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Review

The neuroscience of impulsive and self-controlled decisions

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Abstract

Impulsiveness and self-control are two antagonistic choice patterns. Whereas impulsive decisions can be exemplified by the preference for a small, immediate over a large, delayed reward, self-control can be characterised as the opposite preference order. This review focuses on current developments in investigating the neuroscience of impulsiveness and self-control, with particular emphasis on the neuroanatomy, psychopharmacology, and electrophysiology of this class of decision making. The role of the avian forebrain in representing and processing temporal reward discounting – a chief psychological mechanism responsible for producing impulsiveness – is especially highlighted. In addition to its role in impulsive decision making, the avian forebrain also appears to be involved in processing the key functions required for action- and self-control. In particular, recent electrophysiological studies indicate that single forebrain neurons reflect aspects of response omission strategy and the temporal scheduling of response withholding when execution of action needs to be controlled. In conclusion, the significant advances in this field of research may help to explain neuropathologies that are characterised by exaggerated impulsivity, or lack of self-control, as for instance attention deficit disorders, frontal lobe syndrome, drug addiction, or pathological gambling.

Keywords: Decision making; Impulsivity; Self-control; Temporal discounting; Pigeons; Electrophysiology; Prefrontal cortex; Nidopallium caudolaterale (NCL); Reward

1. Review of the current literature

1.1. Impulsivity and self-control as antagonistic choice dispositions

Virtually all living species frequently make decisions that promise a benefit on the short run, but turn out to be detrimental on the long run. At the same time, humans and other animals have developed more or less efficient ways to manage the temptation of instant gratification whenever the immediate outcomes of a choice are less desirable than the future prospects. The two dispositions that govern decisions about future consequences are called 'impulsivity' and 'self-control'. To simplify matters, we will exclusively use the following definitions of the terms 'impulsivity' and 'self-control', in accordance with numerous other authors (Ainslie, 1975; Logue, 1988; Evenden and Ryan, 1996; note that different definitions of the terms exist; cf. Evenden, 1999a). Whereas 'impulsivity' will be defined as the preference for a small, immediate over a large, delayed reward throughout this review, 'self-control' will refer to the opposite behaviour, i.e. the preference for a large, delayed over a small, immediate reward, unless stated otherwise. With the term 'temporal reward discounting', we refer to the delay-dependent subjective devaluation of a reward, as reflected by a decreasing preference for an increasingly delayed reward. Note that, although the opposite of impulsivity–self-control–may simply result from the lack of impulsivity, self-controlled choices may as well require additional, more complex cognitive control mechanisms, as will be discussed below. This review will focus on some of the recent work on the neuroscience of impulsivity and self-control.

1.2. Preference as a function of reward amount and time-to-reward

An abundance of behavioural studies on the factors influencing the subjective value of a reward has confirmed

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that the selection of an action is influenced by the anticipated reward amount and the delay between response and reward delivery (McDiarmid and Rilling, 1965; Ainslie, 1975; Mazur, 1988; Grossbard and Mazur, 1986; Logue, 1988; Rachlin et al., 1991; Reynolds et al., 2002). Mazur and colleagues developed an adjusting delay procedure to systematically investigate the relationship between subjective reward value, reward amount and delay-to-reward (Mazur, 1988; Grossbard and Mazur, 1986). In this procedure, pigeons chose between a standard alternative, where reward amount and delay were always constant, and an adjusting alternative, where either the reward amount or the delay could be systematically varied. The authors assumed that an equal distribution of choices to both alternatives would indicate the equivalence of the subjective values of both alternatives. They carried out a number of experiments varying delay or reward amount. The equation that described the animals' preference patterns most accurately was a hyperbolical function, suggesting that the subjective value of a response decreased hyperbolically with increasing delay duration. This is an important finding, as the hyperbolical nature of temporal discounting, in contrast to exponential discounting, results in the disproportionate devaluation of future rewards, which is the reason for the preference reversal typical for impulsive decisions (Ainslie, 1975). Most studies on impulsivity cited in this paper used variants of the adjusting delay procedure (Evenden and Ryan, 1996).

