A qualitative and semi-quantitative combined theory of addiction

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Abstract

The proposed hypothesis bundles a number of well-known human traits to obtain a more comprehensive picture of human behavior in general and of addiction in particular. It posits that the major driving force of human decisions and actions are hedonistic such as pleasure seeking and discomfort avoiding located in the neuronal reward centers such as the nucleus accumbens. This drive is evaluated and controlled by "will power" or "self-control" to avoid negative consequences with its neuronal basis in the prefrontal cortex. Both traits are secondarily influenced by memories of previous experiences as well as risk taking assessments originating mostly in the hippocampus and amygdala. In a healthy individual, these 4 traits interact to the well-being of the individual. In addiction, however, these four traits are either overly active or overly inactive and their interactions become dysfunctional leading to addictive behaviors. Here, it is posited that an overly active or poorly satisfied reward system is not satisfied by natural stimuli but demands artificial stimuli like psychoactive drugs to achieve full satisfaction. This additional desire is secondarily poorly controlled by a weak or dysfunctional control system allowing the reward centers to become dominant and to force the individual to abuse drugs. Additionally, previous experiences and their memories and risk taking assessments do negatively affect the first two traits further strengthening the reward and weakening the control systems. It is further posited to assess the strength of each of the four traits as obtained from interviews, psychometric tests or physical measures. This could be done in that the strength or activity of each trait receives a number ranging from 0 to 10 like it is done in a pain scale. The strength of each trait and sum of all four trait numbers will provide a semi-quantitative measure if an individual is or is not at risk of developing an addiction or about the major contributing factor or factors contributing to an existing addiction. Assessment of the strength and activity of each of these four traits and their contributions to addictive behaviors will help the therapist to devise a more specific treatment plan to treat the main components leading to or maintaining an addiction as well as preventing relapses after abstinence.

Key words

Addiction, hedonism, gratification, control, memories, risk assessment, reward center, nucleus accumbens, prefrontal cortex, hippocampus, amygdala, addiction risk calculator, therapeutic intervention of addiction.

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1) Introduction

Currently, a variety of models of addiction are being considered. The neuro-adaptive model proposes that substances or behaviors sensitize and program certain neuronal systems which then lead to use, abuse and addiction. In contrast, the sensitivity model states that sensitive neuronal systems exist before exposure to a substance or behavior which then determines its use, abuse or addiction. The first model is generally espoused by non-professional lay people while the second appears to be more accepted by scientists (Squire et al., 2012). Other models deal with the psychological aspects of addiction per se. A more widely accepted model describes addiction as a progression from positive reinforcement to negative reinforcement. Initially there is an impulse control disorder where tension or arousal leads to impulsive acts leading to pleasure and gratification which later leads to regret, guilt and ultimately to tension. This circular pattern appears to be followed by a compulsive disorder where anxiety and discomfort leads to repetitive substance use- behaviors which is then followed by relief of anxiety and discomfort followed by obsession/substance use and back again (Squire et al.2012). Biological theories of addiction mostly involve proposed disorders of the prefrontal cortex and/or the nucleus accumbens (Goldstein and Volkow, 2011, and Di Chiara et al., 2004) or problems in the connectivity among these and other brain areas (Fingelkurts et al., 2006).

Above models are more global in their interpretations and either rely only on certain traits without assessing their interactions or on brain studies using only one particular trait-brain association. They also do not include a quantitative assessment of the contribution of each trait which might lead to or maintain an addiction. The proposed hypothesis in this paper will identify the most important traits which govern human behavior in general and addiction in particular and will then semi-quantitatively assess their contributions to healthy and addictive behaviors as well as will propose ways to use them in the treatment of addiction.

2) The Psychological and Biological Factors of Normal and Addictive Behavior

The model proposed here is designed to first identify the four most important psychological as well as neuro-biological factors which -among others - seem to be most dominantly involved in any healthy human behavior as well as behaviors which are not considered healthy such as addiction. They can be divided in to two major and two minor traits.

Hedonism and its neuronal reward center.

It is proposed that the first and most fundamental and dominant drive in life is the hedonistic trait or the pursuit of happiness and pleasure and the avoidance of discomfort and displeasure. Scholars and Philosophers over the centuries have expressed similar and supporting ideas. For instance, Aristotle wrote: *All what we do is for our pleasure*. Epicurus stated: *Wellbeing and pleasure are the beginning of a happy life* and Huxley offered in 1950: *The battle of our existence is a battle about wellbeing.* Politically, the constitution of the USA stresses in the beginning that “the pursuit of happiness is an unalienable right of every citizen”. Psychologically, these principles are embedded in the old epicurean and hedonistic theories and the more modern theories of hedonism, desire, objective list and authentic happiness (Zalta, 2016, Seligman and Royzman, 2003). Personal experiences teach us that we try to choose a job, pick a hobby, select food and befriend others all for one reason and one reason only, to enjoy the professional activities, to savor the taste of the nourishment or to enjoy the social interactions while avoiding, procrastinating or grudgingly doing all the things which are bothersome or disliked.

The biological basis of this trait is the reward system identified as being located in the limbic system and consists predominantly of the nucleus accumbens (both core and but mostly shell) and ventral segmental area. The power of this system has been demonstrated both in animals and humans. For example, Olds and Milner observed in 1953 that rats would voluntarily self- deliver electrical impulses to this area while forgoing food intake to the point of starvation and enduring painful foot shocks just to obtain this stimulation (Olds and Milner, 1954, Lowinson, 1997). Similar observations have been made in dogs and monkeys (Rolls et al., 1980). In humans, such experiments are difficult to perform and results are not as definitive. Delgado reported in 1969 about one patient who had received electrical stimulation of the reward area saying that "you can keep me here longer when you give me these shocks which I like" (Delgado, 1969). Heath in 1972 described one patient who self-stimulated his reward circuit experiencing great euphoria and elation and had to be disconnected despite his vigorous protests (Moan and Heath, 1972). Recent studies reported that subjects receiving deep brain stimulation (DBS) described their responses as "cheerful" and "joyful" and felt that they could become "compulsive about the stimulation" capable of stimulating themselves "for the entire day" (Oshima and Katayama 2010**)** . In contrast, under- activity of this center, as in depression, leads to anhedonia which can significantly decrease the quality of one's life. It has been claimed that deep brain stimulation of the limbic center can reverse the feeling of anhedonia and can lead to more enjoyable feelings and activities (Schlaepfer et al., 2008).

