Mechanisms of abstract decisions in the monkey frontal cortex

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Katharina Merten
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Dekan der Math.-Nat. Fakultät:	Prof. Dr. W. Rosenstiel
Dekan der Medizinischen Fakultät:	Prof. Dr. I. B. Autenrieth
1. Berichterstatter:	Prof. Dr. A. Nieder
2. Berichterstatter:	Prof. Dr. U. Ilg
3. Berichterstatter:	Prof. Dr. G. Rainer
Prüfungskommission:	Prof. Dr. A.Nieder
	Prof. Dr. U. Ilg
	Prof. Dr. H. P. Thier
	Prof. Dr. C. Schwarz

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Tübingen, _____ _____

Katharina Merten

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Synopsis

Mechanisms of abstract decisions in the monkey frontal cortex

Katharina Merten

Department of Animal Physiology
Institute of Neurobiology
University of Tübingen, Germany

Introduction

What is a decision?

"If you have made a decision that was entirely based on factual information, you have not made a decision; it was made for you by the facts."

Elliott Jaques

Decisions are indispensable for animals and humans in situations of uncertainty. The choice cannot be based on hard facts only when the available information is ambiguous and noisy, or when rapid decisions are required and the information is incomplete or overwhelming. People often refer to their "gut feeling" when they try to explain their choice. Such subjective judgments arise from internal mechanisms in the brain.

Decision-making is defined as an evaluative process of selecting one particular option from a set of alternatives (Gold and Shadlen, 2007). This cognitive process involves the acquisition, processing, and storage of relevant information from the environment, as well as the interpretation of this information in accordance with internal goals and experiences. Cognitive control mechanisms override reflexive or habitual reactions to allow for a flexible selection of behavioral responses depending on the context of a situation. Thus, decision-making is a central element of human and animal life and essential for what we consider as intelligent behavior (Miller, 2000; Gilbert and Burgess, 2008).

In summary, several characteristics determine a decision (Wang, 2008). First, the choice alternatives have to involve an expected set of options. Second, a decision process must involve the accumulation of relevant information and a deliberate consideration of options. Finally, decisions are essentially risky, as they are made under uncertainty conditions and the commitment to a choice has consequences.

Classes of decisions

Two main classes of decisions can be described based on the type of information that is processed or on the type of choice outcome: value-based decisions and perceptual decisions (Gold and Shadlen, 2007). The processing of rules and algorithms that are used to map input information to particular actions (Miller et al., 2003) are considered by some researchers as a third decision class (Freedman and Assad, 2011). In my view, these tasks do not fulfill the criterion of uncertainty as the acquired information is usually salient and the rules and algorithms are well trained.

Value-based decisions are often referred to as economical decisions and are preliminary based on the value associated with each of the possible alternatives (Glimcher, 2005; Sanfey et al., 2006; Padoa-Schioppa, 2011). Thus, economic decisions can be described as behavior, observed when individuals make choices relying on subjective preferences

only, e.g., the choice of an ice cream flavor in a gelateria or a choice of a house for sale. Value is the unit, which represents the common measure of the multiple dimensions of the choice options. The study of value-based decisions addresses how the values are computed and compared in the brain.

The class of the perceptual decisions is defined by the type of information that is processed to make a choice. Perceptual decisions involve monitoring of sensory information, combination of this information across different sensory modalities, and accumulation in time. Internal brain processes evaluate this information and transform it into categorical choices and appropriate behavioral responses (Gold and Shadlen, 2007; Deco and Romo, 2008). Typical examples are detections of stimuli (de Lafuente and Romo, 2005; 2006), discriminations of stimuli (Newsome et al., 1989; Shadlen and Newsome, 2001; Romo et al., 2004), or categorizations of percepts (Beale and Keil, 1995; Freedman et al., 2001; Nieder et al., 2002; Sigala and Logothetis, 2002; Nieder and Merten, 2007). Perceptual tasks are markedly useful for the study of decision processing. Here, the quantity and the quality of the sensory input can be controlled precisely and the behavioral responses can be quantified easily. The decisions I investigate in my thesis belong to the class of the perceptual decisions.

Detection decisions

The detection of a sensory stimulus is the most elemental perceptual experience and is a prerequisite for any further sensory processing. Perception refers to a subjective process of becoming aware of a physical stimulation (Pomerantz, 2006). Remarkably, when an ambiguous or noisy sensory stimulus is presented, a percept may, or may not be produced. Therefore, the initial stimulus effect on the senses requires further cortical processing that determines whether a subjective experience of this sensory event will be generated or not. From a theoretical point of view, the underlying neuronal substrate of detection could be based on bistable dynamics with two stable states ('stimulus detection' or 'no stimulus'). Both states should coexist for the same stimulus condition. In the simplest case, if no biases for a particular stimulus condition exist, probabilistic fluctuations would drive the system to one or another state (Faisal et al., 2008). In this regime, the processing of percepts appears to be a striking resemblance of decision-making mechanisms (Wang, 2002; Brody et al., 2003), meaning that perception might be regarded as a result of a decision-making process (Deco and Romo, 2008).

The peculiarity of detection decisions is that only one choice alternative, the presence of a stimulus, can arise from a physical sensory signal, whereas the alternative decision about stimulus absence cannot be confirmed by an external sensory event. For this reason, two hypotheses for the neuronal processing of detections can be proposed. First, the choice of stimulus absence might be represented by a default, spontaneous stable state, whereas the other stable state of stimulus-detection would correspond to an active state generating a percept. This view is held by classical psychological and neural models of detection (Green and Swets, 1966; Thompson and Schall, 1999; Shulman et al., 2001; Ress and Heeger, 2003; de Lafuente and Romo, 2005). They suggest that sensory evidence is accumulated for the “stimulus present” decision, but the “stimulus absent” decision is represented by a default (baseline) neuronal response.

Alternatively, both choice options might be represented by two active stable states, whereas the stimulus absence would be encoded as a discrete category and not merely as "noise". The processing mechanism of detection decisions represents the central question of my thesis.

Framework of the study of perceptual decisions

Our understanding of how and where in the brain perceptual decisions are processed has benefited from a study of these processes in an action-based framework. From this perspective, decisions are reduced to choices among motor actions associated with particular stimuli (Schall, 2001; Gold and Shadlen, 2007; Shadlen et al., 2008; Wang, 2008). Because perceptual decisions were studied as intensions to select an appropriate motor response, brain areas were targeted, which are involved in planning and preparation of motor actions. Mainly the lateral intraparietal area (LIP), but also the superior colliculus, and the frontal eye field were shown to participate in dot-motion discrimination tasks and to convert motion evidence into a behavior plan (Horwitz and Newsome, 1999; Platt and Glimcher, 1999; Shadlen and Newsome, 2001; Roitman and Shadlen, 2002; Yang and Shadlen, 2007).

In particular, for detection decisions, Romo and colleagues (de Lafuente and Romo, 2005; 2006) reported that only one choice category (stimulus presence) was actively represented. Neurons in the medial premotor cortex (MPC) were found to modulate their responses categorically during stimulus presence decisions; the decision about stimulus absence was represented as a default (baseline) neuronal response (de Lafuente and Romo, 2005). The proportion of such neurons has been shown to progressively increase from sensory towards higher cortical areas (de Lafuente and Romo, 2006; Hernández et al., 2010).

However, the implications of these findings remain unclear, as the decision about the stimulus remains indistinguishable from the motor report or even might not be represented as a discrete processing step (Cisek and Kalaska, 2010; Freedman and Assad, 2011). In order to study the abstract perceptual decision, one would need to disentangle the processing of the decision from the selection of the motor action in the brain. In such report-independent framework, discrimination decisions have been shown to be encoded by neurons in the LIP independently from how they signaled the corresponding motor response (Bennur and Gold, 2011). Here, the processing of the decision might be regarded as an abstract process. Detection decisions have not been investigated in an abstract framework so far.