1.3. The neuroanatomy of impulsive/self-controlled decisions

Although impulsive behaviour is normal and common to most species, increased impulsiveness and behavioural disinhibition is a key symptom of a large range of pathologies, including attention deficit hyperactivity disorder, drug addiction, pathological gambling, and frontal lobe syndrome. All of these conditions presumably involve a pathological modulation of frontal lobe function. Neuropsychological work on frontal lobe dysfunction has revealed that patients with lesions in their ventromedial prefrontal cortex (VMPFC), which is part of the orbitofrontal cortex (OFC), tend to strongly discount, or even neglect, the future consequences of their decisions, be they appetitive or aversive (Bechara et al., 2000). Due to this and other neuropsychological evidence (Hartje and Poeck, 1997), it was traditionally believed that the prefrontal cortex (PFC) plays a key role in controlling temporal reward discounting and impulsiveness. Recently, animal lesion studies have somewhat challenged this conclusion. Two studies showed that lesions of the rodent (Cardinal et al., 2001) and avian (Izawa et al., 2003) nucleus accumbens (NAc), but not the rodent medial PFC or the anterior cingulate cortex, resulted in a reduced delay tolerance and increased impulsiveness in a modified adjusting delay procedure. Furthermore, lesions of the basolateral amygdala (BLA) increased impulsiveness of rats, but lesions of the OFC and the subthalamic nucleus (STA) actually decreased impulsive choices (Winstanley et al., 2004, 2005a). NAc, BLA, STA, and OFC hence appear to play different roles in impulsive choice behaviour. Winstanley and colleagues conclude that NAc and BLA may be important for representing and maintaining the subjective incentive reward value across the delay, STA may be relevant for permitting basic pavlovian associations, and OFC may play a role in monitoring and updating the representations of the expected rewards. Therefore, lesions of NAc and BLA should increase impulsiveness by impairing the representation or maintenance of incentive salience, but OFC lesions should induce perseveration by impairing the updating of subjective reward value during increasing delays. However, the function of PFC and OFC remain somewhat unclear, as a recent microdialysis study found dissociable roles of medial PFC (mPFC) and OFC in impulsive decision making (Winstanley et al., 2005b; see next section for a more detailed description of this study). The results of this study suggest a direct involvement of the rat PFC in choice behaviour that extends beyond simple outcome monitoring and representation. Because of the heterogeneity in the animal research results, and their (partial) inconsistencies with the clinical reports of increased impulsiveness after PFC and OFC lesions in humans (Hartje and Poeck, 1997), it is questionable whether it is possible to assign a distinct single function to the PFC, or its subparts, in impulsive decision making. It is more likely that the PFC is a part of multiple neural networks that contribute cooperatively or competitively to the generation of choice behaviour. The differential behavioural effects after manipulating parts of these networks depend on the network mechanism, task condition, lesion locus, or experimental manipulation.

In fact, there is evidence from the human imaging literature that several systems in the human brain interact when making decisions between outcomes that differ in their temporal proximity. A functional magnetic resonance imaging study involving choices between rewards with different delays showed that immediate rewards recruited paralimbic areas associated with midbrain dopamine neurons, including NAc, medial OFC, and medial PFC, whereas lateral PFC and the posterior parietal cortex were activated while making choices independent of the delay (McClure et al., 2004). The authors concluded that the impatience associated with the prospect of an immediately available reward was mediated by limbic areas. In contrast, rational and economical planning, and time-reward trade-off were mediated by lateral prefrontal and parietal areas. This conclusion is consistent with the idea of several competing decision-making networks in the brain (McClure et al., 2004; Tanaka et al., 2004; Sanfey et al., 2006). According to this hypothesis, the subjective value of a reward is the result of the interplay between one network processing lower-level automatic processes of reward desiring, the other dealing with the more abstract, future planning and economical reasoning.

1.4. The pharmacology of impulsive decisions

There is ample evidence that the modulation of dopamine (DA) levels as well as dopaminergic areas in the brain affect impulsive choice behaviour. Several studies found that the systemic administration of the D_2 antagonist raclopride and the D_1/D_2 antagonists flupenthixol and haloperidol, but not the D_1 antagonist SCH 23390, increased impulsive choice behaviour (Evenden, 1999b; Wade et al., 2000; Cardinal et al., 2000). The

administration of dopaminergic agonists, as e.g. the psychostimulant *d*-amphetamine, promoted the choice of the large, delayed reward (Richards et al., 1999; Wade et al., 2000), however other studies showed opposite results, namely that the same dopaminergic agonists increased impulsive choices (Evenden and Ryan, 1996). Cardinal et al. (2000) hypothesised that the contradictory effects of *d*-amphetamine might result from the presence or absence of a reward-predicting cue during the delay. They trained one group of rats in an adjusting delay procedure with a reward-predicting cue present during the delay, and another group with no signal. Both groups were systematically treated with varying doses of either the D_1/D_2 agonist *d*-amphetamine, the D_1/D_2 antagonist α-flupenthixol, or the GABA agonist chlordiazepoxide. The results showed that the D_1/D_2 antagonist and the GABA agonist promoted the choice of the small, immediate reward irrespective of the presence versus absence of a cue. However, *d*-amphetamine fostered the choice of the large, delayed reward only in the cued condition, but actually decreased the tolerance for long delays in the no-cue condition. This suggests that D_1/D_2 agonists can improve self-control, but only when the upcoming reward is signalled by a cue during the delay. Other studies showed that the promotion of either impulsivity or self-control by *d*-amphetamine may be dependent on the dose level of the drug (Isles et al., 2003).

