Loss of Willpower: Abnormal Neural Mechanisms of Impulse Control and Decision-Making in Addiction

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Abstract

Addiction is a condition in which the person becomes unable to choose according to long-term outcomes when it comes to drugs. I will argue that this is the product of an imbalance between two separate, but interacting, neural systems: 1) an *impulsive, amygdala-dependent,* system for signaling the pain or pleasure of *immediate* prospects, and 2) a *reflective, orbitofrontal-dependent,* system for signaling the prospects of the *future*. The conditions that lead to this imbalance include (1) a dysfunctional reflective system, and (2) a hyperactive impulsive system. In other words, drugs can acquire properties of triggering bottom-up, involuntary signals through the amygdala that modulate, bias, or even "hijack", top-down goal-driven attentional resources needed for the normal operation of the reflective system and exercising the will.

Keywords: willpower, addiction, prefrontal cortex, amygdala, somatic markers.

Imagine yourself at a party during your first year in college, and you see your friends drinking, using drugs, and engaged in sexual activities. In the back of your mind, you hear the voice of your parents, warning you and asking you not to engage in such activities. What would you do? This is a hard decision, but you are the one who will ultimately decide, with a clear sense of deciding and exercising free will.

Willpower, as defined by the Encarta® World English Dictionary is a combination of determination and self-discipline that enables somebody to do something despite the difficulties involved. This is the mechanism that enables one to endure sacrifices now in order to obtain benefits later. Otherwise, how would one accept the pain of surgery? Why would someone resist the temptation to have something so irresistible, or delay the gratification from something that is so appealing? We will argue that these complex and apparently indeterminist behaviors are the product of a complex cognitive process subserved by two separate, but interacting, neural systems: 1) an *impulsive*, amygdala-dependent, neural system for signaling the pain or pleasure of the *immediate* prospects of an option, and 2) a *reflective*, prefrontal-dependent, neural system for signaling the pain or pleasure of the *future* prospects of an option. The final decision is determined by the relative strengths of the pain or pleasure signals associated with immediate or future prospects. When the immediate prospect is unpleasant, but the future is more pleasant, then the positive signal of future prospects forms the

basis for enduring the unpleasantness of immediate prospects. This also occurs when the future prospect is even more pleasant than the immediate one. Otherwise, the immediate prospects predominate, and decisions shift towards short-term horizons. As suggested by Damasio (Damasio, 1994): “willpower is just another name for the idea of choosing according to long-term outcomes rather than short-term ones”.

We have used the term “*somatic*” (Damasio, 1994) to refer to the collection of body-related responses that hallmark these affective and emotional responses. Somatic refers to the Greek word “soma”, i.e., body. Although during the process of weighing somatic (affective) responses, the immediate and future prospects of an option may trigger numerous somatic responses that conflict with each other, the end result is that an overall positive or negative somatic state emerges. We have proposed that the mechanisms that determine the nature of this overall somatic state (i.e., being positive or negative) are consistent with the principles of natural selection, i.e., survival of the fittest (Bechara & Damasio, 2004). In other words, numerous and often conflicting somatic states may be triggered at the same time, but stronger ones gain selective advantage over weaker ones. With each “thought” brought to working memory, the strength of the somatic state triggered by that “thought” determines whether the same “thought” is likely to recur (i.e., will be brought back to memory so that it triggers another somatic state that reinforces the previous one), or whether that “thought” is likely

to be eliminated. Thus over the course of pondering a decision, positive and negative somatic markers that are strong are reinforced, while weak ones are eliminated. This process of elimination can be very fast. Ultimately, a winner takes all; an overall, more dominant, somatic state emerges (a “gut feeling” or “a hunch” so to speak), which then provides signals to the telencephalon that modulate activity in neural structures involved in biasing decisions **(Figure 1)**. This “winner takes all” view is consistent with the conception of Strack and Deutsch on competition between motor schemata (Strack & Deutsch, 2004) (Deutsch and Strack, Chapter 4).

FIGURE 1 TO APPEAR ABOUT HERE

Addiction is a condition in which the person becomes unable to choose according to long-term outcomes. Choosing according to long-term outcomes rather than short-term ones requires that the pain or pleasure signals triggered by the reflective system dominate those triggered by the impulsive system. Two broad types of conditions could alter this relationship and lead to loss of willpower: (1) a dysfunctional reflective system, which has lost its ability to process and trigger somatic signals associated with future prospects; and (2) a hyperactive impulsive system, which exaggerates the somatic signals from immediate prospects. When drug cues acquire properties for triggering bottom-up, automatic, and involuntary somatic states through the amygdala, this bottom-up

somatic bias can modulate top-down cognitive mechanisms, in which the prefrontal cortex is a critical substrate. If strong enough, this bottom-up influence can interfere or "hijack" the top-down cognitive mechanisms necessary for triggering somatic states about future outcomes.