In addiction, however, the reward system is either overactive or only poorly satisfied by lack of natural stimuli such as job satisfaction, love, happy family life and so forth and, thus, demands full satisfaction through artificial means such as psychoactive drugs. The power of this system in demanding these artificial stimuli has been demonstrated numerous times. For instance, mice, rats and monkeys will self-administer cocaine or morphine solutions intravenously or into the reward area often to the exclusion of water or food and some would die if the experiment is not stopped (Bozart, 1994, Roberts et al., 1999, Denau et al., 1969, Rolls et al., 1980 and Spraag, 1940). Human addicts speak of the most pleasurable and gratifying "highs" or "rushes" following the use of certain drugs. Drugs make them feel good (at least in the beginning) and make them temporarily forget all their misery and discomfort. This urge becomes irresistible. This urge derives from the limbic system and is associated with dopamine. In rats, the author found a correlation in that the amounts of cocaine consumed voluntarily correlated directly with cocaine-induced dopamine changes in the nucleus accumbens (Ferraro et al, 2000). In humans, the limbic system has been found to be enlarged in individuals with substance abuse disorder. However, this enlargement was already present before these individuals engaged in addictive behaviors (Ersche, 2011).

Thus, it could be posited that the pursuit of gratification originating in the reward system is a major driving force of human behavior and a satisfaction of this center by natural stimuli is one important factor for a healthy life. In addiction, it can be proposed that there exists a lack of gratification, an abundance of discomfort or an overly active reward center. Since the reward center is not fully satisfied by natural stimuli, it will now seek gratification by artificial stimuli such as drugs.

Self-control and the prefrontal cortex

The second major factor is self-control or often referred to as "will power". This force is inhibitory and it supports but mostly suppresses excessive hedonistic as well as other traits such as unnecessary risk taking. It prevents one from saying or doing things later regretted or forces us to do things that we do not like to do (Hansen et al., 2010, Duckworth and Seligman, 2005). This activity is frequently encountered – knowingly and unknowingly - in our everyday activities. I would like to play tennis but I will work on the report which I was requested to finish by today. I will only spend $100 in a casino and when lost I will leave. Unfortunately, it has also been shown that self-control is limited in its resources and that it's repeated use can quickly weaken or exhaust its controlling action (Mead et al., 2009, Huston, 2016).

The basis for these controlling activities is found in the executive center located in various areas of the prefrontal cortex (Funahashi and Andreau 2013). The importance of the prefrontal cortex was demonstrated around 1850 by a worker named Phineas Gage. By all accounts he was a nice and hardworking fellow. However, an accident severely damaged his prefrontal cortex. Afterwards, he became irritable, uncontrolled, impatient and incapable of completing any job. Subsequent studies with animals or on patients who had experimental damage or injuries or strokes confirmed this early observation that a weakened prefrontal cortex could result in reduced behavioral control, leading to the development of behaviors aimed at immediate gratification regardless of the long term negative consequences (Cordova et al., 2014, Knoch et al., 2002). For instance, patients with discrete prefrontal lesions showed pronounced impairment on planning and attention and were more prone to exhibit risky decision makings as compared to healthy individuals (Manes et al., 2002). In contrast, electrical stimulation of the prefrontal cortex significantly reduced the quest for pleasurable activities such as food ingestion when hungry or resulted in a marked decrease in risk taking behaviors (Fregni et al., 2008)

In addiction, the executive center is weak and is not able to counteract and suppress the demands of the reward center. This allows the reward center to become dominating and to use drugs for its satisfaction. The excessive self-administration of cocaine by rats can be markedly reduced by activating the prefrontal cortex with electrical impulses. Furthermore, the intensity of the stimulation depended on the degree of self- administration with the most "addicted" rats needing the most stimulation (Chen and Bonci, 2014). Monkeys which self-administered cocaine had a smaller and dysfunctional prefrontal cortex as compared to those which did not (Mcintosh and Hemby, 2013). .In humans, ample evidence is available that the prefrontal cortex is involved in addictive behaviors. A common observation is that the use of alcohol and drug use increases generally in many young adults but drops in most individuals when they reach their early twenties or at a time when the prefrontal cortex has fully matured and can exert a stricter control over such behaviors. In individuals with addiction, a dysfunctional prefrontal cortex with an impaired response inhibition and reduced self-control has been demonstrated repeatedly (Goldstein and Volkow, 2011). Imaging studies in individuals with addictive behaviors have shown that the prefrontal cortex is hypoactivity while the reward center was significantly larger so that it seems that the reward center escaped the weakened control leading to the addictive behavior (Carpenter 2001, Bolla et al., 2004 , Goldstein and Volkow, 2011, Ersche, 2011, Balconi and Finocchiaro 2016), Measurement of the activity of the prefrontal cortex of abstaining persons with addiction resulted in a good prediction in that those with significant hypo-activities were much more prone to relapse (Steward and Paulus, 2015).

Thus, it could be posited that self-control located in the prefrontal cortex is the major control mechanism of our daily decision makings and actions. In addiction, this control is weakened and inadequate and cannot counteract and suppress the demands of the reward center allowing it to satisfy its needs by abusing drugs.

Memories and the hippocampus

The first of these minor forces are our factual and emotional memories of past good or bad experiences which can affect markedly our desires and actions. A very gratifying experience is most likely to be repeated while an unpleasant one is most likely to be avoided. Therefore, it is not surprising that decision making improves with age as the brain matures (Nauert, 2011). Many scientific studies and personal experiences have shown that participants and we having to make a decision will rely heavily on past associated memories.

Processing and recall of memories involve – among other areas – predominantly a well-functioning hippocampus. Damage to this area is associated with significant memory problems. Importantly, the hippocampus can affect both the activities of the prefrontal cortex as well as the reward center in the brain (Courtney et al., 1998, Preston and Eichenbaum, 2013, Fell, 2016, Sweat, 2013).

In addiction, the memories and hippocampal activities have been shown to play a significant role. In animals, selective inactivation of the ventral hippocampus has been shown to attenuate cue-induced reinstatement of drug-seeking in rats (Jason and See, .2007). In humans, addicts remember previous drug related experiences such as the “highs” or “rushes” and such memories can be a strong inducer for the next drug injection or a major cause for relapse after abstinence (Crombag et al., 2008). Brain scans have shown that increased hippocampal activity is a predictor not only of continued cocaine use but also of a high likelihood of relapses after abstinence (Adinoff et al., 2015).

Thus, it is posited that memories of past experiences and the hippocampus are major factors for living a productive life. In addiction, memories often play a detrimental role in that they participate in and foster the initiation, progression and relapse of addictive behaviors.