Frontal cortex as an ideal candidate area for abstract decisions

The substrate for the processing of abstract decisions should be a module that is able to operate functionally separate from the motor effector systems. That means, the link between interpretation of sensory information and action should be more flexible than in brain areas encoding the intended movement purpose. The ideal structure for

abstract decisions should allow for the expression of information in a non-movement related framework, to support independent neuronal processing before any external actions are planned. The structures of the frontal lobe appear to fulfill this requirement.

A candidate frontal cortex region for the processing of abstract computations is the prefrontal cortex (PFC), which is known to operate at the apex of cortical hierarchy (Fuster, 2008). The PFC is interconnected with virtually all sensory neocortical and motor systems and with a wide range of subcortical structures (Goldman-Rakic, 1987; Pandya and Barnes, 1987; Barbas and Pandya, 1991; Fuster, 2008). This provides an ideal infrastructure for integration of a wide range of information and exertion of 'top-down' influences on various brain processes essential for complex intelligent behavior. In particular, the dorsal portions of the lateral PFC are directly interconnected with higher order sensory and motor cortex, so the neurons in this area show multimodal responses (Vaadia et al., 1986; Watanabe, 1992; Rao et al., 1997; Rainer et al., 1998). They are critical for learning of associations between sensory cues (Fuster et al., 2000; Diester and Nieder, 2007), rewards, and voluntary goal-directed actions (Petrides, 1985; Gaffan and Harrison, 1988; Petrides, 1990; Parker and Gaffan, 1998).

Moreover, there are ample interconnections between different PFC areas and higher-order association and premotor cortices (Bates and Goldman-Rakic, 1993; Lu et al., 1994; Wang et al., 2005), which bring together results from a variety of brain processes and allow for the extraction of regularities, general principles, or rules. The PFC involvement has been demonstrated in highly abstract processes: e.g., processing of abstract categories (Freedman et al., 2001; Nieder et al., 2002; 2006; Nieder and Merten, 2007), abstract rules (White and Wise, 1999; Wallis et al., 2001; Bongard and Nieder, 2010), or strategic planning (Genovesio et al., 2005; Mansouri et al., 2007). Humans with prefrontal damage retain their memories, speech, and motor skills, however, they are impulsive and irresponsible so that they have trouble to organize their lives (Damasio, 2008). The ability to override and change established impulses to more appropriate knowledge-driven behavior is impaired as has been shown in the Wisconsin Card Sorting task for humans (Milner, 1963) and in an analogue of this task for monkeys (Dias et al., 1996).

In addition, areas traditionally associated with motor preparatory activities might also be involved in the processing of abstract perceptual decisions. For example, the MPC has been shown to participate in complex cognitive processes such as sensory-motor associations, recall of memories and timing of sequential motor actions (Tanji, 1994; Picard and Strick, 1996; Geyer et al., 2000). Particularly interesting is the presupplementary motor area (preSMA). It projects sparsely to the corticospinal system and the primary motor cortex (Dum and Strick, 1991; Luppino et al., 1994), yet it is extensively interconnected with non-primary motor structures (Luppino et al., 1993). Therefore, preSMA appears to be responsible for more abstract, cognitive, high level motor functions like the sequential organization of multiple movements (Shima and Tanji, 2000; Nakajima et al., 2009). Updating of motor plans (Shima et al., 1996) and switching from automatic to controlled actions (Isoda and Hikosaka, 2007) are further tasks processed by this area. Accordingly, a patient with a lesion in the preSMA had difficulties in a hand-movement change-of-plan task. Once commited to an action, he was unable to switch to an alternative movement (Nachev et al., 2007).

In the cingulate sulcus, the rostral cingulate motor area (CMAr) is a candidate to be involved in cognitive processing. The CMAr receives direct input from the PFC (Lu et al., 1994), has prominent projections to the primary motor cortex (Bates and Goldman-Rakic, 1993; He et al., 1995; Dum and Strick, 2002) and to the corticospinal system (Hutchins et al., 1988; He et al., 1995). This structure has been shown to be involved in the initiation and execution of arm movements (Shima et al., 1991; Procyk et al., 2000). Further, the activity of the CMAr is influenced by emotional and motivational states as it receives input from the limbic system (Amaral and Price, 1984; Morecraft and Van Hoesen, 1998) and thalamic nuclei (Vogt et al., 1987; Vogt and Gabriel, 1993). The anterior cingulate cortex is the main target area of the mesocortical dopamine system (Lewis, 1992; Vogt and Gabriel, 1993), this implicates CMAr in error detection (Gemba et al., 1986; Ito et al., 2003) and converting reward value into action (Shima and Tanji, 1998). Most important, a recent study describes the involvement of this area in abstract rule processing (Vallentin et al., 2012) and highlights the role of CMAr in cognition.

It is of great interest to investigate whether PFC, preSMA, and CMAr are capable of processing a decision as an abstract category. Alternatively, preSMA and CMAr might contribute to decision processing only when information about the motor activity is available (e.g. in a report-dependent framework).

Approaches to study decision processing mechanisms

The question about the mechanisms through which a particular behavior is generated can be ideally addressed at the systems level of neuroscience. Extracellular recordings in behaving animals are typically used to investigate single-cell physiology and anatomical characteristics of a brain function and provide indispensable insights into the representation of these functions.

Additionally, computational modeling is an important tool for characterizing the underlying neural circuits of a processing mechanism. Theoretical approaches help to construct concepts and principles of processing, to build bridges between different levels of neuroscientific descriptions (single cells, populations of neurons, and psychophysics), to simulate particular situations and make predictions about the behavior of the system. Therefore, computational modeling substantially amends electrophysiology.

Computational approach to study decisions

Models of decision-making have been mainly proposed on two levels of description: phenomenological and mechanistic level. Phenomenological models summarize experimental results accurately characterizing the functions of neural circuits. These models might only loosely relate to the biophysical, physiological substrates. The primary goal of these models is to describe phenomena, not to explain them (Dayan and Abbott, 2005). Representative examples of such decision models are diffusion and race models, which are based on accumulation of sensory evidence for different alternatives

until a decision criterion is reached (Gold and Shadlen, 2007). These models capture very well the concepts like trade-offs between speed and accuracy of decision-making (Smith and Ratcliff, 2004; Gold and Shadlen, 2007), but it is difficult to assign biological meaning to the model parameters (Deco and Romo, 2008).

Mechanistic models, on the other hand, are tightly related to the anatomical and physiological findings. These biologically plausible models are based on anatomically plausible architecture. Spiking properties of neurons are described on a high level of accuracy and also the synaptic connections are quantitatively calibrated (Machens et al., 2005; Jazayeri and Movshon, 2006; Deco and Romo, 2008; Wang, 2008).

All decision-making models so far attempt to explain results, or originate from data of decisions studied in an action-based framework. It would be of great importance to construct a model for processing of abstract perceptual decisions on a biologically plausible level, which would allow further insights into the processing mechanisms and networks. Especially, modeling the elemental abstract detections might provide a building block for the understanding of more complex abstract perceptual decisions.

In my PhD thesis, I investigated the processing mechanisms of abstract detection decisions on the neurophysiological and computational levels. In the following, I will summarize the experimental and methodological approaches and describe the main findings of the studies. The final part of the work comprises the discussion of the results of all studies and the conclusions I can draw from my work.