A Somatic Marker Model of Drug Addiction

The somatic marker framework provides a systems-level neuroanatomical and cognitive framework for decision-making, and for choosing according to long-term outcomes rather than short-term ones, and it suggests that the process of decision-making depends in many important ways on neural substrates that regulate homeostasis, emotion, and feeling (Damasio, 1994).

1. Induction of somatic states: Somatic states can be induced from (1) primary inducers, and (2) secondary inducers (Damasio, 1995). *Primary inducers* are innate or learned stimuli that cause pleasurable or aversive states. Once present in the immediate environment, they automatically and obligatorily elicit a somatic response. The actual encounter of a drug by an addicted individual is an example of primary inducers (Bechara et al., 2003). It is important to note that unlike stimuli such as food and sex, the sensations stimulated by drugs are not innately pleasant. However, through learning, drugs acquire properties that are characteristics of a "primary inducer". The process by which a foreign substance,

such as a drug, acquires these primary inducer properties, i.e., a capacity to trigger somatic states automatically and obligatorily like food and sex, is beyond the scope of this discussion.

Secondary inducers, on the other hand, are entities generated by the recall of a personal or hypothetical emotional event, i.e., "thoughts" and "memories" of the primary inducer, which elicit a somatic response. The recall or imagination of a drug experience by an addicted individual is one example of secondary inducers (Bechara et al., 2003).

We have argued that the amygdala is a critical substrate in the neural system necessary for triggering somatic states from primary inducers. It couples the features of primary inducers with the somatic state associated with the inducer. This somatic state is evoked via effector structures such as the hypothalamus and autonomic brainstem nuclei that produce changes in internal milieu and visceral structures along with other effector structures such as the ventral striatum, periacqueductal gray (PAG), and other brainstem nuclei, which produce changes in facial expression and specific approach or withdrawal behaviors (Bechara et al., 2003). In the case of drugs, several lines of direct and indirect evidence support the view that addiction relates to abnormal activity in the amygdala-ventral striatum system, thereby resulting in exaggerated processing of the incentive values of substance-related stimuli (Everitt et al., 1999; Jentsch & Taylor, 1999). Alcoholics showed exaggerated autonomic responses to alcohol

cues (Glautier & Drummond, 1994), and so did cocaine addicts (Ehrman et al., 1992; O'Brien et al., 1992). Similarly, smokers showed exaggerated increase in heart rate to cues associated with smoking (Abrams et al., 1988). Functional neuroimaging studies have revealed increased amygdala activity in response to drug related cues (Grant et al., 1996). We have shown that individuals with alcohol and/or stimulant dependence showed exaggerated autonomic responses to reward in general, e.g., winning a large sum of play money during the Iowa gambling task (Bechara et al., 2002), autonomic responses that we have shown to be dependent on the integrity of the amygdala (Bechara et al., 1999).

Once somatic states from primary inducers are induced, signals from these somatic states are relayed to the brain. Signals from activated somatic states lead to the development of somatic state patterns in brainstem nuclei (e.g., the parabrachial nuclei (PBN)), and in somatosensing cortices (e.g., insular and somatosensory I and II cortices, and cingulate cortices). After a somatic state has been triggered by a primary inducer and experienced at least once, a pattern for this somatic state is formed. The subsequent presentation of a stimulus that evokes memories about a specific primary inducer will then operate as a secondary inducer. Secondary inducers are presumed to re-activate the pattern of somatic state belonging to a specific primary inducer. For example, recalling or imagining the experience of a drug re-activates the pattern of somatic state belonging to the actual previous encounter of that drug. However, the somatic

state generated by the recall or imagination of using a drug (secondary inducer) is usually fainter than one triggered by an actual use of that drug (primary inducer).

Provided that somatic state representations in somatosensing cortices develop normally, triggering somatic states from secondary inducers becomes dependent on cortical circuitry in which the ventromedial prefrontal cortex plays a critical role. The ventromedial prefrontal cortex (which includes the orbitofrontal region) is a trigger structure for somatic states from secondary inducers. It serves as a convergence-divergence zone, which neuron ensembles can couple (a) a certain category of event based on memory records in high order association cortices to (b) the effector structures that execute the somatic state (Bechara et al., 2003).

It is important to note that the anticipatory skin conductance responses acquired during the Iowa Gambling Task are examples of instances where the ventromedial prefrontal cortex couples knowledge of secondary inducer events to covert response effectors (Bechara et al., 1997). Pondering on which deck to choose from is a conscious process, which elicits a covert somatic response, regardless of how much factual knowledge the person has about the goodness or badness of the choices they are making. This covert somatic response is an expression of the *bias* process that leads the subject to choose the correct deck without necessarily knowing why they made that choice. Perhaps in the case of drugs, conscious deliberation on whether to use drugs in an addicted individual

may elicit covert somatic responses that implicitly *bias* cognition in such a way to propel the person to seek drugs, perhaps without much awareness of the choice being made.

