What can the monetary incentive delay task tell us about the neural processing of reward and punishment?

Kai Lutz1,3
Mario Widmer1,2,4
1Department of Neurology, University Hospital Zürich, Zürich, 2Cereneo, Center for Neurology and Rehabilitation, Vitznau, 3Division of Neuropsychology, Institute of Psychology, University of Zürich, Zürich, 4Neural Control of Movement Lab, ETH Zürich, Zürich, Switzerland

Abstract: Since its introduction in 2000, the monetary incentive delay (MID) task has been used extensively to investigate changes in neural activity in response to the processing of reward and punishment in healthy, but also in clinical populations. Typically, the MID task requires an individual to react to a target stimulus presented after an incentive cue to win or to avoid losing the indicated reward. In doing so, this paradigm allows the detailed examination of different stages of reward processing like reward prediction, anticipation, outcome processing, and consumption as well as the processing of tasks under different reward conditions. This review gives an overview of different utilizations of the MID task by outlining the neuronal processes involved in distinct aspects of human reward processing, such as anticipation versus consumption, reward versus punishment, and, with a special focus, reward-based learning processes. Furthermore, literature on specific influences on reward processing like behavioral, clinical and developmental influences, is reviewed, describing current findings and possible future directions.

Keywords: reward, punishment, dopamine, reward system

Introduction

Traditionally, rewards are defined as stimuli an organism is willing to work for and punishments as stimuli an organism is trying to avoid. These concepts have played a central role in the psychology of learning ever since they were introduced by behaviorism last century (see recent overviews Domjan and Miltenberger). They imply that reward and punishment are linked to an operant, ie, to an agent’s action. According to behaviorist concepts, reward increases the probability that a rewarded behavior is shown in the future, whereas punishment decreases this probability. Therefore, reward and punishment are closely related to motivation, providing incentives to actively seek or avoid certain stimuli, and thus can elicit appetitive or avoidance behavior, respectively.

Rewards have been categorized into primary and secondary rewards. Primary rewards consist of stimuli which have a direct positive value for an individual receiving the reward. Many of these primary rewards or punishments have a physiological meaning, like food, beverages, sex, and pain. In contrast, secondary rewards have no immediate direct value, but an individual learns that receipt of such rewards usually has positive consequences. Such rewards can be money, tokens, some forms of social acknowledgement, or similar. Valuation of primary rewards depends on hunger, thirst, or other states of the organism, often making it necessary to deprive an individual under observation of the respective reward, in order to make sure that the stimulus is indeed rewarding. In comparison, secondary rewards are less prone to saturation and thus
possess a relatively stable value. Nevertheless, a multitude of factors exist, influencing the individual valuation of primary as well as secondary rewards.

The neuroscientific study of reward processing flourished with the detailed examination of neuronal activity in rodent brains during consumption and anticipation of rewards and punishment. For a comprehensive review, see Schultz. This work revealed that unexpected presentation of a reward, acting as an unconditioned stimulus, leads to a phasic increase in dopaminergic activity in the substantia nigra/ventral tegmental area. After classical conditioning of such a reward to a conditioned stimulus, the conditioned stimulus elicits a similar phasic increase of dopaminergic activity, but presentation of the unconditioned stimulus does not do so anymore. Correspondingly, if presentation of a conditioned stimulus is not followed by an unconditioned stimulus despite this being expected (leading to extinction), then a phasic decrease of dopaminergic activity can be found at the time when the unconditioned stimulus had been expected. Thus, a wealth of animal studies have led to the description of a reward system and allowed formulation of hypotheses about reward processing in human brains.

Soon after these groundbreaking investigations, research was extended to human subjects, mainly using neuroimaging methods to assess changes in neuronal activity due to the processing of reward and punishment. The most important paradigm used for these studies has been the monetary incentive delay (MID) task. This task consists of the announcement of an incentive, which is linked with a certain contingency to receipt of this incentive. Basically, this reflects the case of classical conditioning. However, the standard version of the MID task requires an individual to react to a target stimulus presented after the incentive cue but before the reward is given. Whether the announced reward is delivered depends then on the individual reaction. Again, contingency can be introduced to make receipt of the reward more or less predictable from the individual action. Examples of such actions include forced choice behavior, memory tasks, and motor tasks. See Figure 1 for a schematic comparison of classical conditioning and the MID task.