Chapter I

Active encoding of decisions about stimulus absence in primate prefrontal cortex neurons

In the first study the implementation of abstract detection decisions, not linked to motor actions, was investigated. For this purpose, a rule-based perceptual detection task was designed, which allowed the separation of the decision process from the initiation of the corresponding motor report. Non-human primates are outstanding model organisms for the study of such highly cognitive tasks. I trained two rhesus monkeys to perform the behavioral task. The monkeys were seated in a primate chair; they fixated a central spot on a computer screen, and grasped a bar to indicate their readiness to perform the task. Randomly, in 50 % of the trials a faint grey object appeared in the middle of the screen; in other half of the trials the stimulus was absent. To introduce uncertainty to the task, the intensity of the visual stimuli varied between nine grey values centered around the perceptual threshold of the animals. During a following delay phase, on each trial, the monkeys were required to make the decision about the presence or the absence of the visual stimulus. Yet, only after the presentation of a rule-cue, a red or a

blue square, the monkeys could start to prepare a motor action to report the decision outcome, because the rule-cue informed the animals about the appropriate motor response. If the stimulus was present, a red cue instructed the monkey to release the bar; the blue cue to keep holding the bar to receive a fluid reward. In the stimulus absent trials, the rule applied in the inverse way: the red cue required the holding of the bar; the blue cue bar release. This task design clearly dissociated the processing of the decision from motor preparation activity and allowed the testing of the hypotheses proposed for the processing mechanisms of perceptual detections.

Both monkeys have reliably learned the complex task. The possible decision outcomes were: hits - correct detections of stimuli; misses - erroneous rejections of a presented stimulus; correct rejections - correct reports of an absent stimulus; and false alarms - erroneous reports of the presence of a stimulus. For trials with a salient stimulus, the monkeys reported in almost 100 % stimulus presence. If no stimulus was presented, in about 90 % of trials stimulus absence was reported. For near-threshold stimuli about half of the trials were hit trials, the other half misses.

While the monkeys performed the detection task, I recorded the activity of 708 neurons from the PFC of both monkeys. To investigate the processing of the abstract decision, I analyzed an early and a late period of the decision, still before motor preparation could take place. During both analysis phases, the discharge rates of single PFC neurons covaried with the monkeys' subjective judgments about the stimulus presence or absence. The responses of the decision neurons were highly relevant for the behavior of the animals. The firing rates of the neurons correlated not only with monkeys reports in correct stimulus present and stimulus absent decisions, but also with erroneous decisions (false alarms and misses). Only a small proportion of decision neurons were additionally weakly modulated by the intensity of the physical stimulus.

During the early decision phase, the detection processing mechanism proposed by the first hypothesis was confirmed: the abstract 'yes, stimulus present' decision was actively encoded by PFC neurons; the 'no, stimulus absent' decision was represented by default, spontaneous neuronal firing rates. However, during the late delay phase, the alternative hypothesis was true: both choice options were represented by two active populations of neurons, which modulated their discharge rates for 'yes' or 'no' decisions respectively, predicting the monkey's subjective decision report. The active encoding of the stimulus absent condition (the 'no' decision) is the main finding of this study. This class of active 'no' neurons represent an abstract category that is neither generated by a specific input (no physical signal was present), nor linked to a preparation of a motor response (as the activity is modulated before the rule-cue is presented). This work has been published in the journal *PNAS* (Merten and Nieder, 2012).

Chapter II

Comparison of abstract decision encoding in the monkey prefrontal cortex, the presupplementary and cingulate motor areas

The second part of my work investigated the contributions of three different frontal brain areas to the processing of abstract perceptual decisions. I recorded the activity of single neurons in the preSMA and the CMAr using the same behavioral protocol as in the first study and compared the processing to the mechanisms I found in the PFC (Merten and Nieder, 2012). In total, I recorded 520 neurons in the preSMA and 149 single cells in the CMAr, simultaneously with the recordings in the PFC, 708 neurons. To compare the representation of abstract decisions in these more motor-related areas to the PFC neurons, implicated in complex cognitive processing, neuronal activity was analyzed during the abstract decision phase (stimulus and delay phase, similar to the first study) and during the motor phase (period short after the presentation of the rule cue, which instructed the motor response).

Interestingly, already during the abstract decision phases both, the preSMA and the CMAr, encoded the subjective decision about the stimulus presence or absence. Just as in the PFC, in the stimulus phase, only active 'yes' neurons encoded the decision; during the delay phase both classes of neurons, active 'yes' and active 'no' decision neurons, represented the subjective judgment of the monkeys. Surprisingly, a significantly higher proportion of preSMA neurons (13 %) compared to 8 % in the PFC encoded the decision during the stimulus phase. Around 11 % of the CMAr neurons covaried with the monkey's decision in the stimulus phase (not significantly different from the PFC and preSMA). During the delay phase, the proportions of the decision cells were comparable 18 %, 21 %, and 18 % for PFC, preSMA, and CMAr, respectively.

I analyzed the selectivity strength of the decision neurons in all three areas using two types of measurements: the coefficients of the stepwise linear regression (SLR) analysis and the choice probability indices derived from a receiver operating characteristic (ROC) analysis. Both approaches identified the preSMA as a more reliable encoder of the abstract decision compared to the PFC. Additionally, the choice probabilities of the preSMA were also significantly larger compared to the CMAr.

During the motor phase all three areas continued to encode the decision in a comparable manner. No differences were found regarding the proportions and selectivity strength of decision cells. However, after the appearance of the rule cue, neurons in all three areas represented (additionally) the required action for the motor response. The proportions of neurons encoding the action were significantly higher in the preSMA and CMAr compared to the PFC. Moreover, preSMA neurons had stronger selectivity for the upcoming motor action than PFC neurons.

These findings demonstrated that the involvement of the investigated premotor areas, in particular the preSMA, is of substantial importance for abstract decision processing,

although both the preSMA and the CMAr participated strongly in the encoding of motor actions. These data allowed the exploration of the substrates of abstract decisions in the parts of the frontal cortex that are traditionally associated with motor processing. Additionally, a comparison of the representations of abstract detections to the mechanisms of detections studied in the action-based framework in the MPC was possible (de Lafuente and Romo, 2005).

Chapter III

A neuronal network model of abstract detections: modeling of active 'yes' and 'no' neurons

The results of the two previous studies (Merten and Nieder, 2012; submitted) revealed the substrates of abstract detection decisions in the frontal cortex. A finding of particular interest was the population of 'no' decision neurons, which actively modulated their discharge rates during 'no' decisions. Because there was no sensory input in the 'stimulus absent' condition, there was no sensory signal, which might have driven the active 'no' encoding. In the third part of my work, I addressed the processing mechanisms of abstract detections at the computational level. This approach aimed for the solution of the inverse problem of finding the connectivity structure from which the measured activity of 'no' neurons possibly emerged.

I designed a simple feedforward network model, which used firing rates of artificial neurons to describe the flow of information between different types of neurons within a neuronal circuit. The underlying architecture allowed the modeling of all classes of decision neurons identified electrophysiologically during both decision phases. All the response properties of these classes of neurons were captured accurately by the model.

The computational results suggest that abstract decisions might be reached at two consecutive processing steps. The activity of the early decision phase, the stimulus phase, might further be processed during the late delay phase. Therefore, the firing rates of the neurons during the stimulus phases might serve as input for the neurons processing the abstract decision during the delay phase. The proposed network implies that 'no' neurons emerged during the delay phase from further processing of 'yes' neurons, which decreased their firing rates actively during the 'yes' decision in the stimulus phase.