In addition to DA, the role of serotonin (5-HT) in impulsive behaviour has been extensively discussed in the context of clinical and basic research. Selective 5-HT reuptake inhibitors as well as full 5-HT agonists decrease impulsive behaviour in pigeons (Wolff and Leander, 2002), and rats (Bizot et al., 1999; Evenden, 1999c). Likewise, lesions of the rat nucleus raphé, which is a main source of 5-HT in the vertebrate brain, results in transient preference for small, immediate rewards (Bizot et al., 1999). However, another study found that 5-HT_2 agonists actually increase impulsivity, whereas 5-HT_{1A} agonists first increase impulsivity at the beginning of a testing session, and then decrease impulsivity at the end of the session (Evenden and Ryan, 1999). A recent microdialysis study contrasted 5-HT and DA modulation of rat mPFC and OFC (Winstanley et al., 2005b). 5-HT efflux was exclusively observed in the mPFC, but not the OFC. Also, increased 5-HT levels were found only under free-choice conditions, but not under rewarded forced-choice conditions (in contrast to free-choice trials, the animals had to make a response for a reward, but could not choose between several response options in forced-choice trials). This suggests that 5-HT levels were related to the actual choice behaviour, and not to the processing of the response–outcome contingencies or the reward. Likewise, increased levels of DA metabolites were found in OFC only under free-choice conditions, whereas increased DA metabolite efflux in mPFC was observed in both free- and forced-choice conditions. This indicates that DA levels in OFC played a role in choice behaviour, whereas DA in mPFC was presumably important for processing reward expectation and/or outcome (Winstanley et al., 2005b). In summary, these data suggest that 5-HT in mPFC, and DA in OFC were directly relevant for making impulsive or self-controlled decisions, whereas DA in mPFC was more relevant for reward processing and/or representing the response–reward contingencies. Furthermore, ethanol (Evenden and Ryan, 1996, 1999), nicotine (Reynolds et al., 2004), and GABA agonists and antagonists (Evenden and Ryan, 1996; Bizot et al., 1999; Cardinal et al., 2000) have also been shown to modulate impulsive choice pattern.

2. Recent evidence for a neural network processing impulsive and self-controlled decisions in the Pigeon

2.1. Decision networks in the pigeon

Despite our increasing knowledge about the anatomy and pharmacology of impulsiveness and self-control, the underlying brain mechanisms are still mainly unidentified. Since pigeons have been the most frequently used species in psychological research to reveal the behavioural processes underlying this type of decision making, they are a suitable animal model to investigate the neuroscience of impulsivity/self-control. In our lab, we have therefore conducted several choice experiments using pigeons.

In a recent study, we attempted to identify the role of the avian forebrain in a task where the preferences for the choice alternatives, as expressed by the animals' relative selection frequencies, were determined by the temporal structure of the response–reward contingencies (Kalenscher et al., 2003). In this task, a concurrent fixed interval schedule, pigeons had to continuously decide to peck on one of two pecking keys. One key, the short-interval key (SI-key), was associated with a time interval of 25 s duration, the other key, the long-interval (LI-) key, was associated with a time interval of 83 s. At the beginning of each experimental session, both interval timers were initiated. Responses on a key during the lapse of the associated interval had no effect, but the first peck once the interval had elapsed resulted in a reward of a fixed amount. Following reward delivery, the timer on the rewarded key was re-initialised and re-started. The pigeons distributed their responses to the two keys according to the matching law (Herrnstein, 1961), which states that the relative rate of responding on a given key should match the relative rate of reinforcement on that key.

Of particular importance, however, was to determine whether the choice frequencies depended on the temporal proximity to the rewards. An analysis of the choice distribution showed that, with decreasing temporal distance to the reward on the SI-key, the response frequency on the SI-key was increasing, whereas the response frequency on the LI-key was falling (Fig. 1A, first panel). Moreover, the frequency of shifts from the SI- to the LI-key was significantly increased just following the delivery of the SI-reward (Fig. 1B, first panel), suggesting that the reward delivery on the SI-key triggered the switch to the other key.