If contingency exists between an action (ie, task processing) and a consequence, the learning process rather fits into the scheme of operant conditioning. In this context, appetitive stimuli are called reinforcers, since they strengthen the reinforced behavior. If the action is not reinforced (eg, because it was not performed to a trainer/teacher’s satisfaction), according to learning theory, this leads to extinction. Note that in the case of classical conditioning, a stimulus is, or is not, followed by a reward. During the MID task, an action is, or is not, followed by reinforcement. However, the MID task allows assignment of different stimuli to different behaviors shown during task processing. One important possibility is to assign reinforcement to one action and an aversive stimulus (punishment) to another action triggered by the preceding cue. This is not the same as assigning a pleasant stimulus (UCS) to a conditioned stimulus in some cases and an aversive (UCS) to the same conditioned stimulus in other cases, since during classical conditioning, presentation of the conditioned stimulus is not controllable by the individual, whereas during the MID task, task processing is. Furthermore, both set ups, ie, classical conditioning and MID tasks, allow the use of pleasant (appetitive) as well as unpleasant (aversive) stimuli to generate reward or punishment, respectively. The most important difference between the set ups is that reward/punishment in the MID task depends on task processing whereas in classical conditioning it depends on the conditioned stimulus.

This paradigm allows investigation of different stages of reward processing, like reward prediction, anticipation, outcome processing, and consumption, as well as the processing of tasks under different reward conditions. The current review gives an overview of the different utilities of the MID task that have been published since its introduction by Knutson et al. The review does not attempt to give an exhaustive overview of the literature, but instead presents selected articles in order to highlight how the MID task has been used to investigate neuronal processes involved in distinct aspects of human reward processing, such as anticipation versus consumption, reward versus punishment, and reward-based learning processes. We further highlight work investigating different influences on reward processing like behavioral, clinical, and developmental influences, as well as reward processing in different contexts. While describing current findings, the review attempts to point to possible future directions of investigation in the human reward system.

Anatomy of the reward system
In order to present an anatomical framework for discussing the neuronal processes involved in reward and punishment,

Figure 1 Schematic drawing of an incentive delay task (B) in comparison with a classical conditioning scheme (A). Note that both settings, instead of using reward/reinforcement, allow for use of aversive stimuli/punishment.
Figure 2 gives an overview of the relevant brain structures, as described by Haber and Knutson.9

**Aspects of processing reward and punishment**

A typical rewarding or punishing situation is a complex phenomenon. It consists of distinct temporal phases and can include different classes of stimuli. In the following sections, the most important aspects, as discussed in the literature, are outlined.

**Anticipation and consumption (wanting/liking)**

As described by Knutson et al8 in their original article introducing the monetary delayed incentive task, a distinction between anticipation and consumption of rewards should be made when interpreting neuronal activity involved in reward processing. Such a distinction has been suggested based on previous observations in animals,10 and on traditional views.11 Consequently, one year after publication of their original article,9 a report about distinct neuronal activity in humans attributable to anticipation versus consumption of rewards was published.12 In short, it reports that reward anticipation activates ventral striatal regions, whereas the receipt of reward outcomes activates the ventromedial frontal cortex, thus replicating earlier studies in monkeys.13 This finding has essentially been corroborated over the years with different types of reward.14–17 Closer inspection of the time course of brain activity involved in reward processing has revealed a more complex pattern: after presentation of monetary gain or loss, activity in the dorsal striatum, particularly the dorsal part of the caudate nucleus, is sensitive to valence (reward/ punishment) as well as outcome magnitude.18 This is true at later stages, approximately 9–12 seconds after outcome presentation, when large rewards elicit the strongest increase and large punishments the weakest. On the other hand, the ventral striatum, especially the nucleus accumbens, seems to be strongly influenced by incentives12 and shows less reactivity to outcome than the dorsal striatum.18 Interestingly, initial feedback-related activity in the dorsal striatum seems to be dependent on incentive values, but after a few seconds, activity seems to depend on the size of outcome.19

The dynamics of brain activity in relation to processing of different reward stages has led to the formulation of a temporal difference model of reward-based learning.20,21 In brief, this model describes how error terms are derived from a mismatch between the predicted reward and that actually received. This mismatch can lead to a positive or negative reward prediction error, meaning that an outcome is better or worse than expected, respectively. Prediction of rewards in response to cues seems to take place in the nucleus accumbens,22 whereas the medial prefrontal cortex seems to (re)calculate expectations of gains in response to outcomes.

While these findings, gleaned by means of functional magnetic resonance imaging, describe brain activities with...
Relatively slow temporal dynamics in the range of seconds, other methods reveal how other brain activities with faster temporal dynamics are related to reward prediction and receipt. Thus, a more complex picture emerges, ie, processing negative prediction errors leads to negativity in the posterior cingulate cortex and striatum, whereas processing of reward expectancy corresponds with electrophysiological activity in the posterior cingulate cortex, anterior cingulate cortex, and parahippocampal gyrus. Furthermore, electroencephalography (EEG) and magnetoencephalographic methods reveal that reward cues are coded by neuronal oscillations in the beta (20–30 Hz) and theta (5–8 Hz) range in the frontal regions. Integration of these results into existing knowledge about the human reward system has only just started, and is likely to benefit from further studies investigating the fast temporal dynamics of human reward processing.