Moreover, I used the computational model layout to address the biological plausibility of the criterion, which was used to evaluate the computational unit activity to determine the decision outcome. The discharges of real experimental decision neurons during the stimulus phase were evaluated using firing rates of neurons, which encoded only the stimulus intensity, but not the decision, during the same period. About 76 % of these

evaluations resulted in appropriate classifications of the activity of the experimental neurons recorded during the stimulus phase. The classification corresponded to the decision reports of the monkeys. These calculations suggest that the activity of the intensity coding cells is well suited to model the criterion for decision evaluations. The results of this theoretical study provide additional insights into the mechanisms of the processing of abstract perceptual detections.

Discussion

Deciding between alternatives is a critical element of flexible intelligent behavior. In my PhD theses, I studied the processing of perceptual decisions on the level of single neurons in the PFC, preSMA, and CMAr of rhesus monkeys. The behavioral protocol used in this work dissociated the processing of the decision from any neuronal activity related to motor planning, thus, ensuring the study of the mechanisms of abstract decisions. My thesis focused on detections because the understanding of the encoding of these most elemental perceptual decisions is requisite to unravel the principles of more complex decisions.

Representation of abstract detections

I investigated whether the representation of abstract detections may be based on neurons encoding both the stimulus-present and stimulus-absent decisions categorically, although by definition only one response category (stimulus present) can rely on sensory input. During the early decision phase, I only found neurons representing the abstract 'yes' decision category, just as it has been reported for action-based detections (de Lafuente and Romo, 2005; 2006). However, during the late processing of the abstract decision, the representation is fundamentally different from action-based decisions. In addition to 'yes' neurons, I found an active encoding of the 'no' decision category.

Comparison of abstract decision encoding in PFC, preSMA, and CMAr

This encoding mechanism was found in all three brain structures investigated in this work. The areas preSMA and CMAr, which are traditionally identified with motor planning, represented the abstract decision about the stimulus presence or absence in a similar way as the PFC, even before any information about the motor action required for the report of the decision became available. In fact, correlates of abstract decisions were more prominent in the preSMA compared to the PFC. During the motor phase, after the instruction of the action, preSMA and CMAr still continued to encode the decision with similar expression strength as the PFC, in spite of their stronger representation of the

upcoming motor action. This finding emphasizes that the encoding capacities of the preSMA and CMAr involve far more abstract and cognitive processing than previously thought.

Modeling of a network for the computation of abstract detections

The physiological results, which argue for the involvement of two discrete processing steps during the abstract decision phase, motivate my computational model of abstract detection decisions. The computation comprises a realistic modeling of 'yes' cells encoding the decision during the stimulus phase. This first processing step might reflect the subjective experience of the stimulus and is largely dependent on the sensory evidence: stimulus presence leads to a modulation of the neuronal responses, whereas stimulus absence results in the maintenance of the baseline firing rate. This early decision activity is used in the model to generate the late decision representation by 'yes' and 'no' cells. In an analogy to the stimulus phase, 'yes' neurons modulate their responses for 'yes' decisions; in contrast, the newly emerging 'no' neurons, modulate their activity during 'no' decisions and remain inactive during 'yes' reports. The second decision processing step seems to be necessary to transform the subjective experience to abstract categories in rule-based detection tasks.

The proposed model architecture provides a plausible connectivity structure using excitatory and inhibitory connections of a local neuronal network, which might constitute a substrate for the suggested two-step computation of abstract detections. Further work is required to implement a biophysically plausible model using spiking integrate-and-fire neurons organized in discrete populations of decision neurons found in my study (active 'yes' and active 'no' neurons). Here, the decision might be modeled as a bistable neurodynamical phenomenon (Deco et al., 2007), in which probabilistic fluctuations cause the transition between the two decision options. Alternatively, to model the decision, the activity of artificial neurons might be evaluated by a threshold value in an analogy to diffusion models (Gold and Shadlen, 2007). This threshold value could be derived analytically from the dynamics of a bistable neuronal model close to the bifurcation point (Deco and Romo, 2008; Roxin and Ledberg, 2008). Another possibility to model the threshold value is suggested by the computational results of my model. The neurons encoding solely the stimulus intensity during the decision task might be implemented as threshold values because I found that their response properties were well suited for such evaluations.

Processing mechanism of abstract decisions

In general, the processing of perceptual decisions can be regarded as gathering of sensory information in order to commit to a plan. Here, the plan can be either a particular movement (action-based decisions) or an implementation of a particular rule, which instructs a movement (abstract decisions). Investigators, who approach the study of decision-making from a motor perspective, propose that the abstract decision is

just a decision to implement a subsequent certain kind of plan and should underlay similar processing principles as motion intention decisions (Shadlen et al., 2008).

The results of my thesis contradict this view. Although the abstract decision is necessary to enact a rule by selecting an appropriate motor response, the implementation of the abstract decision is essentially different from the motor-based decision. I report the emergence of active 'no' neurons, which actively contribute to the processing of abstract detections and have not been reported for motor-based detections. This finding is true even in the preSMA, the same brain area, in which only one population, the 'yes' neurons was found to represent the detection in an action-based framework (de Lafuente and Romo, 2005; 2006); which further demonstrates the flexibility of this brain structure to process the decision dependent on whether an abstract decision is enforced or the decision can be expressed in terms of motor preparation.

Overall, my work suggests that decisions are implemented by the most suitable neuronal representation depending on the framework in which this decision has to be processed (action-based or abstract). Decisions that can be formed as intensions to pursue a particular action might rely on a predefined movement plan, which is modified according to the incoming sensory information. When the sensory information is absent or insufficient, the established movement plan is executed (Romo and Salinas, 2003). The representation by only one population of neurons, actively encoding the 'yes' decisions is adequate for such processing. If a stimulus is detected, 'yes' neurons modulate their responses, so that the default motor plan is modified; otherwise, the predefined motor plan applies.

However, in the abstract framework, in which the appropriate motor response is instructed after the decision is made, the processing of the decision might benefit from a representation by two active neuronal populations actively representing the 'yes' and the 'no' decision. During the abstract decision, a default motor action cannot be defined easily, so "buffering" of the decision in a nonmovement-related framework might constitute a computational advantage. Therefore, when an abstract decision is enforced, the brain seems to deploy a complementary mechanism of decision-making by transforming the subjective experience of a stimulus to an abstract categorical representation (Freedman and Assad, 2011) using active 'yes' and 'no' populations of neurons. Even though sensory stimulation is absent during correct 'no' decisions, the brain constructs a 'no'-signal to meet the computational demands in abstract decision making. This processing mechanism allows the accomplishment of complex operations between interpretation of sensory information and action. Therefore, it appears to be very important for higher cognitive functions and intelligence.

Personal contributions to papers and manuscripts

1. **Merten, K., Nieder, A. (2012). Active encoding of decisions about stimulus absence in primate prefrontal cortex neurons. *PNAS* 109:6289–6294.**

   I designed the experiment together with A. Nieder. I was responsible for animal training, electrophysiological recordings, and data analysis. I wrote the first draft of the manuscript.

2. **Merten, K., Nieder, A. (submitted). Comparison of abstract decision encoding in the monkey prefrontal cortex, the presupplementary and cingulate motor areas.**

   I designed the experiment together with A. Nieder. I was responsible for animal training, electrophysiological recordings, and data analysis. I wrote the first draft of the manuscript.

3. **Merten, K., Nieder, A. (submitted). A neuronal network model of abstract detections: modeling of active 'yes' and 'no' neurons.**

   I developed the idea of the model and programmed all the procedures. I performed data analysis to compare the computational results with the real data acquired in the previous experiments. I wrote the first draft of the manuscript.