To determine the role of the avian forebrain in producing this reward-related modulation of response frequency and key-switching pattern, we temporarily inactivated the avian nidopallium caudolaterale (NCL) with local microinjections of tetrodotoxin (TTX). TTX temporarily and reversibly prevents

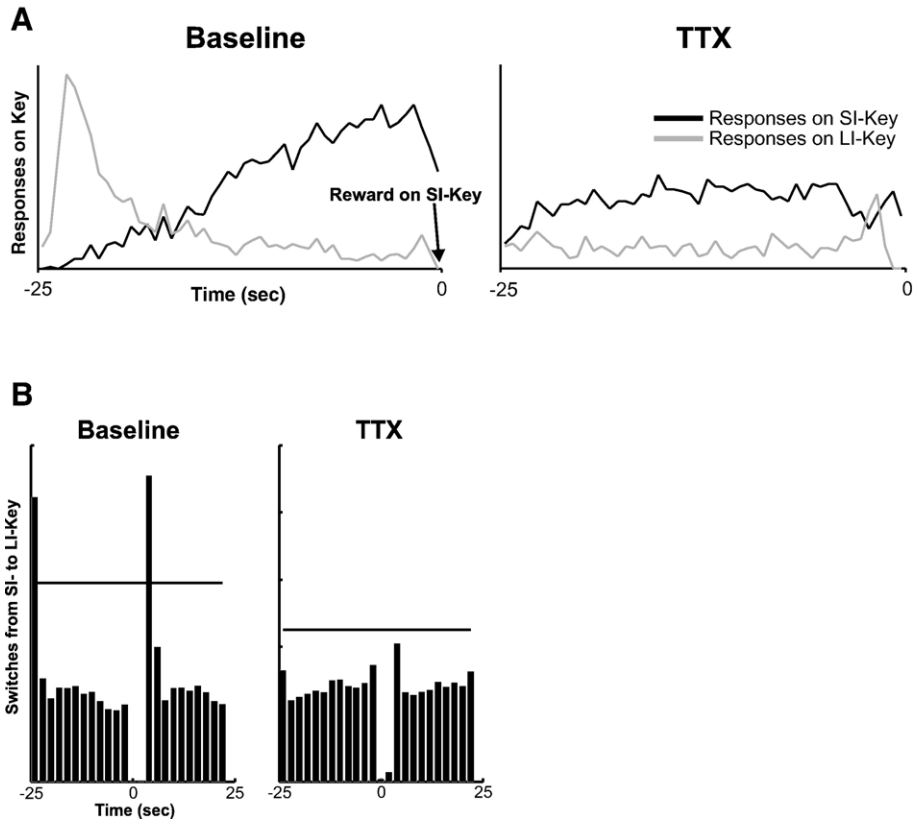

Fig. 1. Effects of NCL inactivation on the choice behaviour in a concurrent interval schedule (Kalenscher et al., 2003). (A) Averaged choice frequencies of the short-interval (SI, black lines) and the long-interval (LI, grey lines) key 25 s before reward delivery following a response on the SI-key. The reward is delivered at time point 0 (right pole of the *x*-axis). The first panel depicts the baseline response frequencies, the second panel depicts the response frequencies following NCL inactivation through microinjections of TTX. (B) Frequencies of changing over from the SI- to the LI-key 25 s before and after reward delivery. Reward is delivered at time point zero at the center of the *x*-axis. The horizontal line depicts the upper threshold of the confidence interval. Modified from Kalenscher et al. (2003), with friendly permission from Blackwell Publishing.

the generation of action potentials, and thus blocks all information processing in the target region (Ambrogi Lorenzini et al., 1997). The NCL is a pallial multimodal association area in the avian brain that is considered functionally equivalent to the mammalian PFC because of cyto-, chemoarchitectonic, connectional, behavioural, electrophysiological and psychopharmacological similarities (Mogensen and Divac, 1982; Kröner and Güntürkün, 1999; Diekamp et al., 2002; Reiner et al., 2004; Jarvis et al., 2005). After TTX injections into NCL, but not after saline control injections, the animals' choice pattern in the concurrent interval schedule was disrupted. Although NCL inactivation did not affect the number of pecks per se, the typical reward-related increase/decrease of the response frequency was significantly flattened, or completely absent in some cases, and the key switching pattern was also disrupted, as pigeons did not systematically change over anymore from one key to another following reward delivery (Fig. 1A and B, second panels).

This change of the response distribution may have several reasons. First, as proposed recently, the forebrain may be necessary to estimate time in interval schedules (Dietrich et al., 1997). This hypothesis implies that, after NCL blockade, the pigeons were impaired in estimating how much time had elapsed since the last reward, and were therefore deficient in predicting the time point of the next reward. Accordingly, the hypothesis predicts that the modulation of the pecking frequency should have been unlocked from interval duration, and the response distribution should have consequently been levelled out. However, this hypothesis fails to explain the change in the key-switching pattern following NCL inactivation. Under baseline conditions, the pigeons switched keys immediately following reward delivery, as explained above. Such reward-triggered switching behaviour could occur even if the pigeons lacked any sense of time. Therefore, the timing-deficiency explanation alone cannot account for the sudden absence of reward-triggered key-switches. Alternatively, the animals may have preserved their ability for time estimation, but they may have been unable to use the time information to integrate it with their reward prediction signal. According to this hypothesis, pigeons would still anticipate a reward at some point in time, but they would be unable to use information regarding reward timing and/or reward probability to translate it into response selection. This hypothesis predicts that the proximity to the next reward should be particularly important for evaluating and weighing the choice consequences, and selecting a response accordingly, and the NCL should play a pivotal role in processing this evaluation and selection process.