**Reward versus punishment**

In addition to the question of temporal dynamics, when discussing rewards, the question remains as to whether rewarding and punishing effects are processed by distinct brain structures. To elaborate on this question, it seems beneficial to briefly overview the positive and negative effects of rewards or punishments; by definition, a stimulus that increases the frequency of a behavior, upon which the stimulus is contingent, is called reinforcement. Reward and positive reinforcement are commonly considered to be synonymous, although a reward is less strictly defined. Positive reinforcement usually consists of the presentation of an appetitive stimulus contingent on an individual’s behavior, whereas negative reinforcement consists of the removal of a noxious or otherwise aversive stimulus. On the other hand, punishment can consist of the presentation of an aversive stimulus or the removal of an appetitive stimulus. The MID task theoretically allows investigation of all of these entities. However, instead of investigating the removal of stimuli, the incentive delay task has usually been used to investigate negative prediction errors, ie, an unexpected decrease of reward magnitude or an unexpected increase in punishment.

There have been several investigations comparing neuronal activity correlated with positive and negative prediction errors. Without distinguishing between anticipation and outcome processing, Delgado et al found stronger involvement of the ventral striatum (approximate region of nucleus accumbens) and the dorsal striatum (caudate nucleus) in trials showing a positive rather than a negative outcome. The latter structure was later shown to code reward magnitude in a parametric manner. Since the task used in the study of Delgado et al involved gambling, and cues were not manipulated to induce expectancies, reward anticipation is unlikely to have varied systematically and therefore should not have influenced these findings.

Rogers et al showed that activity in the medial prefrontal cortex (posterior orbitomedial cortex and pregenual anterior cingulate cortex) increases when positive outcomes are given, relative to the situation when subjects are confronted with a loss. Importantly, these outcomes, due to the nature of the task, were unpredictable, so positive outcomes represent a positive prediction error. While Rogers et al only reported increased brain activity due to processing of positive outcomes versus negative outcomes, and not vice versa, Ramnani et al investigated both types of prediction error separately. Their results corroborate the finding that unexpected rewards activate, among other regions, the medial prefrontal cortex. They also showed that unexpected omission of rewards activates a distinct region of the medial prefrontal cortex, more anterior to the aforementioned areas. Negative outcomes in these studies were operationalized as not receiving an expected reward. Alternatively, negative outcomes can be explicitly defined as a loss by deducting a certain amount of money from a participant’s credit. In doing so, distinct regions are revealed that code positive (gain) and negative (loss) reward prediction errors. Whereas unexpected reward is confirmed to activate the ventral striatum, unexpected loss is shown to correlate with neuronal activation in the amygdala. Interestingly, using this design, not only receipt of outcomes (prediction errors) but also their anticipation involved activation of the ventral striatum and amygdala; anticipation of positive outcomes activates the ventral striatum, whereas anticipation of negative outcomes activates the amygdala. Further evidence for involvement of the amygdala in anticipation of outcomes comes from a study using a different task. A wheel-of-fortune game presented subjects with several possible gains in some rounds and with possible losses in other rounds. The results differ from those reported by Yacubian et al in that activation of the amygdala was increased during anticipation of loss as well as reward in the study by Breiter et al, but only during anticipation of loss in the study by Yacubian et al. Although speculative, the difference might be explained by the subjects’ role in the tasks. The wheel-of-fortune task did not give the subjects any control over the outcome, whereas during the guessing task used by Yacubian et al, subjects might have had a feeling of agency, ie, being responsible for the outcome. Thus, anticipation of reward might depend on whether subjects perceive themselves to have control over the outcome or not.
Additionally, introducing high-incentive versus low-incentive trials (operationalized as monetary gain/loss versus knowledge of performance without monetary consequence, respectively), it has been shown that the dorsal striatum/caudate nucleus is mainly sensitive to monetary incentive, even during outcome processing.\textsuperscript{19}

**Reward-based learning**

One of the most important functions of reward processing is to enable the organism to adapt behavior in order to maximize reward and minimize punishment. Reward prediction error indicates that a cue is not associated with the expected consequence. Thus, in the future, expectations connected to that cue should change. This forms the essence of classical conditioning. As a result, being confronted with the respective cue might be avoided or advanced in the future. Similarly, if reward is dependent on an individual’s behavior (eg, choice behavior or motor accuracy), a prediction error informs the individual that the behavior does not lead to the expected outcome. According to learning theory, behaviors are chosen so that expected reward is maximized and/or expected punishment is minimized. Thus, behaviors leading to reward are strengthened and behaviors leading to punishment are weakened. This is the principle of operant (or instrumental) conditioning.