2. Operation of somatic states: During the pondering of a decision, somatic states are triggered by primary (drug cues) or secondary inducers (thoughts about taking drugs). Once induced, they participate in two functions (**Figure 2**). (i) In one they provide a substrate for feeling the emotional state. (ii) In the other they provide a substrate for biasing decisions:

FIGURE 2 TO APPEAR ABOUT HERE

(i) Feeling the emotional state: The insular/ Somatosensory I and II cortices are necessary, although they may not be sufficient, for feelings of an emotion to occur (Damasio, 1995; Damasio, 1999). Evidence suggests that there may be two variant forms of feelings dependent on partially separate neural sectors. This evidence is derived from studies on pain showing dissociation between two sensory aspects of pain. One is related to feeling the pain itself, so called “pain sensation”, and the other is related to discomfort and the desire to avoid the pain, so called “pain affect” (Rainville et al., 1997). In the case of drugs, Berridge and Robinson (Berridge & Robinson, 1995, 1998) have proposed a model that

dissociates the “liking” from the “wanting” effects of drugs. The “liking” effects include feelings of pleasure and affective facial reactions during the pleasurable state. The “wanting” effects include the desire and urge to obtain the drug. We suggest that the insular/somatosensory cortices are necessary substrates for the feeling of euphoria (not action related). On the other hand the supracallosal sector of the anterior cingulate cortex is necessary for the feeling of craving (related to the action of seeking, obtaining, and consuming the drug). In support, studies have revealed changes in activity in the insular and somatosensory cortices in association with euphoric experience of acute doses of opiate and stimulant drugs (Breiter et al., 1997; London et al., 2000; Volkow & Fowler, 2000). Craving has also been linked to activity in the supracallosal sector of the anterior cingulate cortex in functional neuroimaging studies (Childress et al., 1999).

(ii) Biasing the decision to select a response: In order for somatic signals to influence cognition and behavior, they must act on appropriate neural systems:

One target for somatic state action is the striatum. Evidence suggests that in the striatum, the operation of somatic states is implicit, i.e., the subject learns to select a correct response, but without awareness of whether the response is correct. Studies of patients with Parkinson disease (PD), and patients whose brain damage involved both medial temporal lobes, a portion of the orbital prefrontal cortex and the anterior cingulate, but spared the striatum/ basal ganglia

completely, suggest that the striatum is both necessary (Knowlton et al., 1996) and sufficient (Tranel & Damasio, 1993) to modify behavior through the influence of somatic states at a covert (implicit) level. This supports the notion that this region plays a role in "knowledge without awareness". This is consistent with several investigations that suggested that the amygdala-ventral striatum system is important for drug stimulus-reward (incentive) learning (White, 1996), and the control of drug-related cues over behavior (Cador et al., 1989).

In the supracallosal sector of the anterior cingulate, and perhaps the adjacent supplementary motor area (SMA), the biasing mechanism of response selection is conscious or explicit, i.e., there is "action with awareness of what is right or wrong"; the decisions are "voluntary" or "willful", and guided by knowledge, awareness, and premeditation. Evidence shows that the anterior cingulate plays a role in the implementation of "voluntary" or "willful" decisions; decisions that are guided by "knowledge with awareness". Studies have shown that performance on target detection tasks and the Stroop interference task is associated with activity in the anterior cingulate (Pardo et al., 1990; Posner & Petersen, 1990; Posner et al., 1988). Another study (Frith et al., 1991) compared willed acts requiring explicit deliberate choice to automatic/ routine acts and detected significant increase in activity in the supracallosal anterior cingulate during the willed acts. These results suggest that the supracallosal anterior cingulate is involved in response selection when a wide range of novel choices is

required, and when the response selection is driven by conscious/ explicit knowledge.

There are other neural sites where ascending somatic signals exert influence on cognition. At the level of the lateral orbitofrontal and dorsolateral prefrontal region, the biasing mechanism of somatic states is explicit, but it is at the level of "thought" or "memory", and not behavioral action. In other words, as one is deliberating on several options and scenarios held in their working memory, the biasing effect of somatic states is to endorse some options and reject other ones, before any of these options are translated into actions.

Neural Mechanisms of Willpower

Based on the somatic marker framework, willpower (or lack of) emerges from the dynamic interaction between two separate, but interacting, neural systems: (1) an *impulsive* system that triggers somatic states from primary inducers, and (2) a *reflective* system that triggers somatic states from secondary inducers.

