the cognitive rationality is elastic and can be influenced by various factors, such as deep trans-cranial magnetic stimulation, chemicals, or behavioral treatment. We thus propose that caregivers should evaluate the level of rationality and its elasticity first by designing and administering questionnaires. Using fMRI to measure the level of activity in brain areas related to compulsive behavior and inhibitory control may serve as another tool for evaluating the level of rationality. This knowledge may serve as a method to identify people who have a predisposition for addictive behavior and provide clues for individualized treatment strategies.

While higher animals are perhaps more elastic in their cognitive rationality due to their working memory and long term planning ability, accompanied by an increased volume of prefrontal cortex, we propose that one can still design an animal model that may chose to stop drugs-use. This will enable the future concentration on the areas pertaining to the cognitive rationality directly.

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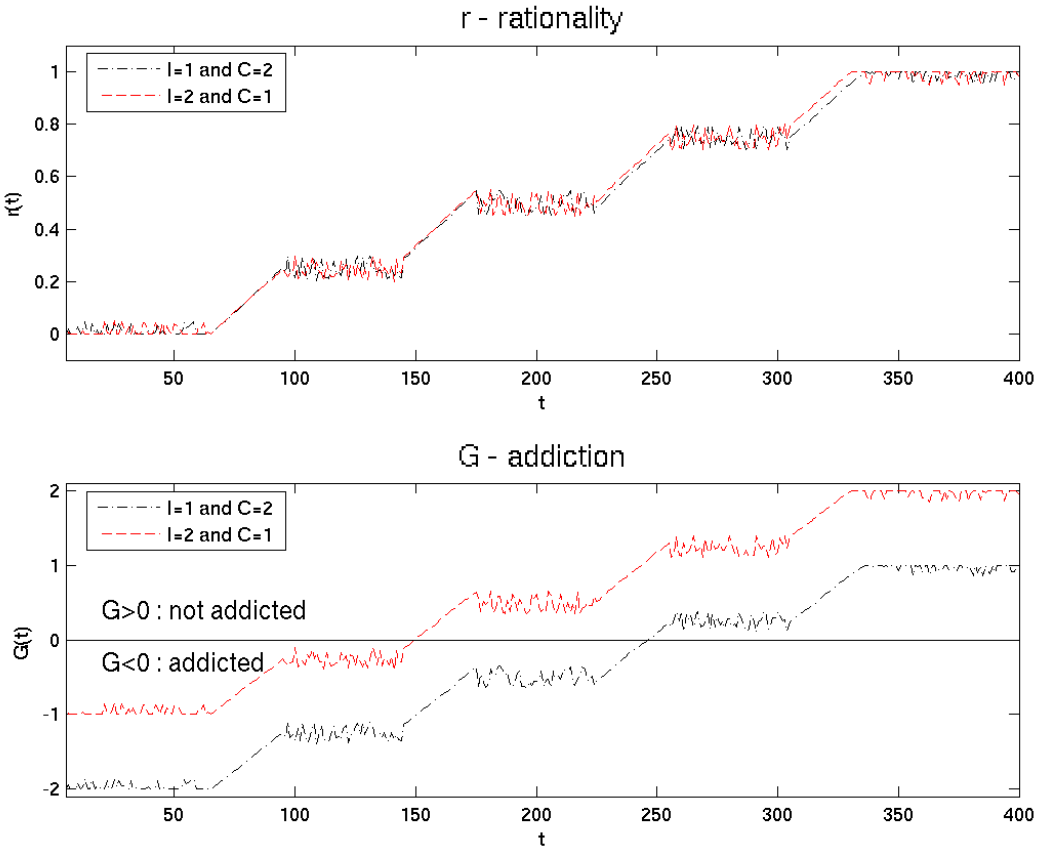

Fig. 1. The top graph features the cognitive rationality (r), and the bottom graph depicts the corresponding global addiction (G) value for the same two profiles of the compulsion (C) and the inhibition (I). Different values of r are required to assure the agent is drug free ($G > 0$). In the first profile where $I = 1$ and $C = 2$, the subject is not addicted when $r > 0.67$, while the subject is drug free when the r value is as low as $r > 0.34$ in the second profile where $I = 1$ and $C = 2$.