As a variant of the classical MID task, early studies\textsuperscript{27,29} gave rewards contingent on goal-oriented activities or contingent on stimuli unrelated to behavior. A main result was that if not contingent on any behavior, unpredicted rewards evoked activity in the orbitofrontal cortex, the frontal pole, the parahippocampal cortex, and the cerebellum. If a monetary incentive is present while a visually triggered action is selected and planned, this results in enhanced activity within the prestriate visual cortex, the premotor cortex, and the lateral prefrontal cortex as compared with action selection and planning without a monetary incentive. These findings, based on goal-oriented behavior, do not involve striatal structures, which makes it hard to integrate them into the reward literature existing at the time. In fact, there is the possibility that focusing on goal-oriented motor behavior might involve different structures than those involved in focusing on the decision process. However, no direct comparison of classical versus operant conditioning processes was performed in these studies. O’Doherty et al\textsuperscript{10} applied a task requiring a two-alternative forced choice in which fruit juice could be gained as a reward upon selecting the right reactions in response to corresponding cues, thus forming a non-monetary instrumental conditioning task. The investigators compared this task with a condition in which the subject had no influence on the outcome, but the selection was made by a computer (coupled with the subject’s previous selections), thus forming a classical conditioning situation in which motor activity is comparable with instrumental conditioning. This approach allows the conditioning process to be viewed within the framework of an actor-critic model, where the actor chooses actions according to expected action outcomes and the critic controls whether the actions lead to the expected rewards (reward prediction error). In this setting, an actor was only assumed to be active in the instrumental conditioning condition. The results show that ventral striatum activity correlates with reward prediction error signal in both types of conditioning. The prediction error signal during classical conditioning was related to activity in the ventral putamen and the prediction error signal during instrumental conditioning was related to the nucleus accumbens. The dorsal striatum, on the other hand, was more strongly activated due to outcome processing in instrumental conditioning than in classical conditioning, suggesting its involvement in the role of an “actor”. Importantly, in another study, the dorsal striatum (head of the caudate nucleus) was activated only when a reward was perceived to be contingent on an action.\textsuperscript{31}

Considering reward following cues versus reward following actions, Gläscher et al\textsuperscript{32} have set up an experiment discriminating between the two. They found that activity in the ventromedial prefrontal cortex corresponds to the expected reward following actions as well as external cues. On the other hand, using an operant conditioning paradigm, FitzGerald et al\textsuperscript{33} distinguished action values (the value ascribed to a specific action) from choice values (the value ascribed to either of two choices). They were able to show that the ventromedial prefrontal cortex along with thalamic and insular structures decode action-specific values, and are thus likely to be involved in operant conditioning. This is partly consistent with studies showing brain activity in the ventromedial prefrontal cortex to correspond to the expected value of actions or choices.\textsuperscript{34,35}