2.2. Single forebrain neurons integrate reward amount and time-to-reward to represent the subjective reward value during impulsive decision making

To address this issue more closely, we trained pigeons in an adjusting-delay self-control task (Kalenscher et al., 2005b). In this paradigm, the values of the available choice consequences were systematically varied by manipulating the timing of the reward. Hence, time was the crucial, choice-determining factor. The animals had the choice between two pecking keys. Responses on one key resulted in the delivery of a small reward with a constant short delay between response and delivery. Responses on the other key resulted in a large reward that was also delivered with the same short delay at the beginning of each session, but that was increasingly delayed as the sessions progressed. Typically, pigeons began a session by preferring the large reward, but they showed a characteristic within-session preference shift to the small, immediate reward once the delay preceding the large reward exceeded an individually different tolerance limit. This behavioural result was in line with the literature cited above in that it shows that preference for a reward depended on its subjective value, which was a function of reward amount and delay-to-reward.

Many studies have shown that the individual constituents of this function are represented in the brain. The amount of an anticipated reward is encoded by single cells in various parts of the brain, including the dorsolateral and orbitofrontal cortex (Leon and Shadlen, 1999; Wallis and Miller, 2003), single units in PFC and other areas have been shown to play a role in time estimation (Brody et al., 2003; Leon and Shadlen, 2003), and single neurons also represent the relative preference for a reward (Tremblay and Schultz, 1999). However, it is unknown how these constituents are neurally integrated to represent the temporally discounted subjective value of an expected reward.

We therefore conducted single cell recordings in the NCL while the pigeons performed the self-control task described above (Kalenscher et al., 2005b). Many recorded neurons exhibited significantly enhanced and sustained delay activity during the period between response and reward delivery. It was of particular interest whether these units showed differential activity patterns before vs. after the pigeons performed the characteristic preference shift from the large, delayed to the small, immediate reward. And in fact, some of these neurons systematically decreased their activation level with increasing delay length across trials preceding the preference shift (Fig. 2A), whereas they showed no variation in their activation magnitude after the preference shift, i.e., when the pigeons chose the small reward and the delay was, thus, constant (Fig. 2B). Hence, the activation magnitude of these cells was inversely proportional to the duration of the delay, and thus appeared to encode delay length. In addition, further analysis showed that, when the delays to both rewards were equivalently short, the same neurons were more active in anticipation of large rewards compared to small rewards (Fig. 2C). This illustrates that the neural activation was not only modulated by a single choice parameter, but by both parameters 'delay length' and 'reward amount'. In other words, their compound activation seemed to represent the integration of delay and reward amount, and hence the temporally discounted subjective value of the anticipated reward. Moreover, the neural signal was best approximated by a hyperbolic compared to an exponential or linear model. This observation coincides with the psychological studies cited above showing that the behavioural results in similar self-control tasks are also best described by a hyperbolic function (Ainslie, 1975; Mazur, 1988; Grossbard and Mazur, 1986).

Recent evidence indicates that the neural representation of temporally discounted reward value is not an exclusive capacity of the pigeon brain. In one study, time- and reward amount coding cells were identified in the monkey OFC (Roesch and Olson, 2005). The authors trained their animals in a forced-choice task where either the reward amount or the delay between task onset and response execution were systematically, but not simultaneously varied. They found that the same neurons that encoded the pre-response delay in one task also encoded the amount of the upcoming reward in a second task. This study suggests that the reported neurons were tuned to represent both reward dimensions, and that they presumably coded the temporally discounted value of the upcoming reward, albeit it did not show a neural integration of reward amount and delay. In addition, there is preliminary evidence presented at a recent neuroscience conference that units in the rat OFC (Roesch et al., 2005), monkey lateral intraparietal area (Louie and Glimcher, 2005), monkey dorsolateral PFC (Hwang and Lee, 2005), and possibly also human amygdala and striatum (Gregorios-Pippas et al., 2005) integrate reward amount and delay in adjusting delay tasks.

In conclusion, the two crucial parameters 'reward amount' and 'time-to-reward' that determine the temporally discounted subjective reward value in impulsive decision making, are integrated on the level of single forebrain neurons. A dysfunctional integration, e.g., an over-weighting of the time component, may result in an accelerated rate of temporal discounting, and may thus account for the exaggerated and detrimental impulsive choice behaviour that is characteristic for various pathologies, such as drug addiction, gambling, frontal lobe syndrome, and attention disorders.