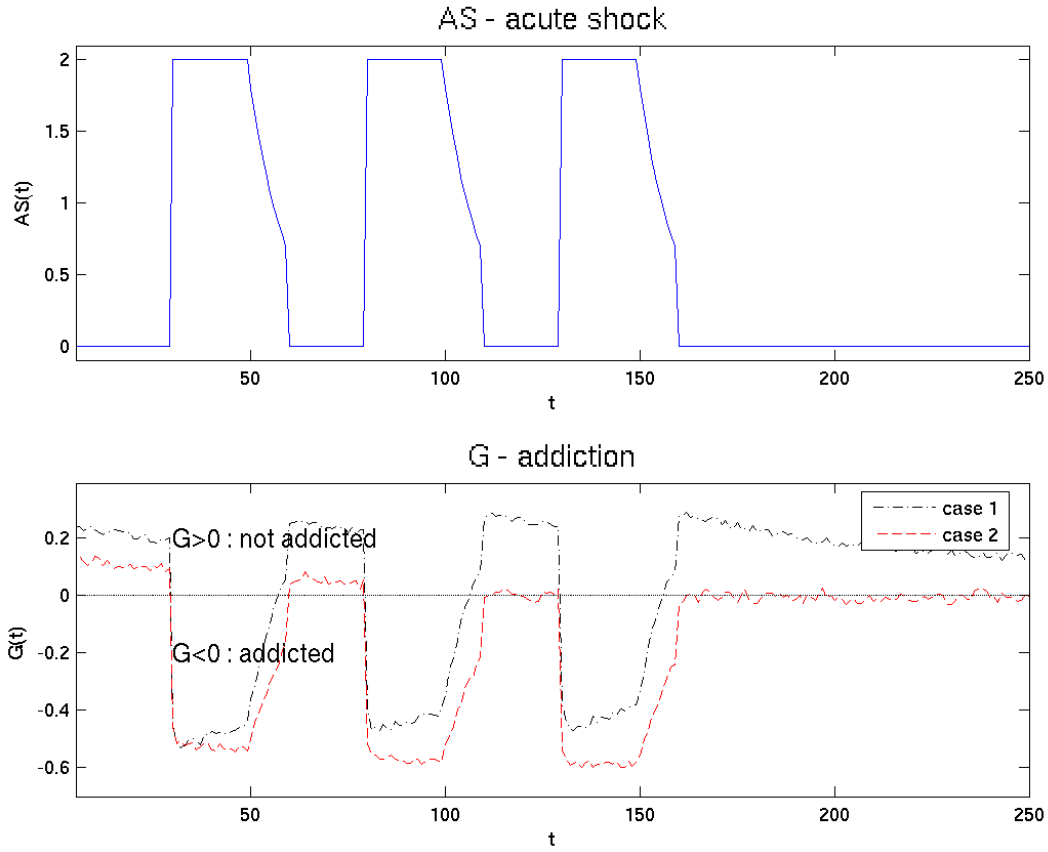

Fig. 2. The top graph features a profile of a series of acute shocks. The bottom graph shows the corresponding global value (G) to the acute shocks, but with two different starting points. In the higher starting point (around 0.24) the subject may use drugs for a limited period of time but will return to its relatively stable non-addicted condition. The second starting point of G (around 0.12) is also non-addictive but is less stable, hence the acute shocks are enough to cause the subject in this case to become addicted.