Fear, risk-taking and the amygdala

The second minor force is our assessment of fear and risk in exploring and in reacting to our environment. Such decisions have to be made daily when crossing a busy road, investing money or deciding to go sky diving. High-risk takers are easily bored and often engage in sensation and thrill seeking with risk seeking increasing and then declining with age again as the prefrontal cortex matures (Lang et al., 2000, Rolison et al., 2013). Risk decisions are often based on perceived and actual risks and many people fear flying with a low risk factor more than driving a car on a public street with a high risk factor.

The basis of this trait involves mostly the amygdala (Purves et al., 2001). In general, stimulation of the amygdala in animals and humans will increase fearful behavior while damage to this area will reduce it (Kilts 2001, Edwards 2005). Gambling studies have shown that healthy individuals would show proper risk evaluation while patients with lesions in the amygdala could not evaluate the risk of losses and would gamble even if the losses would outweigh the gains (De Martino, 2005). The amygdala also has been shown to interact with both the prefrontal cortex and the nucleus accumbens (Gold et al., 2015, Jackson and Moghaddam, 2001).

In addiction, rats with damage to the amygdala were significantly more sensitive to cocaine, more prone to consume this substance voluntarily and more willing to re-instate cocaine consumption after abstinence (Chambers et al., 2007, Fuchs, 2002). For humans, there are often two risks to consider such as evaluating the danger of the drug per se and the legal consequences of using illegal drugs. Here, high risk takers have been found to have a higher incidence of drug use (Laviola et al 1999, Conway et al., 2004). In contrast, many patients taken prescription opioid analgesics state that they are afraid and fear to become addicted and train themselves to just adhere to the prescribed doses at the proper times (Metcalf, 2012) . The number of smokers has steadily decreased over the last five decades and many adult smokers being aware of the dire health consequences of smoking have stopped partially due to the fear of dying from cardiovascular diseases or lung cancer.

Thus, it is posited that fear and risk evaluation is a significant factor in our daily decisions and actions and necessary for our survival. In addiction, low fear and high risk taking without properly judging the consequences do favor the use and abuse of drugs.

3) Interrelationships of these four Traits in Healthy and Individuals with Addiction

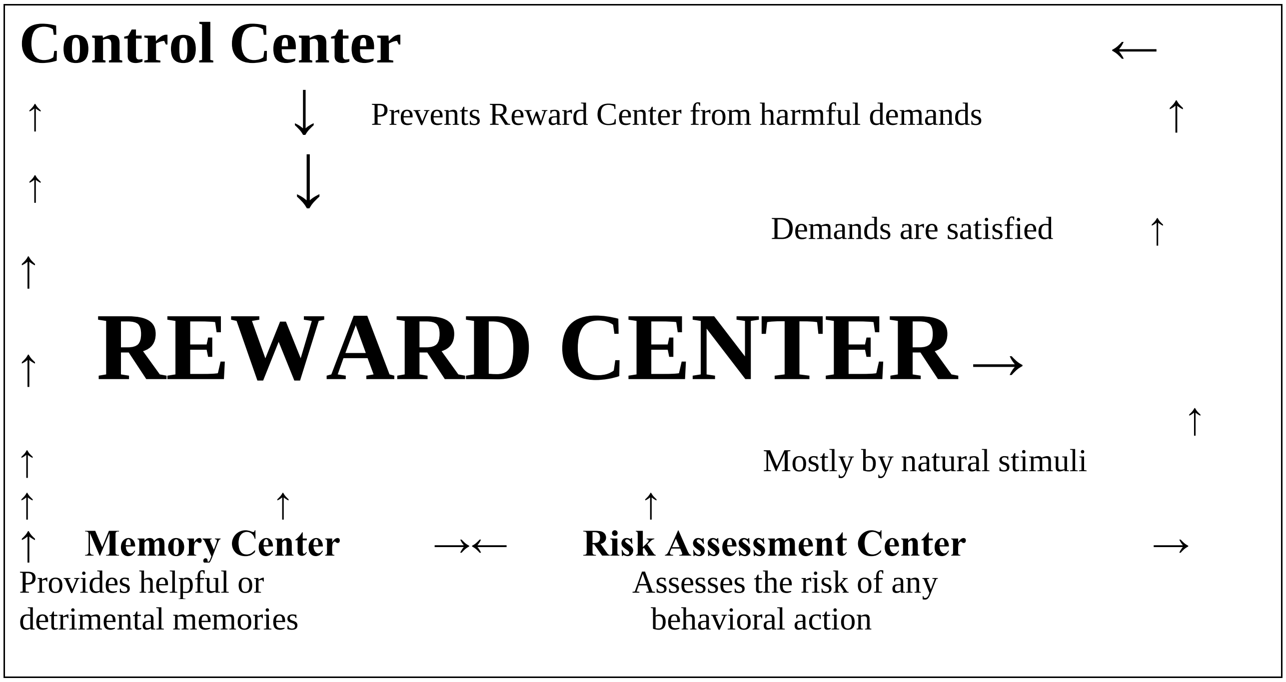
Each of these four traits and their neuro-biological bases are derived from genetic, epigenetic and environmental influences and will slightly vary over a life time. Thus, all individuals will all have these four traits and neuro-biological bases but they will differ in their strengths and activities.

Interaction of these four parameters in healthy individuals.

The interaction of these four traits and their centers differing in strengths and activities will now determine our personalities and the degrees of our happiness, unhappiness, will power and decision making, memories of past experiences and risk assessments of current situations. It can be posited that in healthy individuals the reward center again takes central stage and is well satisfied by natural stimuli such as job satisfaction, healthy family, social and professional experiences and other beneficial factors. If the reward center wants to deviate from its healthy pattern then the control center will spring into action and bring the reward center into line to avoid negative consequences. Both are supported by pleasant and unpleasant memories and by fear of future negative consequences. Thus, a” healthy” balance is present among the four factors and will be maintained leading to a gratifying life (with minor ups and downs) and not getting the individual into significant trouble. This individual has no need for any major artificial stimuli such as drug abuse.

This is depicted in Figure 1.

Figure 1: Interaction between the proposed factors which mostly influence our daily decisions and actions



Interaction of these four parameters in individuals with addiction.