2.3. Neural correlates of action control

The above promoted definition of self-control implies that individuals are self-controlled as long as the subjective value of the temporally distant reward exceeds the value of the proximal reward. However, if this was the only cognitive self-control mechanism, organisms would decide impulsively, and would always opt for the potentially disadvantageous, but immediately available alternative as soon as the value of the distant reward dropped below that of the immediate reward, e.g., due to the increasing delay. According to this view, self-control would be defined as the absence of impulsivity. Consequently, impulsiveness and self-control should be just two sides of the same medal, i.e., of the same mental process.

Yet, humans, and possibly other animals too, are (at least occasionally) able to control their actions by sheer will-power. This somewhat more intuitive concept of self-control

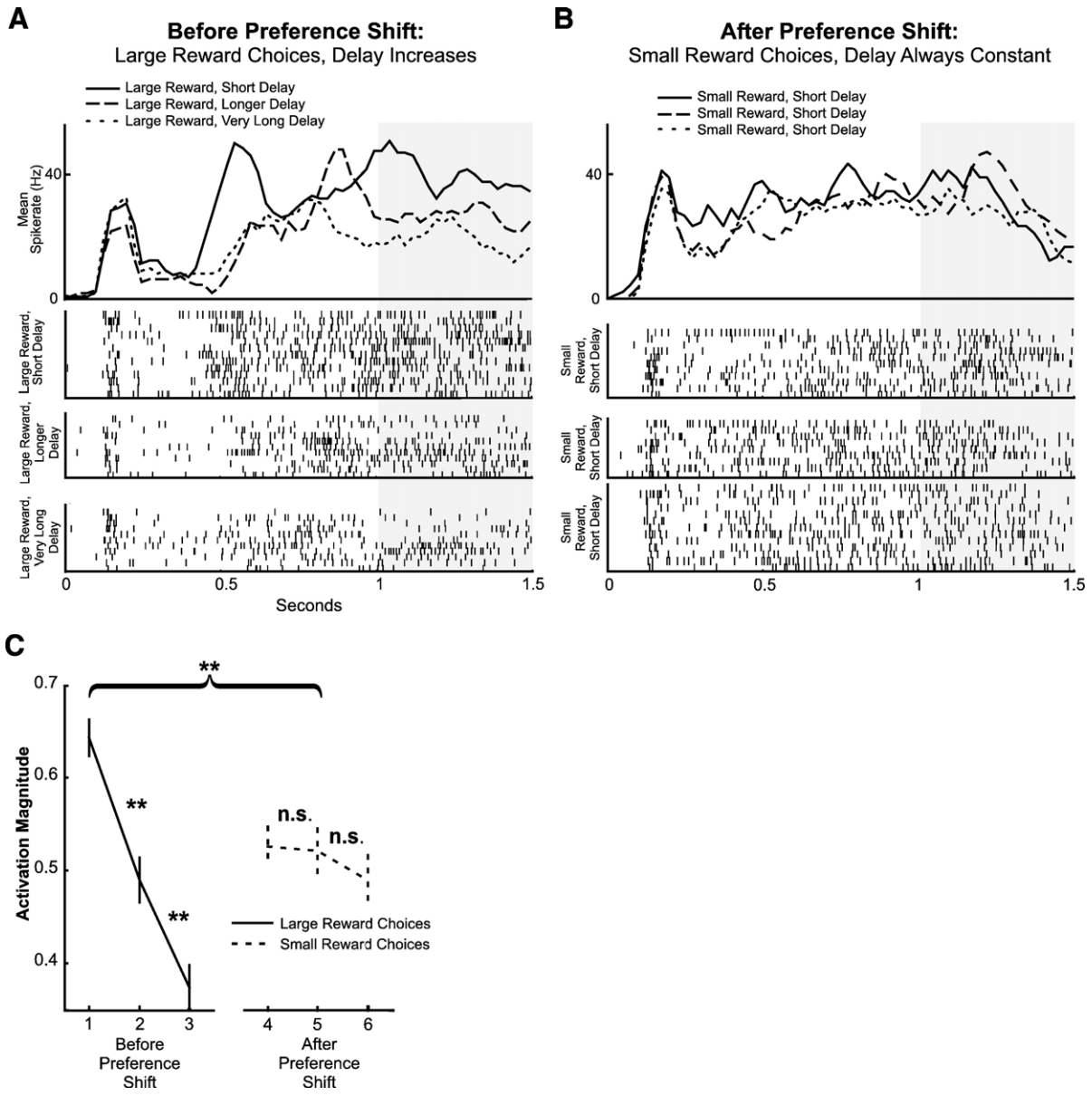

Fig. 2. Neural correlates of temporally discounted subjective reward value during impulsive decision making. Neural activity before and after the preference shift from the large, delayed to the small, immediate reward. (A) Averaged and smoothed peri-stimulus time histograms (PSTHs) and raster plots of the sustained delay activity of one neuron across trials where the pigeon prefers the large reward (before the preference shift). The PSTHs indicate the neuron's discharge rate, each vertical bar in the raster plots represents one spike, each row corresponds to one trial. The delay between response and reward is gradually increased. The solid black line indicates the PSTH for early trials where the delay was minimal, the dashed line indicates the PSTH in trials where the delay was somewhat longer, and the dotted line indicates the PSTH in trials where the delay was maximal, and the preference shift to the small, always immediate reward was just about to occur. The grey box indicates the final level of neural activation. (B) PSTHs and raster plots of the same neuron across trials following the preference shift where the pigeon prefers the small, always immediate reward. (C) A measure of the activation pattern of all neurons of interest. The left part of the panel (tick marks 1–3 on the *x*-axis, the tick marks are referring to block numbers, the delay is increasing across blocks of trials) shows the development of the activation magnitude across trials before the preference shift, i.e., pigeons prefer the large reward and the delay length is increasing. The right part of the panel (tick marks 4–6) shows the activation pattern across trials following the preference shift, i.e., pigeons prefer the small reward and the delay length is constantly short. This figure confirms that the neural activity is negatively correlated with delay duration, but it also shows that the same neurons have higher activity in anticipation of large compared to small rewards when the delay preceding both rewards is equivalent (tick mark 1 compared to tick marks 4, 5, or 6; horizontal bracket). $^{**}p<0.01$. Modified from Kalenscher et al. (2005b), with friendly permission from Elsevier.

incorporates supplementary psychological mechanisms in addition to those responsible for producing impulsiveness. Such processes include the ability to control and suppress a prepotent tendency to make a particular choice or execute a particular response. Hence, in order to capture the neural character of this type of self-controlled decisions, it is important to target the mechanisms underlying the ability for response inhibition. We therefore recorded single-cell activity in NCL while pigeons performed a delayed Go–NoGo task – a classic paradigm to investigate response inhibition (Kalenscher et al., 2005a). The behavioural results suggested that the pigeons needed working memory to correctly perform the Go-trials, but refrained from