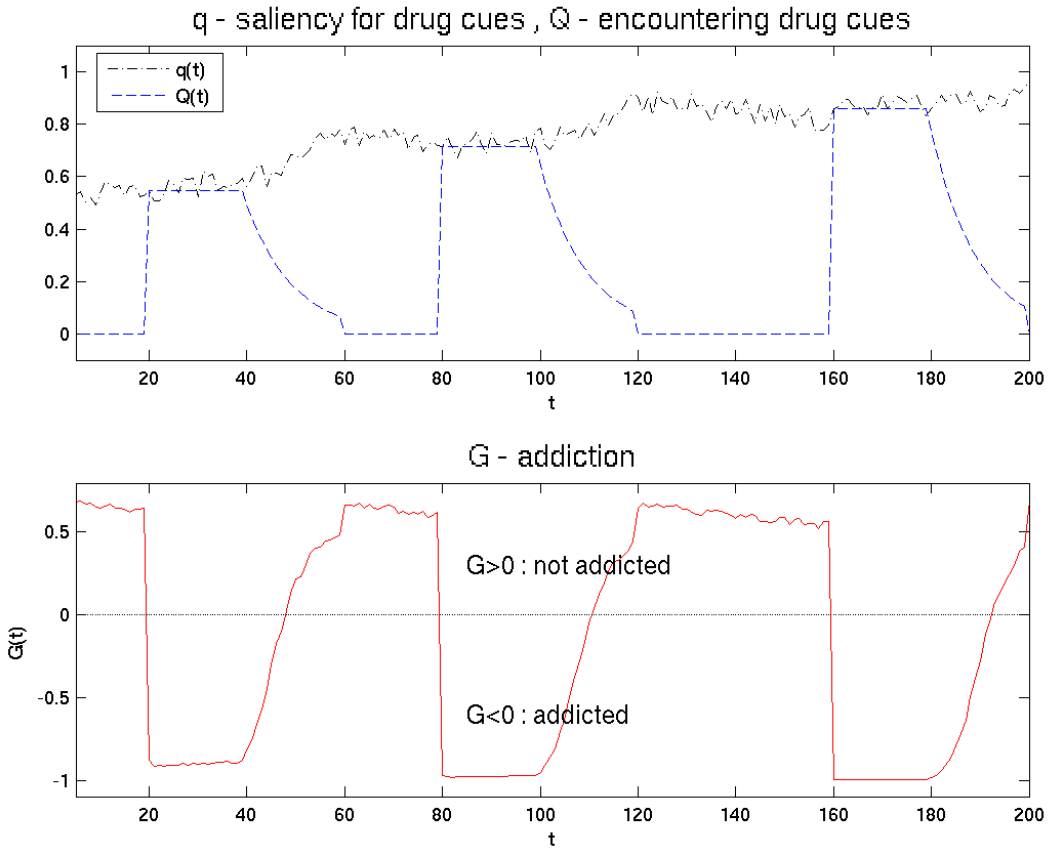

Fig. 3. The top graph demonstrates drug cues Q arriving at times 20, 80, and 160. The value q describing the saliency of drug cues is automatically updated with respect to the history of the cues. The value q affects the height of the next cue: as q increases, the height of Q also increases. The bottom graph shows how the value of G goes down when there are drug cues. The higher the cue values are the longer G remains low.