The reflective system controls the impulsive system via several mechanisms of impulse control. However, this control of the reflective system is not absolute: hyperactivity of the impulsive system can overwhelm or "hijack" the influence of the reflective system. This model is consistent with the Berridge and Robinson model (Berridge & Robinson, 1995, 1998) in that reward systems

(e.g., dopamine) become sensitized to the incentive effects of drugs, so that drug cues become capable of eliciting more intense "wanting" effects that override any conscious attempt by the reflective system to suppress or control that urge.

It is important to note that at the process level, the characteristics of the "impulsive" and "reflective" neural systems are similar to the two-system view of Kahneman and Tversky on "intuition" versus "reasoning" (Kahneman & Tversky, 1979), or that of Strack and Deutsch on reflective and impulsive determinants of social behavior (Strack & Deutsch, 2004) (Deutsch and Strack, Chapter 4). In all cases, the distinction is between the operations of one system that are typically fast, automatic, effortless, implicit, and habitual, and the operations of another system that are slow, deliberate, effortful, explicit, and rule governed. The distinct characteristic of our model is the assignment of neural substrates and physiological mechanisms for the operations of these systems.

More specifically, exposure to primary inducers (e.g., drugs) triggers fast, automatic, and obligatory somatic states via the amygdala system. Somatic states triggered by the amygdala are short lived and habituate very quickly (Buchel et al., 1998; Dolan et al., 1996; LaBar et al., 1998). Secondary inducers trigger somatic states via the ventromedial prefrontal cortex from perceived or recalled mental images. While the amygdala is engaged in emotional situations requiring a rapid response, i.e., "low-order" emotional reactions arising from relatively automatic processes (Berkowitz, 1993; LeDoux, 1996), the ventromedial

prefrontal cortex is engaged in emotional situations driven by thoughts and reflection. Once this initial amygdala emotional response is over, “high-order” emotional reactions begin to arise from relatively more controlled, higher order processes involved in thinking, reasoning, and consciousness (Schneider & Shiffrin, 1977). Unlike the amygdala response, which is sudden and habituates quickly, the ventromedial prefrontal cortex response is deliberate, slow, and lasts for a long time.

Thus the prefrontal cortex, especially the ventromedial prefrontal cortex part, helps predict the emotion of the future, thereby forecasting the consequences of one’s own actions. The forecasting properties of this reflective system are also consistent with the view of Deutsch and Strack (Deutsch & Strack, Chapter 4). Neurally speaking, the ventromedial prefrontal cortices contain convergence-divergence neuron ensembles, which hold a record of temporal conjunctions of activity in varied regions (i.e. sensory cortices and limbic structures) caused by external and internal stimuli. When parts of certain exteroceptive-interoceptive conjunctions are re-processed, consciously or non-consciously, their activation is signaled to ventromedial prefrontal cortices, which in turn activate somatic effectors in hypothalamus, and brainstem nuclei. This latter activity is an attempt to reconstitute the kind of somatic state that belonged to the original conjunction.

A large number of channels convey body information to the central nervous system (e.g., spinal cord, vagus nerve, humoral signals). Evidence

suggests that the vagal route is especially critical for relaying somatic signals (Martin et al., 2004). Although research in this area is still in progress, early evidence suggests that the biasing action of somatic states on behavior and cognition is mediated by the release of neurotransmitters in neural structures belonging to the reflective system. Indeed, the cell bodies of the neurotransmitter dopamine (DA), serotonin (5-HT), noreadrenaline (NA), and acetylcholine (Ach)) are located in the brainstem; the axon terminals of these neurotransmitter neurons synapse on cells and/or terminals all over the cortex (Blessing, 1997). When somatic state signals are transmitted to the cell bodies of serotonin neurons, for example, the signaling influences the pattern of serotonin release at the terminals. In turn, changes in serotonin release will modulate synaptic activities of neurons subserving behavior and cognition within the reflective system. This chain of neural mechanisms provides a way for somatic states to exert a biasing effect on decisions **(Figure 3)**.

FIGURE 3 TO APPEAR ABOUT HERE

Thus once somatic states are enacted, in the body (body-loop) or in the brain stem (as-if-body-loop) via direct and indirect connections between the amygdala and the ventromedial prefrontal cortex, and the neurotransmitter nuclei within the brainstem (Blessing, 1997; Nauta, 1971), they can then influence activity in (1) regions involved in *body mapping*, i.e., holding patterns of somatic

states that help generate *feelings*; (2) regions involved in the triggering of somatic states (e.g., amygdala and ventromedial prefrontal cortex), so that the threshold for triggering subsequent somatic states is increased or decreased; (3) regions involved in *working memory* (e.g., lateral orbitofrontal, dorsolateral prefrontal, and other high order association cortices), so that a particular representation is strengthened or weakened; and finally (4), somatic state signals influence activity in regions concerned with motor responses and behavioral actions (e.g., striatum and anterior cingulate/ supplementary motor area (SMA)).