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Publication I

Active encoding of decisions about stimulus absence in primate prefrontal cortex neurons

Katharina Merten and Andreas Nieder

Department of Animal Physiology
Institute of Neurobiology
University of Tübingen, Germany

Active encoding of decisions about stimulus absence in primate prefrontal cortex neurons

Katharina Merten and Andreas Nieder[1]

Animal Physiology, Institute of Neurobiology, University of Tübingen, 72076 Tübingen, Germany

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Judging the presence or absence of a stimulus is likely the most basic perceptual decision. A fundamental difference of detection tasks in contrast to discrimination tasks is that only the stimulus presence decision can be inferred from sensory evidence, whereas the alternative decision about stimulus absence lacks sensory evidence by definition. Detection decisions have been studied in an intentional, action-based framework, in which decisions were regarded as intentions to pursue particular actions. These studies have found that only stimulus-present decisions are actively encoded by neurons, whereas the decision about the absence of a stimulus does not affect default neuronal responses. We tested whether this processing mechanism also holds for abstract detection decisions that are dissociated from motor preparation. We recorded single-neuron activity from the prefrontal cortex (PFC) of monkeys performing a visual detection task that forced a report-independent decision. We not only found neurons that actively encoded the subjective decision of monkeys about the presence of a stimulus, but also cells responding actively for the decision about the absence of stimuli. These results suggest that abstract detection decisions are processed in a different way compared with the previously reported action-based decisions. In a report-independent framework, neuronal networks seem to generate a second set of neurons actively encoding the absence of sensory stimulation, thus translating decisions into abstract categories. This mechanism may allow the brain to "buffer" a decision in a nonmovement-related framework.

perceptual detection | abstract decision | single-cell recordings | rhesus monkey

Perceptual decisions are choices among alternatives based on sensory information. To arrive at distinct choices, sensory input has to be classified into behaviorally meaningful categories. The detection of a stimulus (decision about its presence or absence) is the most basic form of a perceptual decision. The peculiarity of detection decisions is that only one choice alternative can be based on sensory evidence, whereas the alternative decision about stimulus absence lacks sensory information. How does the brain arrive at categorical stimulus-absent and stimulus-present decisions when only one response category (stimulus-present) can rely on sensory input?

The neuronal underpinnings of perceptual decisions have been studied extensively in an intentional, action-based framework (1–3). Here, decisions are regarded as intensions to choose among actions associated with the stimuli (1, 4). Decision-related neurons showed activity encoding the process of converting sensory information (5–7) or cognitive cues (8–10) into choices. In agreement with the view that detections are discriminations of a stimulus from noise (11), elegant studies by Romo and coworkers (12, 13) reported neurons actively encoding the decision about the stimulus presence. The decision about stimulus absence, however, was represented as a default (baseline) neuronal response (12–16) for action-based detection decisions.

When dissociated from action preparation or studied in a report-independent framework, decisions can be seen as distinct processes that are encoded as abstract categories (17–19). In a dot-motion discrimination task, neurons in the lateral intraparietal area were shown to encode the abstract decision about motion directions independently from how they signaled the associated motor response (20). In such discrimination and categorization tasks, subjects decide based on sensory stimuli represented for both alternatives. Thus, two separate neuronal populations encode the respective choice categories.

We investigated how abstract detection decisions, not linked to motor actions, are implemented by single neurons in the prefrontal cortex (PFC) of rhesus monkeys. To ensure report-independent decisions, we designed a rule-based visual detection task that allowed a clear dissociation of a decision about the stimulus from motor preparation. In such a protocol, also the stimulus absent decision is not just "noise" but a discrete category.

Results

We trained two rhesus monkeys to report the presence or absence of a visual stimulus in a rule-based delayed detection task that allowed a clear dissociation of the decision about the stimulus from motor preparation (Fig. 1*A*). The visual stimulus was presented at different intensity values centered around perceptual threshold. For stimuli of identical intensities, the internal status of the monkey determined whether it had ("yes" decision) or had not ("no" decision) seen the stimulus. Three different visual objects were used to ensure that the monkeys relied on the mere presence of the stimuli, whereas ignoring low-level object properties. Because a rule cue informed the animal about the appropriate motor action of how to report the decision, the monkey could not prepare any motor response during the delay period. The possible decision outcomes were classified according to signal detection theory (Fig. 1*B*). The proportion of "yes" decisions for each stimulus intensity was used to create psychometric detection curves for both monkeys (Fig. 1 *C* and *D*). The monkeys were only rewarded in correct trials (hits and correct rejections). No reinforcement was given in trials in which the monkeys failed to detect stimuli (misses), even if they were presented below the perceptual threshold. This reward contingency leads to a small bias of the monkeys to erroneously report the presence of a stimulus in some of the stimulus absent trials (false alarms) (Fig. 1 *C* and *D*).

While the monkeys performed the detection task, we recorded the activity of 708 randomly selected neurons from the PFC (Fig. 2*A*). We analyzed neuronal activity during the stimulus phase (immediately after stimulus presentation) to investigate the very early stage of decision formation, and the late-delay phase during which motor preparation was still excluded. We applied stepwise linear regression (SLR) analysis to study the conjoint contributions of stimulus intensity and the subjective "yes" and "no"

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[1]To whom correspondence should be addressed. E-mail: andreas.nieder@uni-tuebingen.de.

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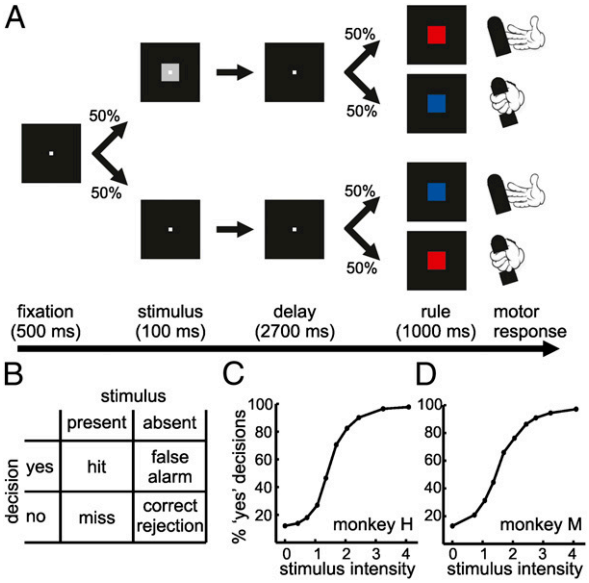

Fig. 1. Visual detection protocol and behavioral performance. (*A*) The monkeys initiated each experimental trial by grasping a lever and fixating a central fixation target. After 500 ms, a stimulus was displayed for 100 ms in 50% of the trials (intensity varied in nine levels, centered around the perceptual threshold). In the other 50% of the trials, no stimulus was shown. Both types of trials appeared randomly. After the delay period (2,700 ms), a color cue appeared to indicate the rule of how to respond to a particular decision. If a stimulus was presented, a red square cue required the monkey to release the lever within 1,000 ms to receive a fluid reward, whereas a blue cue demanded the monkey to keep holding the lever for another 1,200 ms. The rule applied in the inverse way if no stimulus was presented. Thus, movement preparation was excluded during the delay period. (*B*) Signal detection theory classifies an observer's behavioral options (hit, miss, correct rejection, and false alarms) at detection threshold, given two stimulus conditions (stimulus present or absent) and two possible decisions ("yes, stimulus present" and "no, stimulus absent"). (*C* and *D*) Psychometric detection curve for monkey H (*C*) and monkey M (*D*). Stimulus intensity is represented as % visual contrast; visual contrast of 0 indicates absence of stimulus. [Error bars (SEM) are so small that they are hidden behind the markers].