responding in NoGo-trials without employing working memory. This asymmetry in memory usage indicated that the pigeons omitted their responses by default in the NoGo trials (Grant, 1991) – a strategy that was reflected by an asymmetric activation pattern of NCL neurons in Go vs. NoGo trials (Kalenscher et al., 2005a).

Default response omission is a rather passive form of self-control. In order to investigate a more active control of action, we trained pigeons in a paradigm which made it necessary to temporarily inhibit for a limited time the impulse to peck on a key. The task consisted of two conditions. In the 'rapid response' condition, animals had to peck on a response key as fast as possible following the onset of the key illumination. In the 'wait' condition, they had to withhold their response for a short time period (1.5 s) following key onset, and then had to respond within another short time window. The length of the 'wait' period and the following onset of the response window were not indicated, and had to be estimated by the pigeon. Incorrectly timed responses were mildly punished with a short light-off period. This task, hence, required to actively withhold the response, and to estimate the duration of the required 'wait' period.

Single cell recordings of NCL neurons revealed that some units had significantly enhanced activity during the period between key onset and motor execution. Some of these cells showed climbing activity, i.e., a steady increase in discharge frequency following key onset, until a maximum rate was reached (Fig. 3). Interestingly, the slopes of the neural ramps differed between 'rapid response' and 'wait' condition. It was steeper and peaked earlier in rapid-response trials compared to waiting-trials, suggesting that slope and peak of the curves were adjusted to the duration of the required response latency (Fig. 3A). If this hypothesis holds, then one would expect that slope and peak of the climbing function would be incorrectly scaled in error trials. And that is exactly what we found: When pigeons responded prematurely in the 'wait' condition, the activity ramp peaked too early compared to correct trials (Fig. 3B). Likewise, when pigeons responded too late in 'rapid response' trials, the neural function peaked later than normal (Fig. 3C).

Climbing activity is a prominent profile of neural activity observed in prefrontal cortex and other brain areas. Several authors have proposed that the adjustment of its slope and peak time may be causally related to interval time estimation, e.g., in working memory or reward prediction tasks (Brody et al., 2003; Durstewitz, 2003; Reutimann et al., 2004). Applied to the results in the pigeons' self-control task, the ramping activity presumably reflected the animals' internal estimation of the duration of the required 'wait' interval. There are two possibilities how time information could be implemented to solve the present task: 1) The pigeons may have inhibited the already prepared response, and released the response following the estimated lapse of the 'wait' interval, or 2) they may have scheduled the timing of the response, for example, by planning and programming the response latency during the premotor phase by adjusting the slope of the climbing function. Future studies need to determine which scenario best explains the