The significance of this neural arrangement is that regardless of how somatic states are triggered, i.e., impulsively (primary induction) or reflectively (secondary induction), once they are triggered; they can gain access to cortical and subcortical neurons subserving cognition. Thus depending on their strength, they have the capacity to modify and influence cognition.

Loss of Willpower

Early in life, the reflective system is poorly developed, and willpower is relatively weak, behavior is more dominated by the impulsive system—children tend to behave in a manner that they do what they feel like doing right now, without much thought about the future. However, through learning they learn to constraint many desires and behaviors that conflict with social rules, and which lead to negative consequences. This is the first sign of the development of

willpower, and an example of how the reflective system gains control over the impulsive system. This ability, i.e., to choose according to long-term outcomes, and resist immediate desires, requires the normal development and normal triggering of somatic states by the reflective system, which signal the value of long-term outcomes. Deprived of these somatic states, the reflective system loses its control, and willpower breaks down. Indeed, this is what happens when areas of the ventromedial prefrontal cortex are damaged, as described in the case of Phineas Gage who became impatient of restraint or advice when it conflicted with his desires (Damasio, 1994). However, it appears that there is more than one mechanism through which the reflective system exerts control over the impulsive system.

The functional evolution of the prefrontal cortex appears to involve an incremental increase in its capacity to access representations of events that occur in the more distant future. This enhanced "futuristic" capacity coincides with the development of more rostral/anterior regions of the ventromedial prefrontal cortex. Comparative studies of the frontal lobes in humans and non-human primates have revealed that the major advancement in the size, complexity, and connectivity of the frontal lobes in humans relates primarily to Brodmann Area 10, i.e., the frontal pole, (Semendeferi et al., 2001), and not so much to the more posterior areas of the ventromedial prefrontal cortex (Semendeferi et al., 2002).

For this reason, we have argued that there is a distinction between two broad mechanisms of behavioral and cognitive control:

(1) Decision-making, which reflects a tendency to think about the consequences of a planned act before engaging in that act. It requires knowledge about facts and values, and it involves conscious, slow, and effortful deliberation about consequences that may or may not happen in a distant future. To give an example requiring decision-making is finding a briefcase with $100,000 in a dark alley. The decision to take or not take the money may require some deliberation about the ethics, morality, and consequences of such an action. The critical neural region for this mechanism of control is the more anterior region of the ventromedial prefrontal cortex, i.e., those involving the frontal pole and Brodmann Area 10 (Bechara, 2004). We have shown that this decision-making function can be taxed by the Iowa gambling task (Bechara, 2004).

(2) Impulse control reflects inhibition of a pre-potent act (motor impulse control), or a pre-potent mental image/ thought (perceptual impulse control). The learning to quickly and automatically inhibit such a pre-potent act (or thought) is due, in large part, to the triggering of a somatic state (as-if-body-loop), which signals the immediate and certain nature of the consequences. An example of this quick, automatic, and implicit mechanism of impulse control is finding a similar amount of $100,000 spread out on a table inside a bank. Normally, any thought, intention, or impulse to grab the money is inhibited automatically and effortlessly.

The critical neural region for the mechanism of motor impulse control is the more posterior region of the ventromedial prefrontal cortex, i.e., those involving the anterior cingulate (Bechara, 2003, 2004). The Stroop, Continuous Performance Task (CPT), Stop Signal, Go/no Go, delayed alternation, and reversal learning tasks are examples of paradigms that detect deficits in this type of behavioral/motor impulse control. The critical neural region for the mechanism of perceptual impulse control is the lateral orbitoforntal and dorsolateral (inferior frontal gyrus) regions (Bechara, 2003, 2004). Perseveration on the Wisconsin Card Sorting Task (WCST) and inability to shift attentional sets (Intradimensional-Extradimensional (ID-ED) shift), as well as other tasks that require shifting attention from one perception to another are laboratory measures that detect this type of deficit in perceptual impulse control.

It is very important to realize that although these different cognitive and behavioral mechanisms can be dissociated under controlled experimental conditions, they are all inter-related and act together in a functioning brain. Injuries or diseases that affect a single or a combination of any of these mechanisms will have a devastating impact on judgment, decision-making, and the whole social and real-life behavior of the affected individual.

Thus an addict may have abnormalities in any of these top-down control mechanisms of the reflective system, i.e., decision-making and impulse control (motor and/or perceptual). For instance, the choice between another drug use

episode and the family pressure not to use drugs presents a dilemma to individuals with substance dependence, and the choice depends on mechanisms of decision-making. When this mechanism fails, the addict decides to seek the drug, regardless of the consequences. On the other hand, the ability to put a stop and resist another drug use when exposed to an environment with many drug cues depends on intact mechanisms of impulse control. When these mechanisms fail, the individual with substance dependence becomes unable to suppress the "thought" of taking the drug (perceptual impulsiveness), or may actually act quickly, without thinking, and take the drug (motor impulsiveness).