In addiction, these relationships between the four parameters are changed and are different. This is mostly due to the fact that each center exhibits abnormal abnormalities which result in "unhealthy" interactions and outcomes. Again, the main driving force is the reward center which demands satisfaction though gratification and/or avoidance of displeasure. However, full satisfaction cannot be achieved by natural stimuli since the reward center is overactive or there is a lack of natural stimuli. Thus, it looks for artificial stimuli like drugs to achieve full satisfaction. The control center recognizing and anticipating the negative consequences will try to counteract the reward center but it is too weak or dysfunctional to do so. The result is that the reward center gets out of control, becomes dominant and will now indulge in the use of artificial stimuli like drugs. Both of these traits and centers are influenced by memories and risk assessments. First, memories of previous soft and/or hard drug experiences and their rewarding effects strengthen the reward system and weaken the control system even more. Second, risk assessment and fear of possible outcomes is faulty in that it under-evaluates risk factors such as "nothing bad will happen to me" or "I will not get caught by the police

Figure 2 depicts these interactions in addiction..

Figure 2: Interaction between the proposed factors which are mostly are involved in the initiation, progression and cessation of addiction

→ **Control Center** ←

↑ ↓ Weak or dysfunctional and exerting little control

↑

↑ ↓ ↑

Unsatisfied by natural stimuli

Demands to be satisfied ↑

↑ **REWARD CENTER** →

Requires artificial stimuli like drugs ↑

↑

↑ ↑ ↑ ↑

↑ **Memory Center** →← **Risk Assessment Center** →

Provides memories of discomfort

Provides memories of previous "Highs"

Risk assessment is weak or faulty underestimating the dangers of personal or legal implications of illegal drug use

4) Establishment of a Semi-quantitative Hypothesis of Addiction

There are already a number of addiction scales and assessments available like the Michigan alcohol screening test, drug abuse screening test or the Yale food addiction scale. While these scales are quite helpful, they usually only asked general questions like "have you abused drugs" or "have you lost a job because of drug abuse". Some – like the Kimberly internet addiction scale – assign numerical values and then offer a prediction. However, they all seem to be more concerned with the general question – are you or are you not addicted. These are mostly global questions without any indication which of the above traits is responsible to become or not become addicted.

There are also studies available which have linked individual traits or specific brain activities to risks, maintenance and relapse of addiction. However, a risk for or a disease is not diagnosed by one symptom or sign alone but by a combination of many.

Thus, assuming that addiction is a multi-phased disease and that more than one trait contributes to its pathogenesis, we posit to bundle the four above mentioned major traits and their neural bases. The more factors which can be included the better will be the prognosis, diagnosis and treatment. It is further proposed to first assign a number to each trait from 1 to 10 obtained from selective psychometric tests or personal assessments. Then all numbers of the four traits should be added and the sum should be a better indicator to predict or assess an addiction.

This would lead to the following equation:

$$R + C + M + F = \textit{Expected decisions and behavior}$$

Gratification of reward center (R) - fully satisfied, no discomfort = 10 to unsatisfied, lots of

discomfort = 1
Control of reward center (C) - strong control = 10 to weak control = 1
Memories of drug experiences (M) - many good memories = -10 to no, few good memories = - 1
Risk assessment, fear (F) - strong risk assessment, high fear = 10 to weak risk

assessment, low fear = 1

Two examples demonstrate the use and its prediction based on hypothetical numbers:

A well satisfied reward center (e.g. 10) with strong control (e.g.9), no or little drug memories (e.g. -1) and moderate risk assessment (e.g.5) could be, for instance, written as

$$10 + 9 - 1 + 5 = \mathbf{23}$$

In contrast, a partially unfulfilled reward center (e.g. 3), a moderately active control (e.g. 5), many good drug related memories (e.g. -8) and moderate risk assessment (e.g. 5) could be, for instance, written as

$$10 + 9 - 1 + 5 = \mathbf{23}$$

In contrast, a partially unfulfilled reward center (e.g. 3), a moderately active control (e.g. 5), many good drug related memories (e.g. -8) and moderate risk assessment (e.g. 5) could be, for instance, written as

$$3 + 5 - 8 + 5 = \mathbf{5}$$

Thus, a high value would predict a healthy life style. A low value would predict poor and faulty decision making and a behavior with a troubled life style and many negative consequences. While the sums differ by a factor of about 4 to 5, individual trait differences differ much less or can sometimes even be equal.

While it is recognized that assigning numerical values to a trait is quite difficult, psychologists, however, already are doing it by assigning values and numbers in their studies to a particular trait or traits. For instance, if psychologists compare a particular trait between two groups of test individuals, they assign numbers to this trait which are then subjected to statistical analyses. Thus, a numbering system could also be devised for the four traits by researchers specializing in psychometrics.

The following example demonstrates how 3 of the above traits, for instance, can be and have been compared and actually numbered. This example involves the marshmallow test (Mischel, 2014). In this paradigm, a child placed in an empty room on a chair in front of a table with one marshmallow is given two choices: do not eat the marshmallow when I leave and you will get a second marshmallow when I return or to eat the marshmallow but you will then not get a second one. The results apparently depended on how strong the desire was to experience the happiness of eating the marshmallow and how well it was inhibited by the self-control of each individual child. As expected, some children ate the treat quickly while others waited until the experimenter returned. The balance of the reward and control center at an early age can actually predict troubled and addictive behavior later on. A follow-up of children who had taken the marshmallow test showed 40 years later that children with more self-control had a better health profile as adults, were more successful and more prosperous while children with low self-control showed a higher association with getting into trouble with the law and, for this case, showed a higher degree of addiction (Mischel, 2014, Moffitt et al., 2011). However, imaging studies also showed that the prefrontal cortex was more active in high delayers when they were trying to control their responses to alluring temptations (Casey et al., 2011, Mischel, 2014).

The Marshmallow test can also be used to show the influence of memories of past experiences on the interaction between the reward and control center. Here, children were also told that the experimenter would shortly return with a set of crayons and paper to help them bridge the time. In the first group, the experimenter returned with the promised crayons while in another group children were told that they had just run out of crayons. The waiting time in the first group was four times longer than in the second group. The “bad” experience with the crayons influenced the decision to eat the marshmallow since subjects believed that there might not be a second marshmallow (Kidd et al., 2013, Mischel, 2014).

The beauty of this test is not only that it demonstrates the interaction of these 3 parameters (risk assessment has not been done in this test to the best of the author’s knowledge but could easily be incorporated by telling the children if they eat the marshmallow they will get some sort of punishment) but also that the test gives us actual numbers – namely minutes. These minutes can be plugged into the above equation and this will result in a sum which will be a better predictor – in this case – of future choices involving drugs and becoming a person with addiction – then an individual trait alone.

5) Prediction and Therapy of Addiction

The above equation can now be applied to predict an individual’s risk of becoming addicted, to assess the main causative components of an existing addiction and to specifically treat an existing addiction.