These studies of reward-based learning make it clear that distinct mechanisms are likely to be involved when action is or is not required by the subject. However, when acting, we have to consider whether the actions are goal-oriented or not. If rewards or punishments are offered, we can usually assume that the agent’s goal is to maximize reward and to minimize punishment. Some aspects of goal-oriented behavior in the context of reward processing are discussed in the following section.
Goal-oriented behavior and reward
One important distinction between classical and operant conditioning lies in the fact that classical conditioning does not assume an agent’s action to lead to consequences. Instead, during classical conditioning, stimulus effects on the individual are investigated. Operant conditioning, on the other hand, rewards certain behaviors, leading to increased probability that these behaviors take place in the future, possibly in order to receive further rewards. Thus, presentation of rewards is commonly understood to be accompanied by emotional reactions which may trigger motivated behavior. This view brings a series of studies into focus, allowing the question of whether goal orientation might involve distinct components of the reward system to be addressed. An early study pointing in this direction showed dorsal striatum activity in response to the presentation of performance feedback in classification learning tasks.36–38 Interestingly, positive performance feedback did not elicit stronger activity than negative feedback in any subregion of the striatum.37 However, when giving performance feedback under two conditions, one signaling achievement of the subject’s goal and the other signaling the same amount of information but unrelated to any explicit goal, the former condition activated the head of the caudate nucleus more strongly.39 Similarly, Nees et al demonstrated that during a MID task, the anticipation of an optional reward elicited ventral striatum activity dependent on the magnitude of the possible reward. On the other hand, no such dependency existed in a simple guessing task, in which reward magnitude, although being experimentally manipulated, was unrelated to the subject’s behavior. Other studies have used a slot-machine task requiring no action and compared this with tasks in which outcome was contingent on the preceding choice or action.41 Using EEG, the investigators found that action outcomes elicited a transient change in mediofrontal activity when they were unfavorable (errors). On the other hand, when independent of the subject’s action, a similar mediofrontal EEG component was elicited in response to both favorable as well as unfavorable salient outcomes. This finding was later substantiated with a different task, again showing a greater difference between win-related and loss-related EEG frontomedial components, when the outcome depended on the subject’s action.42 These findings can be seen in the context of the abovementioned studies of reward anticipation when there is or is not a likely feeling of agency. To elaborate further on the role that performance feedback plays in the reward circuitry, a recent study compared performance feedback in a motor task when performance was or was not linked to monetary reward.43 In both cases, being informed about good performance activated the ventral striatum. However, in this study, feedback about bad performance led to less activity in this region than feedback about good performance, in contrast with previous findings using other tasks.37 However, in those tasks, information about bad performance was similarly valuable for the overall goal of learning a classification task, whereas the goal in the later study was generally to maximize precision in a motor task that in a subset of trials led to monetary gain. Thus, error was always negatively coupled with reward. Similar results have been found in a study using a category learning task with a monetary incentive in 50% of trials whereas only cognitive feedback was given in the other 50%.44 Both kinds of feedback elicited increases in the activity of several basal ganglia structures during the anticipation phase. Activity in the nucleus accumbens was stronger in monetary incentive trials, corresponded to measures of extrinsic motivation in monetary incentive trials, and corresponded to measures of intrinsic motivation in cognitive feedback trials. Video gaming is another example in which high motivation can be observed without obvious rewards. Performance feedback is stressed in many of these games, and massive release of dopamine into the ventral and dorsal striatum was reported long ago during video gaming.45 An active role of the player seems to be essential for this.46

These studies show that performance feedback, especially if it informs about good performance, elicits neuronal activity in many respects comparable with the neuronal activity elicited by the presentation of reward. Given that performance feedback is not regarded as a classical rewarding stimulus, the question about motivation in these tasks without explicit incentive is interesting. The concept of intrinsic motivation assumes that some tasks are worked on merely because a subject enjoys working on the task. With certain components of the human reward system being involved in the processing of performance feedback and even being connected to measures of intrinsic motivation, versions of the MID task without monetary (or other forms of) incentive seem to provide a valuable approach to investigate intrinsic motivation and its interaction with extrinsic motivation. This interaction in behavioral studies has been discussed controversially in terms of the interesting notion that monetary reward can undermine intrinsic motivation. A pioneering study using a variant of an MID task investigated the size of the midbrain and striatal activation due to positive performance feedback.
under several conditions, ie, when performance was coupled to monetary reward, when performance was not coupled to monetary reward, and when performance was not coupled to monetary reward after having been coupled to it previously. Not differentiating between the dorsal and ventral striatum, the authors found that performance feedback elicited the strongest responses in the midbrain and striatal regions due to feedback of good performance which was monetarily rewarded, and significantly weaker activation if no monetary incentive was given. Interestingly, removing the monetary incentive led to a drop in midbrain and striatal activity to significantly below the level in a control group where monetary incentives had never been present.

These studies show that, in some tasks, performance feedback can serve as task intrinsic reward, so instead of incentive motivation, intrinsic motivation might act. Considering the much discussed advantages of intrinsic motivation versus extrinsic motivation,48,49 closer examination of the neural systems involved in the interaction of these motivational systems would be of interest.

**Reward processing and error monitoring**

A topic closely related to the role of performance feedback in reward processing is the processing of error information in cognitive or motor tasks. As mentioned earlier, processing of error information in a categorical learning task has been shown to elicit activity in the ventral striatum in specific settings.36 Error information is most frequently investigated in tasks showing similarity to the MID task (consisting of the trial cue, action/choice, and outcome), with the difference being that monetary incentive is not usually coupled to error information. Therefore, although the scope of the present paper is focused on the MID task, a brief comment on the interesting link between human error processing and reward systems seems appropriate.