Although dysfunction within these top-down control mechanisms of the reflective system can be responsible for maintaining drug use, the problem can also arise from bottom-up mechanisms of the impulsive system, where hyperactivity in the impulsive system can weaken control of the reflective system. In other words, choosing according to long-term outcomes rather than short-term ones requires that the somatic states triggered by the reflective system dominate those triggered by the impulsive system. Two broad types of conditions could alter this relationship and lead to loss of willpower: (1) a dysfunctional reflective system, and (2) a hyperactive impulsive system. The neural regions of the reflective system, which exert "top-down" control on decision-making (anterior ventromedial prefrontal cortex), motor impulse control (anterior cingulate), and perceptual impulse control (lateral orbitofrontal and dorsolateral) are all targets

for the neural systems that convey “bottom-up” influence of somatic signals. The influence of these somatic signals could be non-conscious and implicit, or conscious and explicit, i.e., accompanied by a certain feeling of urge. Addiction to drugs provides examples of disorders that affect each type of these mechanisms.

1. A dysfunctional reflective system: Patients with bilateral ventromedial prefrontal cortex damage and individuals with substance dependence show similar behaviors. (1) They often deny, or they are not aware, that they have a problem. (2) When faced with a choice to pursue a course of action that brings an immediate reward, at the risk of incurring future negative consequences, including the loss of reputation, job, home, and family, they choose the immediate reward and ignore the future consequences. Research has shown a link between the “myopia” for future consequences seen in ventromedial prefrontal cortex lesion patients and that seen in individuals with substance dependence by finding a relationship between substance abuse and poor decision-making as measured by the Iowa Gambling Task (IGT), as well as other similar decision-making tasks (Bartzokis et al., 2000; Grant et al., 1997, 2000; Grant et al., 1999; Mazas et al., 2000; Petry et al., 1998; Rogers et al., 1999).

Studies have shown that the abnormal mechanisms of processing drug reward in individuals with substance dependence generalize to other rewards, including monetary reward (Breiter et al., 2001; Breiter & Rosen, 1999).

Therefore, we predicted that the abnormalities of individuals with substance dependence in processing somatic states would apply not only to drugs, but also to reward in general, such as the monetary reward used in the Iowa Gambling Task paradigm. We conducted experiments where we tested three groups of subjects: individuals with substance dependence, normal controls, and ventromedial prefrontal cortex lesion patients on the Iowa Gambling Task (Bechara et al., 1994; Bechara et al., 2000). All individuals with substance dependence met the DSM-IV criteria for dependence, with either alcohol or stimulants (meth-amphetamine or cocaine) as the primary substance of choice. The results revealed a significant impairment in the performance of individuals with substance dependence relative to normal controls on the Iowa Gambling Task.

Measuring skin conductance response activity of subjects after receiving reward or punishment (Reward or Punishment skin conductance responses), and before making a choice (Anticipatory skin conductance responses), revealed that a subgroup of individuals with substance dependence was similar to ventromedial prefrontal cortex lesion patients. These individuals with substance dependence triggered normal Reward and Punishment skin conductance responses, but they failed to trigger skin conductance responses (Anticipatory) when they pondered choices associated with high immediate gains, but also with more delayed and more severe losses (Bechara et al., 2002). This showed that individuals with

substance dependence, like ventromedial prefrontal cortex lesion patients, were deprived of a mechanism for triggering somatic states that implicitly (or explicitly) help bias and guide decisions in favor of long-term outcomes.

In addition to decision-making, we examined the integrity of the other impulse control mechanisms of the reflective system in individuals with substance dependence. We assessed response inhibition using the stop-signal task (Crone et al., 2003; Crone et al., 2004). In the stop signal paradigm the participant performs a choice reaction time task requiring responses to left and right pointing arrows. Occasionally and unpredictably the color of the arrows change, instructing participants to inhibit responses. The main dependent variables in this task are the response time (RT) and the estimate of the covert response to the stop signal, by inferring the stop-signal reaction time (SSRT). Relative to normal controls, individuals with substance dependence had significantly longer SSRTs, but shorter RTs, thus reflecting difficulties or impairments in impulse control.

In another experiment, we used a task-switch paradigm requiring participants to rapidly switch between two reaction-time tasks, requiring left or right hand responses to squares and rectangles that could appear as local or global figures (Crone et al., 2003; Crone et al., 2004). The main dependent variable was the difference in reaction time (RT) between task repetition trials and task alternation trials. Individuals with substance dependence showed significantly

larger switch costs than controls, while there was no difference in accuracy of responding.