Assessment of traits contributions

There are already a number of addiction scales and assessments available like the Michigan alcohol screening test, drug abuse screening test or the Yale food addiction scale. While these scales are quite helpful, they usually only asked general questions like “have you abused drugs” or “have you lost a job because of drug abuse”. Thus, they do not give any information as to the contributing traits which might cause the addiction.

The author is not a psychiatrist or psychologist and is only vaguely familiar with psychometric testing. Thus, the following are only suggestions. The four individual traits can be evaluated through personal interviews or appropriate psychometric tests which are already available or can be devised in the future. For instance, gratification or reward intensity can be measured, for instance, using the delay of gratification test either for children or adults or the sensitivity to punishment and to reward questionnaire. Self control can be assessed by various self control tests like the self-control questionnaire.

Memory tests should be applied to test for the presence of hedonic and anhedonic memories. Risk assessment can be evaluated by risk assessment questionnaires or the sensation seeking test (Forstmeier et al., 2011, Connor et al., 2011, Smith, 2010, Neal and Carey 2005, Zuckerman et al.1978). Psychologists can also develop one scale which incorporates one test including all of the four above mentioned traits.

Prediction of risk to develop an addiction

Below are 2 hypothetical examples which hopefully will demonstrate the power of assigning values to each trait and then adding up these numbers to arrive at a sum which is more powerful then the individual trait numbers in predicting risk factors in a person for addiction. Again, numbers are hypothetical and not based on actual tests.

1) Individual A, 16 yrs, is an apprentice to a plumber who loves his job, has a good family life and loves to play lots of basketball (Reward center is fully satisfied and does not demand action or 10). He is always punctual at his appointments, completes his jobs on time and keeps his weight down (Control center very strong or 10). He has some beers and enjoys the taste and their effects but does not get drunk (Memories or -3). He, however, enjoys parachuting (Fear is low or 3) :

10 + 10 --3 + 3 = 20 (Not at risk for addictive behavior but might enjoy some alcohol socially)

2) Individual B, 21yrs, is a college student in relatively good standing. She enjoys college work but is not overly enthusiastic about it (Reward center only partially satisfied or 5). She has trouble being on time or to complete her assignments as asked (Control center weak or 3). She likes to drink beer and smokes once in while (Memories of enjoyment of beer and smoking or -7). She has 2 speeding violations and likes mountain climbing (Fear is low or 3)

5 + 3- 7 + 3 = 4 (she is at risk of developing addictive behaviors)

Again, the sum is a better predictor differing by a factor of 5 while individual traits are less different and sometimes might even overlap. An assessment of all 4 risk factors might allow now to identify those individuals who are at risk of sliding into an addiction and provide health professionals to intervene at an earlier time

While this paper was being prepared, a report about prediction of risk for bipolar depression was published. The authors followed the same thinking as the author of this paper. They studied a group of parents with bipolar depression and evaluated their anxiety, manic symptoms, depressive symptoms, mood lability, poor general social functioning and parental age. They assigned a value to each and then bundled all the data and developed a risk calculator for their children to also become bipolar. This risk calculator was able to differentiate quite accurately between children who showed signs of bipolar depression versus those who remained healthy. This calculator now allows health professionals to indentify children at risk and start intervention early in life (Hafeman et al, 2017).

Using the marshmallow test and combining measurements of all four traits should, for instance, provide a good measure of future risk of developing addictive behavior.

A more specific and directed therapy of addiction

Therapeutic strategies to treat an addict would follow similar lines in identifying the most important factor or factors which contribute mostly to the addictive behavior and then specifically trying to treat these factors. The following offers some suggestions but is not a comprehensive list.

First, the reward system is most likely a major cause of initiation and maintenance of drug use and abuse. Here, the reward center is not fully satisfied and people with addiction will use drugs for their hedonic or pleasurable effects or to counteract any anhedonia and to give them a “high” or make them feel “good”. Thus, treatment of an unsatisfied reward system or existing discomfort is both exceedingly important. Social intervention can channel an individual’s activity into more pleasant activities like new friends, sports or physical activities, hobbies, yoga or a new environment. In particular increased physical activity seems quite promising. In the above mentioned marshmallow test it was observed that children who would wander around the room or would play with toys were more successful in completing the test as compared with children who just sat in front of the table doing nothing (Mischel, 2014). Cognitive behavioral therapy tries to help by making such individuals see the more positive aspects of life. Pharmacotherapy should be directed to satisfy the reward system in other ways or to reduce its activity. For instance, nicotine replacement or verenicline are used to stimulate neuronal nicotine receptors and perhaps replace the stimulation obtained from nicotine obtained by smoking. Recently, ibogaine has been claimed to reduce the activity of the reward center and to help some people with addiction to reduce their cravings but the drug is illegal in the USA and carries a high risk of death and/or brain damage (Brown 2013). Efforts are underway currently to synthesize related drugs which are still effective but less toxic. Other drugs like antidepressants can be used which seem to have a weak effect on the reward system. There is accumulating evidence that Transcranial Magnetic Stimulation could reduce craving for various psychoactive drugs such as alcohol, nicotine and cocaine and might represent a potential therapeutic tool for treating addiction (Martinez and Trifilieff 2015, Gorlick et al., 2014). .In severe cases, deep brain stimulation of the nucleus accumbens has been shown to alleviate anhedonia in depression, which is also a driven force in drug addiction and it might prove to be beneficial here as well (Sclaepfer et al., 2008, Muente et al, 2013).

In case of a weak prefrontal cortex, its activity seen as “willpower” has to be improved (Cummins 2013). People with addiction often want to quit but lack the “willpower” to do so. Here, the individual has to be instructed to improve its “willpower” but also to use it carefully and not to use it for minor decisions but to save it for major decisions since “willpower” can be easily depleted. It is often suggested that the individual should plan ahead in order to avoid (the AA/NA adage of avoidance people, places and things) situations where his or her will power may fail. Various behavioral therapies such as Cognitive Behavioral Therapy, Contingency Management Intervention, Community Reinforcement Approach, Implementation Intention Therapy and the 12 Step Facilitation Therapy can help and have shown beneficial results. These therapies try to increase self control by strengthening good intentions (Walters, 2000). In addition, studies using the marshmallow test have shown that children raised by mothers to be more independent and to express what they want to do did much worse on this test than children who were raised by more authoritarian mothers and who were told what to do (Ayduk, 2017). This finding might not only help to increase "willpower" from childhood on but might also show that patients with addiction should be exposed to a more authoritarian therapeutic approach. There is no known specific pharmacotherapy to stimulate the executive center and treatment still has to rely on the accepted drugs for various addictive problems. Cranial electrical stimulation of the prefrontal cortex has been shown to reduce alcohol intake significantly in people with alcohol problems (Martinez and Trifilieff, 2015).