Processing error information in decision tasks has been studied intensively using electrophysiological methods, mainly EEG. Event-related components, time locked to erroneous behavior (error-related negativity), and time locked to feedback about an error (feedback-related negativity) have been identified as the most important and most reliable neuronal correlates of error processing. An influential model, the reinforcement learning theory of error processing assumes that whenever information indicates that an action does not result in an expected consequence, disinhibition of the anterior cingulate cortex mediated by the basal ganglia leads to a negative EEG deflection in the frontocentral electrodes. The precise location and involvement of the basal ganglia, along with the anterior cingulate cortex and other structures not readily amenable to investigation by EEG, have been identified by functional magnetic resonance imaging studies of error perception.50-52 The theory is eloquently described by Holroyd et al.53 The stronger the expectation of a certain action outcome that is missed, the greater the EEG deflection. Thus, the reinforcement learning theory of error processing only applies if stable expectancies concerning action outcome can be formed, allowing a reward prediction error to be generated. In motor learning theory, the capacity to predict action outcomes is inherent in an internal model mapping actions to consequences on the environment.54 Confirming the reinforcement learning theory of error processing and its applicability to motor learning, a recent study has shown that error-related negativity increases with buildup of such an internal model while learning audiomotor mappings on a manipulated piano keyboard layout.55 The evidence presented here demonstrates that reward prediction errors seem to play a greater role than would be expected from the investigation of MID tasks. Rather, reward prediction and outcome monitoring seem to have important features in common. As proposed by Kaplan and Oudeyer,56 the goal to minimize prediction error in several domains might be driving intrinsically motivated behavior like playing and exploration, and the nucleus accumbens may play a pivotal role in this process. Interestingly, novelty, as encountered when exploring new environments, activates a neuronal system partly overlapping with the reward network, and contextual novelty seems to boost activity in the striatum.24,57,58

**Discounting of delayed reward**

MID tasks also allow investigation of other aspects of reward processing, not mentioned so far. One important aspect of the value of the reward is determined by the temporal availability of the reward; if available immediately, a reward is valued more highly than if it is available only after a certain period of time. Thus, introducing a choice between small and immediately available or large and not immediately available rewards enables study of the process of devaluation due to temporal delay, known as delayed reward discounting. A wealth of literature has accumulated showing how different periods of delay influence the subjective perception of reward value in different populations. A recent overview of this topic, including underlying neural mechanisms, has been published by Peters and Büchel.59 Subjective discounting seems to take place in a neural system comprising the ventromedial prefrontal cortex,
ventral striatum, and posterior cingulate cortex. Further, the amygdala and hippocampus are involved in delay discounting. The specific contribution of these structures is not yet fully understood, but abnormal delay discounting has been linked to neuropsychiatric disorders related to impulsivity, as well as to addictive behaviors. Typically, addicts discount delayed rewards at a much higher rate than control subjects.\(^{60,61}\) Moreover, this impulsive discounting behavior has been shown to be largely independent of the particular drug of abuse and thus seems to be a reliable trait marker for addiction, especially given that it has been observed not only for drug rewards, but also for nondrug rewards, such as money.\(^{59}\) The latter makes the MID task an ideal tool for the study of addictive behavior in the context of reward and loss. The way in which the neural response to reward differs between addicted and healthy subjects is discussed in the following section concerning individual influences on reward processing.

**Individual influences on reward processing**

With the observation that certain clinical populations show abnormal delay discounting, a further field of investigation using the MID task is now introduced, along with a few examples, ie, a detailed description of alterations in reward processing in clinical populations, as well as influences of personality traits and changes across the lifespan. This can help to increase our knowledge about the relevant diseases and find new treatment approaches.