In a separate study (Noel et al., 2003; Noel et al., 2005), we tested the hypotheses that alcoholics suffer from deficits in their cognitive control mechanisms of "stopping" and of "shifting" and that these deficits are exacerbated by cognitive biases for alcohol-related stimuli. Noel designed a laboratory task called the "Alcohol Shifting Task", in order to examine distinctly motor inhibition, shifting attention, and the influence of alcohol-related stimuli on these functions in detoxified poly-substance abusers with alcoholism. The Alcohol Shifting Task involves the presentation of alcohol-related versus non-alcohol related words on a computer screen. The subject is instructed to press the bar key when a non-alcohol related word appears on the screen and withhold the response if an alcohol related word appeared instead. After establishing a habit for responding this way, the contingencies would reverse unexpectedly in the task so that the subject must now withhold responding to non-alcohol related words and respond to alcohol related words. In a second cycle, there is a return to the first contingency, i.e., respond to non-alcohol and withhold responding to alcohol cues followed by a reversal. Relative to control subjects, we found that alcoholics were slower to respond to neutral, but not alcohol, stimuli in both stopping and shifting conditions. In addition, when subjects were supposed to withhold responding to an alcohol or neutral stimulus, alcoholics made more errors than controls in both

'stopping' and 'shifting' conditions. Most important, the failure of alcoholics to inhibit their responses ('stopping' condition) was significant when alcoholics had to suppress their response to an alcohol stimulus, but not when they had to withhold their response to a neutral stimulus. In contrast, in 'shifting' condition, alcoholics made more errors in both neutral and alcohol words conditions. However, the deficit was much more pronounced when alcoholics had to shift attention from alcohol to neutral cues, but not so much when they shifted attention from neutral to alcohol cues.

Together, the results reflect disorders in the reflective system of individuals with substance dependence at both the level of decision-making as well as the ability to control impulses.

2. A hyperactive impulsive system: Somatic states work through neurotransmitter systems, and neurotransmitters modulate synapses of cortical neurons within the reflective system. Therefore, a hyperactive impulsive system subserved by an amygdala-ventral striatal (nucleus accumbens) neural circuit, which exaggerates the somatic response of reward stimuli, can weaken the reflective/ prefrontal system, thus gaining control over behavior and cognition.

We have shown that many individuals with substance dependence may suffer from a hyperactive amygdala system that exaggerates the processing of reward, which result in poor decision-making as measured by the Iowa Gambling

Task (Bechara, 2003). We have described this condition as "hypersensitivity to reward", in which a subgroup of individuals with substance dependence expressed exaggerated responses to reward and relatively weak responses to punishment (Bechara, 2003). Specifically, we used different versions of the Iowa Gambling Task, where the contingencies were reversed, so that the punishment was immediate and the reward was delayed. When testing individuals with substance dependence on this variant task, a subgroup of individuals with substance dependence behaved on the original and variant versions of the Iowa Gambling Task in such a way that they were drawn to choices that yielded larger gains, irrespective of the losses that were encountered. This subgroup showed higher magnitude Reward skin conductance responses, in comparison to normal controls. Furthermore, during the anticipation of a reward, this subgroup of individuals with substance dependence showed higher anticipatory skin conductance responses, in comparison to controls (Bechara et al., 2002). On the basis of these behavioral and physiological results, we have described this sub-population of individuals with substance dependence as hypersensitive to reward, so that the presence or the prospect of receiving reward dominates their choice and behavior.

Conclusions: implications for treatment and directions for future research

Advances in the study of cognition and emotion can improve our understanding of the implicit and explicit mechanisms that govern decisions to abuse drugs. This

chapter began with addressing the role of willpower in the decision to use substances. Although the act of using substances can be resisted under extreme conditions (e.g., a gun to the head), in most cases there is no gun to the head. The research discussed provides evidence that the loss of willpower in individuals with substance dependence is likely the result of their experiencing the world differently. Addiction is a condition in which the person becomes unable to choose according to long-term outcomes. However, this inability can result from a dysfunction of one or more of several mechanisms of cognitive and behavioral control within the reflective system, or hyperactivity of the impulsive system. The breakdown of one or more of these cognitive and emotional mechanisms constitute one of the principal mechanisms responsible for the switch from a controlled to uncontrolled and compulsive behavior. Thus future research should address the reasons for why these mechanisms breakdown: is it genetic, e.g., abnormal neurotransmitter transporters? Is it developmental, e.g., environmental stress or exposure to drugs during a time window in adolescence where the prefrontal cortex has not yet developed completely? Other questions should address the mechanisms of “predisposition” versus “specificity”. Acquisition of addictive behaviors may depend on at least two steps: 1) a predisposition to becoming addicted to anything, and 2) specificity to an addictive stimulus. Breakdown in the mechanisms of decision-making and impulse control may explain the issue of predisposition. But what determines the specificity of an

addiction? For instance, why certain people become pathological gamblers but not drug addicts?