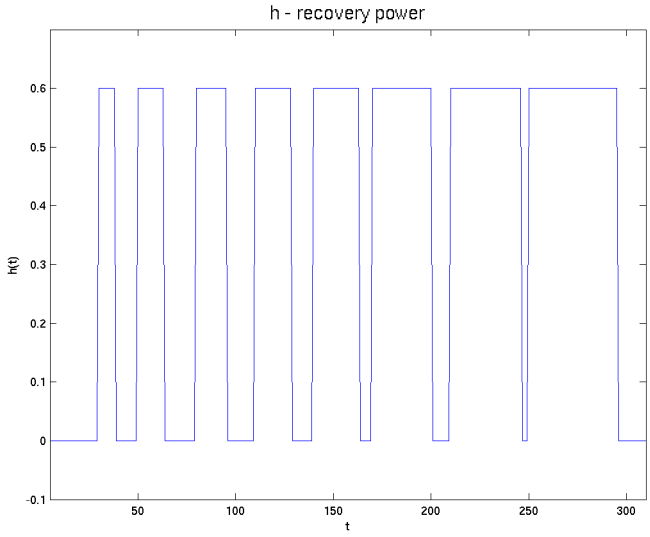

Fig. 4. The recovery power (h) has memory. Here we see a series of eight recovery power events. If the previous h event was recent, the next burst has a longer duration. A sequence of relatively frequent recovery power signals may lead to a stable recovery power value.

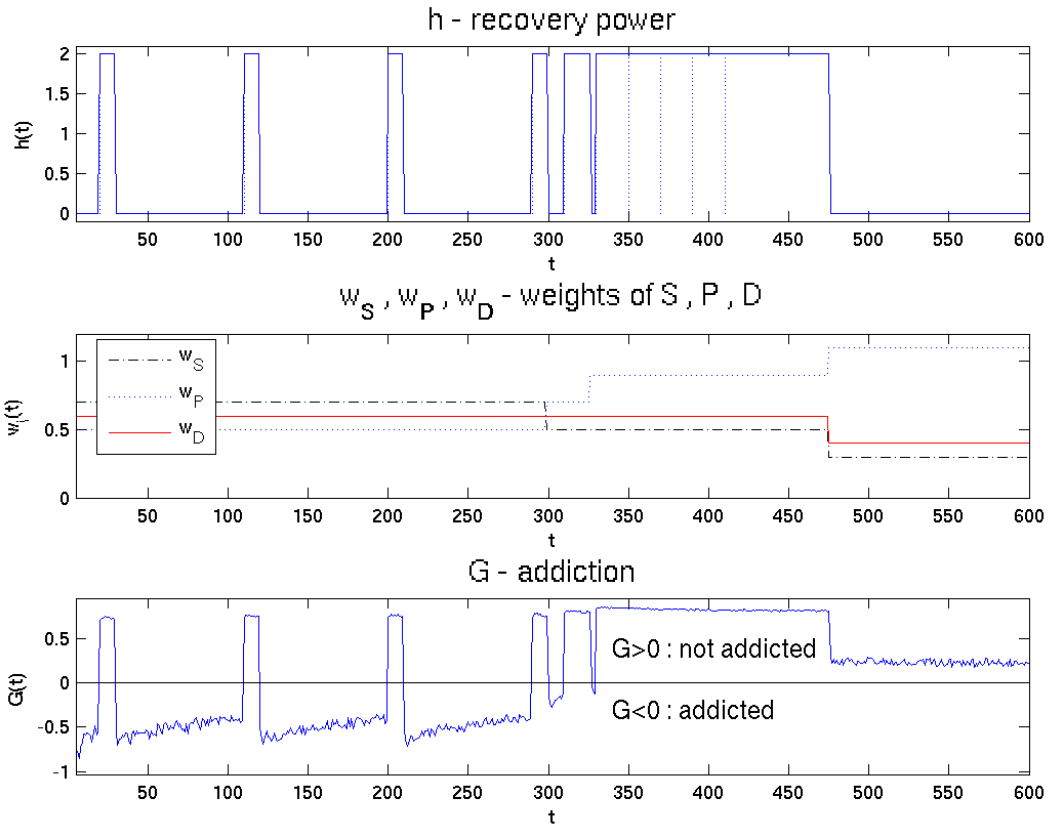

Fig. 5. The top figure demonstrates a recovery power series with memory. In the middle figure we see that the recovery power has the ability to stochastically affect the weights of the basic parameters of the cognitive rationality factor, such as stress (S), pain (P), and dopamine related craving (D). The bottom figure shows how the G value which started with a negative (addictive) value increases and stays permanently positive due to the influence of the recovery power shown at the top.