For instance, many authors have used the MID task to understand reward and loss in addicts. The observation of steeper delay discounting in addicts raises the question of whether increased discounting is a consequence or a cause of addiction. That is, do genetic factors result in an impulsive personality and thereby increase the likelihood of drug abuse, or is impulsive discounting a repercussion of changes at the neural level due to long-term drug abuse? Generally, while addicts show an increased response of the reward system to drug-related cues,\(^{62}\) overall the data imply that addiction is associated with reduced activation of the valuation network (ie, the ventral striatum and orbitofrontal cortex, including the ventromedial prefrontal cortex) during processing of non-drug rewards.\(^{59}\) Recent evidence from a longitudinal genetic neuroimaging study links decreased reward sensitivity during the anticipation phase of an MID task to a certain haplotype of the ras protein-specific guanine nucleotide-releasing factor 2 (RASGRF2) gene in 14-year-old males.\(^{63}\) This haplotype has previously been linked to addictive behavior,\(^{64}\) and thus represents a possible genetic risk factor for drug addiction. In contrast with this reward deficiency hypothesis, other studies have observed increases in ventral striatal activity during the anticipation of monetary gains in chronic cannabis users,\(^{65–67}\) and a blood-oxygen level-dependent response in the right ventral striatum was found to be significantly correlated with lifetime use and reported lifetime cannabis joints consumed.\(^{67}\) Therefore, the relationship between chronic cannabis use and activity in the ventral striatum might be qualitatively different from that involving other drugs.\(^{68}\) Concerning the question of cause or consequence, a recent study by Patel et al,\(^{69}\) in addition to corroborating the reward deficiency hypothesis, investigated reward processing in former and current cocaine users. Both groups differed similarly from control subjects, but between-group differences were found in the ventral tegmental area during loss outcome and in prefrontal regions during loss anticipation. The authors concluded that current cocaine use may influence reward processing circuits, and that even long-term cocaine abstinence does not normalize most drug-related reward circuit abnormalities. Since both groups showed elevated impulse-related factors that relate to loss, the authors further suggested that these tendencies may predate cocaine addiction. Further, genetic factors have been shown to be associated with altered reward processing in alcoholism.\(^{70}\) Certain variants in the inhibitory \(\gamma\)-amino butyric acid \(\alpha_2\) receptor subunit (GABRA2) gene are linked with higher insular cortex activity during anticipation of reward and punishment, as well as with impulsiveness and familial alcohol abuse. Here, however, changes in dopaminergic activity have not been directly reported, since GABRA2 acts on the production of GABA\(_{\text{A}}\) receptors. All in all, further studies are needed to investigate the extent to which functional differences in former users of cocaine and other drugs reflect pre-existing features, exposure, and recovery.

As another example of changed reward processing in a clinical population, patients with attention deficit hyperactivity disorder show decreased activation in the ventral striatum during anticipation of gain, but increased activation of the orbitofrontal cortex in response to gain outcomes.\(^{71}\) However, these observations of decreased activation of the putamen,\(^{72}\) while being partially confirmed in adults with persistent symptoms of attention deficit hyperactivity disorder, did not prevail in symptom-free adults with childhood attention deficit hyperactivity disorder,\(^{72}\) and behavioral changes in reward processing were not confirmed in other studies.\(^{73,74}\) Thus, although the phenomenon of striatal hypoactivation during reward anticipation is well known in patients with attention deficit hyperactivity disorder,\(^{71,72}\) it would be premature to draw firm conclusions.
Schizophrenia is another disease that has been linked to changes in reward processing. During reward anticipation, schizophrenics show significantly less activation in the ventral striatum, anterior cingulate cortex, and dopaminergic midbrain regions than healthy controls, possibly explaining the symptoms of apathy commonly present in schizophrenia. This attenuation was reduced by treatment with the dopamine agonist amisulpride or with olanzapine. However, this attenuation has not consistently been replicated in other studies. Although there is no clear picture as yet regarding how the reward system may be modified in patients with schizophrenia, probing the integrity of this system may lead to identification of subgroups and tailored treatment concepts.

A recent meta-analysis of the literature on reward processing in major depressive disorder has summarized the results of 22 functional magnetic resonance imaging studies, of which five used variations of the MID task and another seven used conditional learning or guessing tasks with or without rewards to patients. This work yielded rather heterogeneous results, possibly due to the great heterogeneity in the experimental paradigms used. One general finding seemed to be decreased reward-related activity in the subcortical and limbic areas and an increased response in cortical areas. The authors concluded that “future studies may be strengthened by paying careful attention to the types of reward used as well as the different components of reward processing examined”.

As mentioned above, addictive behavior is linked to changes in reward processing, possibly via greater impulsiveness or altered reward sensitivity in addicted individuals. However, in nonclinical populations, reward sensitivity, as measured by questionnaire is a stable trait associated with changes in, eg, reward-based learning and inhibitory control. This trait also has neurophysiologic correlates. For example, individuals with high reward sensitivity show increased responses in the nucleus accumbens and midbrain to reward anticipation, as measured during performance of MID tasks. Further, structural and functional correspondence to high trait reward sensitivity, not directly related to MID task processing, has been described and complement our understanding of individual differences in reward processing. Such changes include diminished striatal volume, increased strength of the white matter tract between the nucleus accumbens and amygdala, more random resting neural dynamics in the nucleus accumbens and orbitofrontal cortex, and less functional connectivity between the midbrain and medial orbitofrontal cortex.