We have suggested that the different mechanisms of cognitive and impulse control of the reflective system could be assessed by different sets of cognitive tasks, and linked to abnormalities in different neural sectors. Characterization of individuals with substance dependence on the basis of neurocognitive criteria has strong implications for prognosis and rehabilitation. For instance, many individuals with substance dependence do not show signs of prefrontal impairment, and it is possible that these are the individuals who decide at some point to quit their addiction habit and they succeed. These individuals seem in full control of their behavior and this is why they possess the capability to control their addiction. On the other hand, individuals who show profiles of cognitive deficits similar to ventromedial prefrontal cortex lesion patients probably have the worst prognosis. Such individuals may fall into one trouble after the other and repeat one mistake after the other and can never shift their behavior towards long-term thinking and avoiding future negative consequences on their own. Individuals who show only signs of hypersensitive to reward may fall somewhere in between. We speculate that the weakness of these individuals and their loss of behavioral control are precipitated primarily in the presence of reward or irresistible cues. In other words, they may have the cognitive capacity to learn to

stay way from the situations that make them vulnerable to succumbing to their addiction.

We have begun pharmacological research aimed at understanding the chemical deficiency in the reflective/prefrontal system of individuals with substance dependence, which underlies their decision-making impairment and loss of control over their behavior. We found that the stimulation or blockade of both dopamine and serotonin interfere with the ability to make advantageous decisions in the Iowa Gambling Task, but the dopamine effect seemed restricted to decisions guided by covert knowledge, i.e., decisions under ambiguity. In contrast, the serotonin effect seemed restricted to decisions guided by conscious knowledge of which choices are good or bad, i.e., decisions under risk (Bechara et al., 2001). The results suggest that covert biasing of decisions might be dopaminergic, whereas overt biasing might be serotonergic. These findings have implications for the treatment of addictive disorders in that more than one neurotransmitter system may be involved in the addictive process, and thus different aspects of the addictive process may need different pharmacological treatments. Most important, pharmacological treatments may never work alone, i.e., without cognitive and behavioral rehabilitation. The idea is that the poor prefrontal mechanisms of decision-making in individuals with substance dependence are in part related to learning in the presence of a deficiency in the chemicals that modulate non-conscious (e.g., at the level of the striatum) or

conscious (e.g., at the level of the cortex) decisions. Thus decision-making and poor learning to control certain behaviors are flawed in part because of this deficiency. Reversal of this chemical deficiency alone is not sufficient for learning to decide advantageously. The individual must re-learn how to think and behave in a particular situation related to drugs or gambling while treated with medications, which correct the chemical imbalance. Thus, only re-learning (i.e., rehabilitation) in the presence of normal pharmacology (i.e., drug treatment) is perhaps the most effective way to restore advantageous decisions in an addicted individual.

Figure Captions

Figure 1: A diagram illustrating the interaction of the reflective and impulsive systems in relation to their triggering of somatic states and the ultimate emergence of a net or overall somatic state that plays a critical role in biasing decisions.

Figure 2: A schematic model of somatic state activation and decision-making. **(a)** The amygdala is a trigger structure for emotional (somatic) states from primary inducers. It couples the features of primary inducers, which can be processed subliminally (e.g., via the thalamus) or explicitly (e.g., via early sensory and high-order association cortices), with effector structures that trigger the emotional/somatic response. **(b)** The ventromedial prefrontal (VM) cortex is a trigger structure for emotional (somatic) states from secondary inducers. It couples knowledge of events held temporarily in working memory (which is dependent on dorsolateral prefrontal (DLF) cortices) to effector structures that induce the somatic responses, and to structures holding representations of previous feeling states (e.g., Insula and Somatosensory I (SI) and Somatosensory II (SII) cortices).

During the pondering of a decision, somatic states are triggered by primary (drug cues) or secondary inducers (thoughts about taking drugs). Once induced, their ascending feedback signals participate in two functions (**c**): in one they provide a substrate for feeling the emotional state, through the somatosensing

cortices (Insula/SII, SI); in the other they provide a substrate for biasing decisions through motor effector structures such as the striatum (Str.) and anterior cingulate cortex (AC) and adjacent cortices.

Figure 3: A diagram illustrating three different levels at which somatic states can bias decisions via the release of neurotransmitters (NT). (1) Dopamine biases decisions covertly (perhaps through action in the striatum and affective sector of anterior cingulate (Brodmann Area (BA) 25 and lower 24,32). (2) Serotonin biases decisions overtly (perhaps through action in the cognitive sector of anterior cingulate and probably the adjacent SMA (Supplementary Motor Area)). (3) Somatic states also bias working memory in the LOF (lateral orbitofrontal and dorsolateral regions of the prefrontal cortex); They help endorse or reject "thoughts", "options", or "scenarios" brought to mind during the pondering of decisions, i.e., before their translation into action. The neurotransmitter system that mediates this biasing function remains to be determined

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