Memories play an important part in the initiation, progression and relapse in addiction. Thus, erasing unwanted memories would be important if these are main contributors to the problem. Memories can be erased in animals by chemically modifying the brain of mice or rats either by using xenon gas or blebbistatin with the latter selectively erasing dangerous addiction-associated memories. Such avenues could be eventually developed into a useable therapy for humans (Young et al., 2017). At present, Cognitive Behavioral Therapy could be used to modulate unwanted memories and the use of anti-anxiety drugs before therapy has been shown to be beneficial in PTSD and should prove to be helpful in addiction as well. A new technique called Memory Reconsolidation weakens memories and this technique would help to erase memories which might contribute to the maintenance of addiction or its relapse after abstinence (Quirk, 2010, Klemm, 2012). Again, no specific drug therapy to increase wanted or depress unwanted memories is available.

If the activity of the amygdala and its fear and risk assessing features are insufficient, they need to be strengthened. While it has been shown that fear evoking strategies to prevent drug abuse usually do not work well in young individuals, in older individuals the threat, for instance, of developing lung cancer in smoking adults has had some success (Graham et al., 2016). While cognitive behavioral strategies are often employed to decrease fear in general they could be adjusted to also increase fear of the negative consequences of addiction (Nebhinani et al., 2012). The author is not aware of any pharmacotherapy which could be employed.

Thus, the main therapy has to be applied to one or more of the psychological factors or brain areas which are the main contributor to the problem. If the reward center is hyperactive, for instance, requiring constant satisfaction and the self control center already works at full capacity, then any therapy geared to strengthen the control center alone will not produce therapeutic effects but the main efforts must be directed to satisfy the reward system in ways other than the use of drugs.

Acknowledgements

The author wishes to acknowledge the helpful suggestions and the critical review of this paper by Stephen Weinstein and Robert Sterling both from the Department of Psychiatry and Human Behavior, Jefferson Medical College of Thomas Jefferson University, Philadelphia, PA.

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References

B.Adinoff H. Gu, H, C. Merrick, M. McHugh, H. Jeon-Slaughter4, H. Lu , Y. Yang, E. A. Stein. Basal Hippocampal Activity and Its Functional Connectivity Predicts Cocaine Relapse. Biological Psychiatry. 1;78(7) (2015) pp.496-504.

O. Ayduk. African farmer's kids ace the willpower test. www.sciencenews.org (2017) August 5,.

M Balconi and R Finocchiaro.Left Hemispheric "Imbalance" in Drug Addiction Neuropathology of Drug Addictions and Substance Misuse, edit V. R. Preedy Elsevier Inc (2016) pp.229-238

K.Bolla, M.Ernst, ; K Kiehl, M .Mouratidis, M. D.Eldreth, C.Contoreggi, E. London Prefrontal Cortical Dysfunction in Abstinent Cocaine Abusers. The Journal of Neuropsychiatry and Clinical Neurosciences. 16 (4) (2004) pp. 456–464. .

Bozart 1994 M.A. Bozarth Pleasure systems in the brain. In D.M. Warburton (ed.), Pleasure: The politics and the reality. New York: John Wiley & Sons. (1994) pp. 5-14

T.K. Brown.Ibogaine in the treatment of substance dependence. Current Drug Abuse Review 6(1) (2013) pp. 3-16

S. Carpenter.Cognition is central to drug addiction American Psychological Association 32 (2001) http://www.apa.org/monitor/jun01/cogcentral.aspx

B.J. *Casey, L H. Somerville, I. A. Gotlib, O Ayduk, N. T. Franklin, M.K. Askren, M K.; J. Jonides, M. G. Berman, N. L. Wilson, T.Teslovich, G. Glover, V. Zayas, W.* Mischel, *Y.* Shoda *Behavioral and neural correlatesof delay of gratification 40 years later* Proceedings of the National Academy of Sciences. *108 (36) (2011) pp. 14998–15003.*

R. A. Chambers, T. J. Sajdyk, S, K. Conroy, J. E. Lafuze, S.D. Fitz, A. Shekhar Neonatal Amygdala Lesions: Co-Occurring Impact on Social/Fear-Related Behavior and Cocaine Sensitization in Adult Rats Behavioral Neuroscience. 121(6) (2007) pp 1316–1327.

B Chen, A Bonci, Prefrontal Cortex Stimulation Stops Compulsive Drug Seeking in Rats NIDA NOTES January 06, 2014

R. M. O'Connor, C. R. Colder , L.W. Hawk Jr. Confirmatory factor analysis of the Sensitivity to Punishment and Sensitivity to Reward Questionnaire Personality and Individual Differences (37) (5) (2004) pp. 985–1002

K.P. Conway, J. D. Swendsen, B.J.Rounsaville, K. R.Merikangas Personality, drug of choice, and comorbid psychopathology among substance abusers. Drug Alcohol Dependence. 65(3) (2002) pp :225-34.

C A. Cordovaa, D. Jackson K. D. Langdon, K A. Hewlett, D Corbett. Impaired executive function following ischemic stroke in the rat medial prefrontal cortex Behavioural Brain Research 258 (2014) pp 106–111

S. M. Courtney, L. Petit, J. V. Haxby, L. G. Ungerleider. The role of prefrontal cortex in working memory: examining the contents of consciousness. Philosophical Transactions Royal Society Lond B Biological Sciences 29; 353(1377) (1998) pp 1819–1828.

A qualitative and semi-quantitative combined theory of addiction

H.S. Crombag, J. M. Bossert, E. Koya, Y. Shaham.Context-induced relapse to drug seeking: a review Philosophical Transactions. Royal Society B 363 (2008) 3233–3243

D. Cummins. How to Boost Your Willpower Psychology Today June 2013 https://www.psychologytoday.com/blog/good-thinking/201306/how-boost-your-willpower

J.M. R. Delgado. PHYSICAL CONTROL OF THE MIND- Toward a Psychocivilized Society. http://www.wireheading.com/delgado/index.html

B. De Martino. Brain location for fear of losing money pinpointed -- the amygdala Science News February 9 2005 https://www.sciencedaily.com/releases/2010/02/100208154645.htm

G. Di Chiara, V. Bassareo, S. Fenu, M.A. De Luca , L. Spina , C. Cadoni , E.Acquas , E. Carboni , V. Valentini, D. Lecca. Dopamine and drug addiction: the nucleus accumbens shell connection. Neuropharmacology 47 Suppl 1, (2004) pp. 227-41.