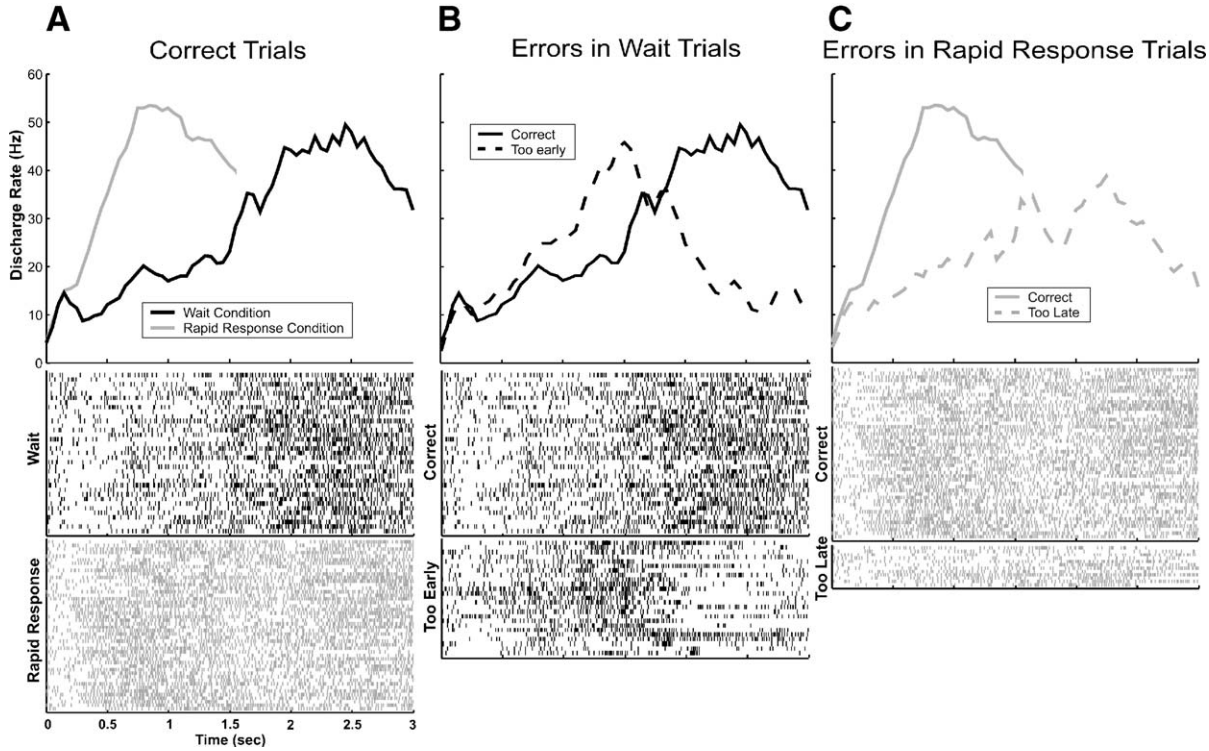

Fig. 3. Neural correlates of active action control in a temporal response scheduling task. PSTHs in the three seconds following the onset of key activation. (A) Discharge rate (Hz) and raster plots of a single NCL neuron of correct trials in the 'wait' (black lines) and the 'rapid' response condition (grey lines). Each vertical bar in the raster plots represents one spike; each row corresponds to one trial. (B and C) Discharge rate of the same neuron in error trials (dotted lines and lower raster plots) in comparison to correct response trials (solid lines and upper raster plots).

present results. Whatever the underlying response control mechanism was, we believe to have identified the neural correlates of an essential aspect of action control: the use of time information for response scheduling and inhibition.

2.4. Summary

This review has summarised a selection of the most recent literature on the neuroscience of impulsive and self-controlled decisions. In mammals and birds, dopaminergic and serotonergic systems and their origin and target structures are involved in shifting the choice disposition between self-control and impulsiveness. Mammalian and avian forebrain structures appear to play a key role in representing the temporally discounted subjective reward value, and reflecting the computational processes underlying some of the most crucial requisites of self-control, i.e., when and for how long a response needs to be inhibited. The PFC may, therefore, be an essential part of a set of inter-connected neural networks that are distributed across the entire brain, and that work in concert to link the different processing levels in the sensory–cognitive–motor loop (Başar et al., 2000; Fuster, 2003; Başar, 2005).

3. List of abbreviations

5-HT	serotonin
BLA	basolateral amygdala
DA	dopamine
LI-key	long interval key
mPFC	medial prefrontal cortex
NAc	nucleus accumbens
NCL	nidopallium caudolaterale
OFC	orbitofrontal cortex
PFC	prefrontal cortex
SI-key	short interval key
STA	subthalamic nucleus
TTX	tetrodotoxin
VMPFC	ventromedial prefrontal cortex

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