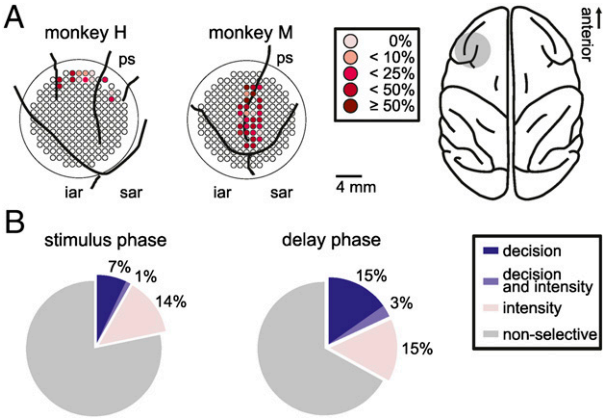

Fig. 2. Recording sites and proportion of selective cells. (*A*) *Right* shows a top view of a monkey brain. The gray area marks the chamber location. The circular panels on *Left* show the precise recording sites inside each recording chamber in the lateral PFC for both monkeys. The proportion of decision neurons at individual recording sites is color-coded. iar, inferior arcuate sulcus; ps, principal sulcus; sar, superior arcuate sulcus. (*B*) Proportions of neurons coding stimulus intensity and decision in both phases.

decisions on the discharge rates of the neurons. During both analysis phases, we found a proportion of neurons significantly coding the subjective judgments of monkeys about the stimulus presence or absence [Fig. 2*B*; 8% (58/708) during the stimulus phase and 18% (128/708) during the delay phase, $P < 0.05$, SLR analysis]. A proportion of 14% of the cells (96/708) during the stimulus phase and 15% of the neurons (106/708) during the delay phase only coded the intensity of the stimulus ($P < 0.05$, SLR analysis). Only 1% and 3% of the recorded neurons were modulated by both the factors stimulus intensity and the subjective decision during the stimulus and delay phase, respectively (Fig. 2*B*). Neurons significantly covarying with the monkey's choices were termed "decision neurons." Overall, we found a significantly higher proportion of decision neurons in the delay phase compared with the stimulus phase, ($P < 0.01$; χ^2 test).

Receiver operating characteristics (ROC) analysis was used to quantify the probability with which the decision of the monkey could be predicted from the neuronal responses. Choice probability indices were calculated for "yes" decisions in clearly visible, salient stimulus trials (hits) versus "no" decisions in stimulus-absent trials (correct rejections), as well as for "yes" (hits) versus "no" (misses) decisions in threshold trials when stimuli were presented close to the perceptual threshold.

Neuronal selectivity of a given neuron is usually determined by the experimental condition that elicits the highest discharge rate. This approach ignores that suppressive effects (decreases in firing rates relative to baseline discharge) are sometimes the dominant influences of a particular stimulus. Thus, we subdivided and classified decision neurons according to their active modulation of neuronal activity (modulation strength) during "yes" or "no" decisions rather than highest discharge rate. Neurons modulating (increasing or decreasing) their firing rates more strongly for "yes" decisions were termed "yes" neurons, cells modulating their discharges more strongly to "no" decision were called "no" neurons.

"Yes" Neurons Actively Encode Decisions During the Stimulus Phase. During the stimulus phase, virtually all decision neurons (98%) modulated their discharge rates only for "yes" judgments (merely one neuron was classified as a "no" cell; summary in Table S1). Fig. 3*A* shows an exemplary "yes" cell that increased its discharge rates for hits in salient stimulus trials, whereas the firing rates for correct rejections in stimulus-absent trials remained at baseline level. Neuronal responses for threshold trials correlated significantly with the judgment of the monkey: for "yes" decisions, neurons increased their activity, mirroring the firing rate in salient stimulus trials. For erroneous "no" decisions (misses), activity remained at baseline level, just as in stimulus absent trials. The choice probability indices for salient and threshold trials are depicted as a function of time in Fig. 3*A*, *Lower*. Indices significantly above chance level indicate that these discharges of neurons reliably predict the decision of the monkey ($P < 0.05$; ROC analysis, bootstrapping). This effect was also present on the neuronal population level (34 cells; Fig. 3*B*). Several cells showed transient suppression of the firing rate for "yes" decisions (Fig. 3*C*); the neuronal population data (23 units) are depicted in Fig. 3*D*. The population analysis includes the neuronal responses during false alarms. Interestingly, decision neurons increased (Fig. 3*B*) or decreased (Fig. 3*D*) the firing rates for this erroneous "yes" decisions in a similar way as during hit trials, already during this early decision phase. The average peak latencies of the neuronal responses for false alarms and hits were comparable (neurons increasing the firing rate: hit latency = 242 ms, false alarms latency = 289 ms; neurons decreasing firing rates: hit latency = 346 ms, false alarms latency = 341 ms). Overall, during the stimulus phase, PFC neurons represented "yes" decisions by either increasing or decreasing their responses, whereas "no" decisions were represented by default discharge rates.

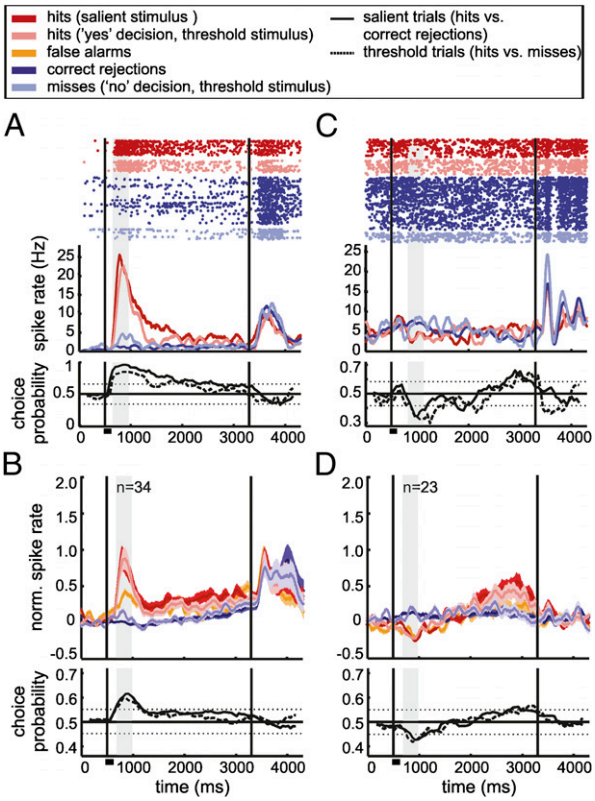

Fig. 3. Decision coding by "yes" neurons during the stimulus phase. (*A* and *C*) Responses of two example neurons coding the "yes" decision by increasing (*A*) or decreasing (*C*) their firing rates during the stimulus phase (analysis window highlighted by the gray shaded area). *Top* depict dot raster plots; *Middle* represent the corresponding spike density histograms averaged and smoothed with a Gaussian kernel for illustration. The vertical black lines indicate the presentation of the stimulus (at 500 ms) and the rule cue (at 3,300 ms). Stimulus duration is marked by a small horizontal bar underneath the *x* axis of each plot. *Bottom* show the choice probability indices as a function of time. Dotted lines mark significance levels. (*B* and *D*) Averaged and normalized responses (*SI Materials and Methods*) and choice probability indices of decision neurons grouped by response type. Shaded regions indicate SEM; n, number of neurons.