G. *Deneau, T.Yanagita M.H. Seevers .Self-administration of psychoactive substances by the monkey. Psychopharmacology. 16 (1) (1969) pp. 30–48.*

A. Duckworth , M. Seligman, Self-discipline outdoes IQ in predicting academic performance in adolescents. Psychological Science, 16, (2005) pp. 939-944.

S. Dwyer. Brain Stimulation Shows Promise in Curing Bulimia https://www.thefix.com/content/brain-stimulation-shows-promise-curing-bulimia.

S.P Edwards. The Amygdala: The Body's Alarm Circuit http://www.dana.org/Publications/Brainwork/Details.aspx?id=43615

K. Ersche. Brain Reward System May be Linked to Cocaine Addiction http://www.goodtherapy.org/blog/brain-reward-system-cocaine-addiction/

A. Fell. Memory replay prioritizes high-reward memories https://www.ucdavis.edu/news/memory-replay-prioritizes-high-reward-memories/

T.N. Ferraro, G.T. Golden, W.H. Berrettini, E. Gottheil, C.H. Yang, G.R. Cuppels and W.H. Vogel: Cocaine Intake by Rats Correlates with Cocaine-Induced Dopamine Changes in the Nucleus Accumbens. Pharmacology Biochemistry & Behavior, 66, 397-401, 2000.

A.A. Fingelkurts, R.Kivisaari, T.Autti, S.Borisov, V.Puuskari,O. Jokela, S.Kähkönen Increased local and decreased remote functional connectivity at EEG alpha and beta frequency bands in opioid-dependent patients. Psychopharmacology (Berlin).188(1),(2006) pp.42-52.

F.Fregni, F Orsati, W. Pedrosa S..Fecteau, F A.M. Tome, M A. Nitsche, T Mecca, E C. Macedo , A. Pascual-Leone, P. S. Boggio. Transcranial direct current stimulation of the prefrontal cortex modulates the desire for specific foods Appetite 1,2008 (2008) pp. 34–41

S. Forstmeyer, R. Drobetz, A. Maerker. The delay of gratification test for adults: Validating a behavioral measure of self-motivation in a sample of older people http://citeweb.info/20110498413

A. L. Gold, R.A. Morey, G. McCarthy. Amygdala–Prefrontal Cortex Functional

Connectivity During Threat-Induced Anxiety and Goal Distraction Biological Psychiatry. 77(4) (2015) pp. 394–403.

D.A. Gorelick, A.Zangen, M.S George. Transcranial magnetic stimulation in the treatment of substance addiction. Annals New York Academy of Science 1327(2014) pp:79-93.

J.M. Funahashi. J.M.J. Andreau . . Prefrontal cortex and neural mechanisms of executive function. .Journal of Physiology (Paris). 107(6) (2013) pp. 471-82.

, R.Z.Goldstein and N.D. Volkow. Dysfunction of the prefrontal cortex in addiction: neuroimaging findings and clinical implications. National Review of Neuroscience 12(11) (2011), pp.:652-69.

A. L Graham, K.M. Carpenter, S. Cha, S. Cole, M.A. Jacobs, M. Raskob, H. Cole-Lewis Systematic review and meta-analysis of Internet interventions for smoking cessation among adults Substance Abuse and Rehabilitation Substance Abuse and Rehabilitation 18(7) (2016) pp55-69

D M Hafeman, J. Meranko, TR Goldstein, et al. Assessment of a person-level risk calculator to predict new-onset bipolar spectrum disorder in youths at family risk. JAMA Psychiatry, published online July5, 2017)

R. Hansen, K.Ochsner, Y. Trope. Self-control in society, mind and brain, Oxford Press, (2010)

M. Huston Does Self-Control Have a Limit? https://www.psychologytoday.com/articles/201509/does-self-control-have-limit

M. E. Jackson, B. Moghaddam .Amygdala Regulation of Nucleus Accumbens Dopamine Output is Governed by the Prefrontal Cortex Journal of Neuroscience 21 (2) (2001) pp 676-681

J. L. Rogers and R. E. See. Selective inactivation of the ventral hippocampus attenuates cue-induced and cocaine-primed reinstatement of drug-seeking in rats Neurobiology Learning Memory 87(4) (2007) pp.: 688–692.

Quirk, 2010, G. J. Quirk, D. Paré, R. Richardson, C. Herry, M. H. Monfils, D. Schiller, A. Vicentic. Erasing fear memories with extinction training Journal of Neuroscience. 30(45) (2010) pp: 14993–14997.

Kidd et al. 2013 C Kidd; H. Palmeri, R.N. Aslin. Rational snacking: Young children's decision-making on the marshmallow task is moderated by beliefs about environmental reliability. *Cognition. 126 (1) (2013) pp: 109–114*

C.D.Kilts. Imaging the roles of the amygdala in drug addiction Psychopharmacological Bulletin 35(1) (2001)84-94.

W.R. Klemm. Therapy Erases Bad Memories Psychology Today October 7 2012 https://www.psychologytoday.com/blog/memory-medic/201210/behavioral-therapy-erases-bad-memories

D. Knoch L.R. Gianotti, A. Pascual-Leone, V. Treyer M. Regard M.Hohmann, P. Brugger
Disruption of right prefrontal cortex by low-frequency repetitive transcranial magnetic stimulation induces risk-taking behavior. Journal of Neuroscience 14;26(24) (2006) pp.6469-6472.

P. Lang, M. Davis, A. Ohman, A. Fear and anxiety: animal models and human cognitive psychophysiology. Journal of Affective Disorders, 61,(2000) pp137-159

G. Laviola, W. Adriano, M.L Terranova, G. Gerra. Psychobiological risk factors for vulnerability to psychostimulants in human adolescents and animal models Neuroscience, Biobehavioral Reviews 23(7) (1999) pp. 993-1010.