Other personality factors have also been shown to relate to reward processing. For example, Wu et al have investigated the affective traits of positive arousal and negative arousal, as derived by factor analysis from several standard affective personality subscales (ie, the extraversion and neuroticism scores from the NEO-Five-Factor Inventory; actual high-arousal positive and actual high-arousal negative scores from the A Values Inventory; and behavioral inhibition, behavioral activation-reward, behavioral activation-drive, and behavioral activation-fun scores from the behavioral inhibition/behavioral activation scale). These authors demonstrated that during anticipation of large gains, the nucleus accumbens show significantly increased activity bilaterally, whereas during anticipation of large losses, activity in the anterior insular cortex is significantly increased bilaterally. Interestingly, activation increases in the left nucleus accumbens during anticipation of large gains correlate with positive arousal scores, whereas activation increases in the right anterior insula during anticipation of large losses correlate with negative arousal scores.

Further, recent studies have shown that reward processing can be influenced by environmental factors such as stress. Treadway et al demonstrated that subjects reporting a greater impact of stressors had smaller neural responses in the medial prefrontal cortex in response to both monetary gains and losses in an MID task. Similarly, acute stress, induced before performing a guessing task, blunted activation increases in the dorsal striatum and orbitofrontal cortex when compared with a control group not subject to stressors. These studies, although not directly corroborating each other, nevertheless draw a comparable picture, revealing a decrease in mediofrontal reward-related brain activity under conditions of perceived stress, which might relate to the role of stress as risk factor for addictive behavior.

Another topic warranting brief discussion here is the development of reward processing over the lifespan. Although it could be argued that a comparison between healthy adolescents and adults reflects intraindividual development rather than interindividual differences, no longitudinal studies on reward processing beyond adolescence are available, to our knowledge (note, however, the IMAGEN trial following a cohort of 2,000 adolescents and describing, among other things, functional genetics and neuroimaging of the MID task). Thus, studies using the MID task to investigate gain and loss in developmental populations are discussed in this section. Adolescents are of particular interest in this context because of their increased willingness to take risks. Bjork et al were the first to compare patterns in the reward circuit in response to incentive cues
and outcomes between adolescents and adults. They observed lower right ventral striatal and right-extended amygdala activation due to gain anticipation (but not consumption) in adolescents. These findings were subsequently replicated by the same group.97 In contrast, other studies investigating win versus no-win demonstrated stronger activation of the ventral striatum in adolescents, but observation of stronger activation in the amygdala of adults was documented, thus suggesting that “maturing subcortical systems become disproportionately activated relative to later maturing top-down control systems, biasing the adolescent’s action toward immediate over long-term gains”.98,99 The divergence of findings from these different studies has been attributed to sensitivity of the incentive-motivational neurocircuitry to the nuances of the incentive task or stimuli, such as behavioral or learning contingencies and to the specificity of the component of instrumental behavior, such as anticipation versus notification.100 More recently, it was found that, compared with adults, adolescents show less of a linear increase in ventral striatal activity during anticipation of increasing reward magnitude.101 In this study, adults, but not adolescents, demonstrated greater ventral striatal activity in response to the same absolute reward when it was the preferred of two possibilities (ie, $1 versus $0.20 compared with $1 versus $5), indicating that ventral striatal activity in adolescents is less sensitive to relative reward value. Further, reduced ventral striatal sensitivity to absolute anticipated reward correlated with a higher level of trait impulsivity. This finding is consistent with that of another study, in which healthy young subjects, who happened to be steep delay discounters, showed lower responses in the left ventromedial caudate during anticipation of potential reward.102 All in all, although their findings may diverge in some aspects, researchers agree on the attribution of increased risk-taking and impulsive behavior during adolescence to developmental differences in neural processing of rewards. Moreover, with the development of a child-friendly version of the MID task,102,103 the investigation of reward processing in developmental populations can now be validly expanded to children.

Conclusion

We conclude with a short final valuation and synopsis of the use of the MID task. One of the most important achievements of the MID task is to provide a paradigm flexible enough to allow investigation of many facets of reward processing and yet allowing comparison between studies. By parsing the whole process of reward processing, from incentive presentation, task performance, display of approach or avoidance behavior, possible discounting of reward due to delay, and finally reward consumption, researchers are free to focus on any of these steps in a multitude of populations, using different reward modalities and introducing other variations. We have briefly mentioned current developments, eg, the use of the MID task in prospective genetic neuroimaging studies on the development of psychiatric disorders. We have pointed to relationships with other tasks, eg, some forms of conditioning or error processing, thereby placing a special focus on the possible role that agency and goal orientation might have in the processing of rewards and punishments. These relationships should be further explored in future studies, thus integrating knowledge gathered in different fields of research. Some fields of integration are already emerging, eg, elucidating the role played by reward processing in learning mechanisms connected with novelty, or investigating the processing of performance feedback in the framework of reward processing, which may yield new insights into the mechanisms of intrinsic motivation.

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Disclosure

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