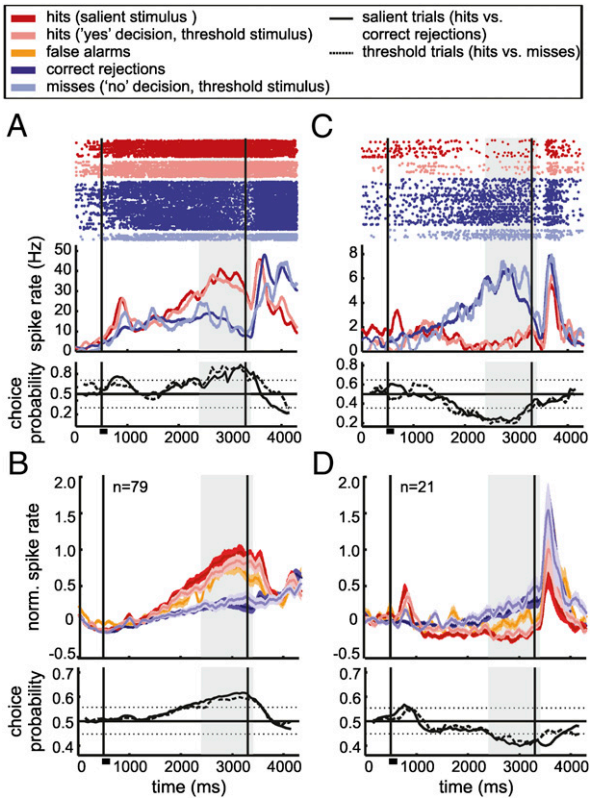

Fig. 4. Decision coding by "yes" and "no" neurons during the delay phase. (*A* and *C*) Raster plots, spike density functions, and choice probability indices for neurons increasing their activity for "yes" decisions (*A*) or for "no" decisions (*C*) during the delay phase. (*B* and *D*) Normalized averaged responses (*SI Materials and Methods*) of the corresponding groups. Active "no" decision neurons newly emerged during the delay phase. Same layout as in Fig. 3.

"Yes" and "No" Neurons Actively Encode Decisions During the Delay Phase. In striking contrast to the findings in the sample phase, the processing of decisions in the delay phase was based on "yes" (Fig. 4 *A* and *B*) as well as active "no" responses (Fig. 4 *C* and *D*) (summary in Table S1). Just as in the stimulus phase, we found neurons increasing (79 neurons; Fig. 4*B*) or decreasing (25 units) their firing rates for "yes" decisions (hits and false alarms). In addition, however, a new class of decision cells, "no" neurons, exhibited significantly increased discharge rates whenever the monkey decided to report the absence of a stimulus (correct rejections and misses) (Fig. 4*C*; average responses of 21 neurons in Fig. 4*D*). Three cells were classified as decreasing their firing rate for "no" responses. These active "no" neurons represent an abstract category that is neither generated by a specific input nor linked to a preparation of a motor response.

Finally, we also investigated the neuronal selectivity of delay phase decision neurons to the rule cue and the instructed motor action during the rule cue phase. For both "yes" and "no" decision neurons, decision activity remained the dominant factor well into the rule cue phase (Fig. 5 *A* and *B*). To identify the proportions of decision neurons responding to decision, stimulus intensity, rule cue, and motor action during the cue presentation, we next performed a sliding SLR analysis by using these factors (Fig. 5*C*). Selectivity for the color cue or the motor action was absent during the delay analysis period. Only after a latency of ≈100 ms after rule cue onset, decision cells started to encode the color of the rule cue and, most dominantly, the instructed motor action.

Discussion

We found single neurons in the PFC that encode abstract "yes" and "no" decisions during a visual detection task. In this perceptual decision task that dissociated the decision both from low-level sensory processing and preparatory motor activity, the neuronal activity covaried with the subjective reports of monkeys about the percepts. A very small proportion of decision neurons showed an additional significant effect of the intensity of the visual stimulus; thus, we report a predominantly categorical, binary activation pattern of "yes" or "no" decision coding. During the stimulus phase, decision neurons exclusively either increased or decreased their firing rates for "yes" decisions, whereas "no" responses were represented by baseline discharge rates. During the delay period, however, neurons also actively encoded "no" decisions. We propose that the coding of abstract, report-independent decisions is fundamentally similar to the representation of abstract categories (21), even if one choice alternative is devoid of sensory evidence. Our data thus extend previous findings about the representation of perceptual decisions in detection tasks (12).

Behavioral Relevance of the Perceptual Decision Encoding. Decision neurons modulated their firing rates according to the sensory percept of monkeys: Activity signaling categorical "yes" decisions (hits and false alarms) was different from neuronal responses to correct rejections and misses (as shown by SLR analysis). The

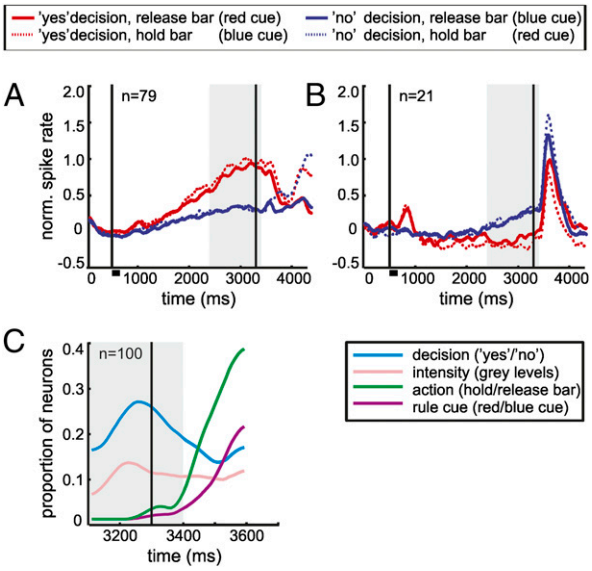

Fig. 5. Selectivity of decision cells during rule cue presentation. (*A* and *B*) Averaged neuronal activity of "yes" (*A*) and "no" delay phase decision neurons (*B*) is shown throughout the trial during "yes" and "no" decisions separated according to the rule cue (requiring a particular motor action). The figure has the same layout as in Fig. 3. (*C*) Proportion of all "yes" and "no" delay phase decision neurons significantly selective for the factors decision, stimulus intensity, motor action, and rule cue during the cue phase. The vertical black line at 3,300 ms depicts the onset of the rule cue. On average, the monkeys performed a motor action 300 ms after the rule cue onset in release trials. The gray area highlights the analysis window of the delay phase. No selectivity for the rule cue or the motor action is present during the delay phase analysis window.

behavioral relevance of these responses becomes clear in the analysis of error trials. Miss trials clearly mimicked the responses to correct rejections during stimulus and delay phase. Similarly, a population analysis revealed that false alarm responses resembled the neuronal representations of hit trials. (The small number of false alarm trials precluded an analysis for individual cells). The slightly lower response amplitude of average false alarm responses compared with hit activity most likely reflects the different causes for such erroneous "yes" decisions that can appear during the course of a trial.

"No" Neurons. The presence of active "no" neurons—in addition to active "yes" neurons—is an important finding of our study. During the delayed decision process, "no" cells encoded the decision actively by modulating their activity more strongly for "no" decisions, even in the absence of sensory evidence. One possible explanation for our finding is that decisions irrespective of motor preparation require additional neuronal representations compared with decisions in previous task designs (12, 13, 22, 23). Deco and coworkers used the term "type 'no' neurons" for cells that showed a transient peak activity during stimulus presentation and suppressed activity during the delay period whenever the monkey reported stimulus presence (24). Importantly, these neurons were reported to maintain baseline activity if no stimulus was presented. According to the definition we use in our study, these neurons would most likely correspond to "yes" neurons increasing their firing rate in the stimulus phase and decreasing the firing rate during the delay phase for "stimulus present" decisions.