J. Lowinson, P. Ruiz,; R. Millman, J. Langrod, Neuroanatomy and Physiology of the “Brain Reward System” in Substance Abuse
Substance Abuse: A comprehensive Textbook 3rd Edition. Williams & Wilkens

F. Manes, B. Sahakian, L. Clark R., Rogers, N. Antoun, M. Aitken, T. Robbins.
Decision-making processes following damage to the prefrontal cortex
Brain 125(3) (2002) pp 624-639

Martinez and Trifilieff. Stimulation as a Potential Treatment for Addiction http://www.asam.org/magazine/read/article/2015/08/14/brain-stimulation-as-a-potential-treatment-for-addiction

S. Mcintosh, S.E. Hemby. Dopaminergic Dysregulation in Prefrontal Cortex of Rhesus Monkeys Following Cocaine Self-Administration Frontiers in Psychiatry 4 (2013) pp. 88-102

N. L Mead, R.F. Baumeister, F. Gino, M.E. Schweitzer, D.Ariely. Too Tired to Tell the Truth: Self-Control Resource Depletion and Dishonesty. Journal Experimental Social Psychology . 45(3) (2009) pp.594-597.

E.Metcalf. Pain Medication: Are You Addicted? WebMD June 19,2012 http://www.webmd.com/pain-management/features/pain-medication-addiction#1

W. Mischel. The Marshmallow Test: Mastering Self-Control Published September 23rd by Little, Brown and Company (2014)

C,E. Moan, R.G. Heath . Septal stimulation for the initiation of heterosexual activity in a homosexual male. Journal of Behavior Therapy and Experimental Psychiatry, 3, (1972) pp.23-30
.
T. E. Moffitt, L. Arseneault, D. Belsky, N. Dickson, R. J. Hancox, H. Harrington, R. Houts, R. Poulton, B. W. Roberts, S. Ross, M’;R. Sears, W. M. Thomson, A. Caspi. A gradient of childhood self-control predicts health, wealth, and public safety. Proceedings of the National Academy of Sciences, 108, (2011) pp. 2693-2698

T.F.Muente, H.J.Heinze, V. Visser-Vandewalle. Deep brain stimulation as a therapy for alcohol addiction. Current Topics in Behavioral Neuroscience 13 (2013) pp.709-27.

R. Nauert. Decision-Making Improves with Age, Experience Psychiatry Central August 23, 2011 http://psychcentral.com/news/2011/08/24/decision-making-improves-with-age-experience/28884.html

D.J.Neal, K.B. Carey, A follow-up psychometric analysis of the self-regulation questionnaire. Psychology of Addictive Behaviors 19(4) (2005) pp. 414-422.

N.Nebhinani , S.Sarkar, S.Ghai, D.Basu. Reasons for help-seeking and associated fears in subjects with substance dependence. Indian Journal of Psychological Medicine 34(2) (2012) pp:153-8.

A qualitative and semi-quantitative combined theory of addiction

J. Olds, P. Milner. Positive reinforcement produced by electrical stimulation of septal area and other regions of rat brain. Journal of Comparative and Physiological Psychology. 47(6), (1954) pp.419-27.

H.Oshima and Y Katayama. Neuroethics of deep brain stimulation for mental disorders: brain stimulation reward in humans. Neurology Medicine Chirurica (Tokyo). 50(9) (2010) pp.845-52.

A. R. Preston H. Eichenbaum. Interplay of Hippocampus and Prefrontal Cortex in Memory Current Biology 23 (17) (2013) pp 764-773

D. Purves, G. J Augustine, D.Fitzpatrick, L. C Katz, A-S LaMantia, J O McNamara, S M Williams edts . The Importance of the Amygdala Neuroscience, 2nd edition,(2001)

D.C.Roberts , R.Phelan, L.M. Hodges, M.M.Hodges, B. Bennett, S. Childers H. Davies
Self-administration of cocaine analogs by rats Psychopharmacology (Berl). 144(4) (1999) pp.389-397

J. J. Rolison1 Y. Hanoch, S. Wood, P.-J. Liu. Risk-Taking Differences Across the Adult Life Span: A Question of Age and Domain Journal of Gerontology (10) (2013) pp 23-36

E.T. Rolls, M.J. Burton, F. Mora. Neurophysiological analysis of brain-stimulation: reward in the monkey. Brain Research 194 (2} (1980), pp. 339–357

T.E.Schlaepfer, M.X. Cohen, C. Frick, M. Kosel, D.Brodesser, N. Axmacher, A.Y.Joe, M.Kreft, D. Lenartz, V., Sturm. Deep brain stimulation to reward circuitry alleviates anhedonia in refractory major depression. Neuropsychopharmacology. 33(2) (2008), pp.368-377

M.E.P Seligman, E.Royzman. Authentic Happiness https://www.authentichappiness.sas.upenn.edu/newsletters/authentichappiness/happiness

, B. Sonnenschein, K. Conover, P. Peter. Growth of Brain Stimulation Reward as a Function of Duration ans Stimulation Strength. Behavioral Neuroscience. 117(5),(2003), pp. 978-994

J. Smith. Willpower and Self-Control: Do You Need to Improve Your Self-Discipline? Psychologia http://psychologia.co/willpower-and-self-control-test/

S,D.Spragg. Morphine addiction in chimpanzees. Comparative Psychology Monographs. 15 (7) (1940) pp. 1–132.

L Squire, D. Berg, F.E. Bloom, S. du Lac, A. Ghosh, N. C. Spitzer, L. R. Squire, Fundamentals of Neuroscience, 3rd edition, Elsevier Publisher (2012) – Addiction, pp.999 -1031, 2012

J. Stewart, M. Paulus.Brain imaging predicts relapse to cocaine addiction NIDANotes September 14, 2015

J.L. Stewart, C.G. Connolly, A. C. May, S. F. Tapert, M. Wittmann, M. P. Paulus
Cocaine dependent individuals with attenuated striatal activation during reinforcement learning are more susceptible to relapse Psychiatry Res. 223(2) (2014) pp. 129–139.

S.T. Sweat . How the brain remembers pleasure: Implications for addiction Science News August 25, 2013 https://www.sciencedaily.com/releases/2013/08/130825171530.htm

G.D. Walters. Behavioral self-control training for problem drinkers: A meta-analysis of randomized control studies. Behavioral Therapy 31 (2000) pp.135-149.

E.J.Young, S.B. Briggs, G.Rumbaugh, C.A.Mille. Nonmuscle myosin II inhibition disrupts methamphetamine-associated memory in females and adolescents. Neurobiology of Learning and Memeory 7 (2017) pp: S1074-7427

Zalta Pleasure *The Stanford Encyclopedia of Philosophy* ttp://plato.stanford.edu/entries/pleasure/ *Fri Jun 17, 2016*

M. Zuckerman, S.B.J. Eysenck, H.J. Eysenck. Sensation seeking in England and America: Cross-cultural, age, and sex comparisons. Journal of Consulting and Clinical Psychology, 46(1) (1978) pp 139-149.