Two Processing Steps of Abstract Decisions. Our physiological results argue for two discrete processing steps involved in abstract decisions in detection tasks, implemented by "yes" cells in the stimulus phase and by "yes" and "no" cells during the delay phase. During the stimulus phase, the responses might reflect the subjective experience of the stimulus, based on the accumulation of sensory information (12). The emergence of "no" neurons in the delay phase likely constitutes a second active decision-processing step transforming the subjective experience to abstract categories in rule-based detection tasks.

In an abstract, report-independent decision protocol, in which the appropriate motor response is instructed later, a default motor action cannot easily be defined. From the computational perspective, "buffering" of the decision in a nonmovement-related framework (21) and applying two sets of active decision neurons ("yes" and "no" cells) would constitute an advantage. The principle of using two sets of active neurons is also implemented in (delayed) report-dependent (6, 7, 25–27) and report-independent (20) coding and models of decisions in discrimination tasks. In such comparison tasks, decision can be based on the evaluation of sensory evidence (e.g., "rightward" versus "leftward" motion), so the information of two sets of neurons actively coding the two alternative categories can be "translated" into a movement-related framework. With the applied detection task, we show that this coding scheme is a fundamental principle in representing abstract decisions. Our data show that, if sensory evidence is not available in the absence of sensory stimulation, the second set of active coding neurons is purposefully generated in neuronal networks.

The question of how the second active decision-processing step and the emergence of "no" neurons in abstract decisions is generated requires further investigation. One speculation might be that information during the stimulus phase is transferred and further processed throughout the delay phase. Another possibility might be that this late decision processing is triggered by midbrain dopamine (DA) neurons. A recent study reports high levels of DA activity for high uncertainty, which arises internally because of the evaluation of a sensory stimulus (28). Because stimulus-absent events carry a high level of uncertainty, this DA activity might account for the active "no" decision responses we measured in the PFC.

To guide behavior, the accuracy of neuronal decision signals should improve if information is combined across neurons. Sensory-related decisions have been found to rely on neurons with increasing and decreasing response profiles (13, 25). We find that both "yes" and "no" decision categories are encoded by facilitation and suppression. However, combining both apparently opposing information streams by a simple linear summation or averaging pooling rule would diminish/cancel out the information. A mechanistically similar situation occurs during the discrimination of opposite directions. Here, computational models suggest pooling profiles that specify how each neuron (tuned to its preferred direction) contributes to the decision (29). These pooling profiles result in opposite weighting of the contribution of neurons tuned to opposite directions. The difference of the weighted responses is used to determine the decision. Cells found in our study that encode the same decision category based on increasing and decreasing activity (but not opposing decisions) could exploit the same pooling principle within a decision category. To take full advantage of both information streams, pooling might rely on the difference between averaged subpopulations of neurons increasing and neurons decreasing their responses. This pooling-rule might be achieved if a subpopulation of increased-discharge decision neurons excites a downstream neuron, whereas a subpopulation of suppressed neurons inhibits this neuron.

Intentional and Report-Independent Frameworks. Our data suggest that the best-suited neuronal representations of decision may be implemented depending on the nature of the behavioral task (intentional or report-independent). Decisions that can be formed as intensions to pursue a particular action may not require an abstract decision; thus, a direct link between stimulus activity (sensory input) and premotor activity (motor output) might be established. Therefore, the abstract decision may not even be represented as a discrete processing step at all (21, 30).

Our data indicate a complementary mechanism of decision processing, one that is deployed by the monkey brain when an abstract decision is forced. According to this hypothesis, deciding does not inevitably mean to plan a motor response (31). Rather, if required, decisions can be represented in an abstract processing step separated from motor effector systems, thus permitting complex operations between decision and action. Our results suggest that, if a rule cue were to be introduced in action-based detection tasks, the same kind of mechanism as observed in the current detection study would presumably emerge.

Brain Areas Encoding Abstract Decisions. Although early sensory brain areas reflect the physical properties of a stimulus (12, 32), the correlation between neuronal discharges and interpretation (subjective experience) of a stimulus progressively increase across higher cortical hirarchy and result in a choice of an appropriate behavior (13, 33). We selected the PFC, a classical association area known to operate at the apex of the cortical hierarchy, as a candidate structure. PFC neurons have been shown to be engaged in highly abstract processes (34) including evaluation of sensory information (19, 35), decision-related processes (25, 36, 37), and abstract behavioral planning (38–40). Moreover, human fMRI suggested this area as an abstract decision-making module that is functionally separate from the motor systems (31, 41). We show that neurons in the PFC are strongly involved in the processing of abstract decisions.

However, other highly associative brain areas might also be strong candidates for the processing of abstract decision information. The medial premotor cortex (MPC) has been reported to be crucial for linking sensory information to action investigated from a motor perspective (37, 42, 43). The anterior cingulate cortex (ACC) has also been shown to reflect the intention for a particular action based on sensory (44) or reward information (45). It would be interesting to investigate whether and how these areas encode abstract decisions.

Materials and Methods

Behavioral Protocol. Two rhesus monkeys (*Macaca mulatta*) were trained to report the presence or absence of a visual stimulus (Fig. 1*A*). The stimulus consisted of a gray object (4° of visual angle) presented at nine levels of contrast close to the perception threshold (monkey H: 4.1%, 3.2%, 2.4%, 2.0%, 1.7%, 1.4%, 1.1%, 0.7%, 0.4%; monkey M: 4.1%, 3.2%, 2.4%, 2.8%, 2.0%, 1.7%, 1.4%, 1.1%, 0.7%), measured with a J16 Digital Photometer (Tektronix). The shape of the object was chosen randomly from a set of three objects: square, circle, and hexagon for monkey H; cross, triangle, and rhomboid for monkey M. The area of the object was kept constant to maintain the same visual contrast of the stimulus across different shapes.

Monkeys kept their gaze within 1.75° of visual angle of the fixation target during stimulus and delay period. Eye movements were monitored with an infrared eye-tracking system (ISCAN). CORTEX program (National Institute of Mental Health) was used for experimental control and behavioral data acquisition. For the behavioral analysis, we gathered the proportion of "yes" decisions for stimulus present (hits) and stimulus absent (false alarms) trials (15021 and 14830 trials for monkey H; 14207 and 14326 trials for monkey M). For each stimulus intensity and type of decision, we pooled trials requiring lever release and holding trials from all recording sessions (Fig. 1 *B* and *C*).

Neurophysiological Recordings. Extracellular single-cell activity was recorded by using arrays of four to eight glass-coated tungsten microelectrodes of 1 MΩ impedance (Alpha Omega) (*SI Materials and Methods*). All of the surgery procedures were carried out under aseptic conditions and under general anesthesia in accordance with the guidelines for animal experimentation approved by the local authorities, the Regierungspräsidium Tübingen, Germany.

Data Analysis. Data analysis was performed by using MATLAB (MathWorks). We studied all well-isolated neurons and focused our analysis on two decision periods: a 300-ms interval after stimulus onset shifted by the individual response latency of the cell (stimulus phase) and a 1,000-ms window starting 1,900 ms after stimulus onset (delay phase).

Excluding Nonabstract, Object Feature-Selective Neurons. To ensure that the studied neurons encoded abstract object properties irrespective of low-level visual features, we only analyzed cells, whose responses generalized over all three presented objects. We performed a Kruskal–Wallis test to analyze the selectivity of neurons for the three types of objects. For this test, hit trials of all intensities were grouped by object type. Only few neurons showed significantly different discharge rates for at least one of the three object types: (5% during the stimulus and delay phase). These cells were excluded from further analysis.

SLR Analysis. The SLR analysis (46) was used to investigate the relationship of firing rate with stimulus intensity and firing rate with monkey's choice (43, 46, 47). We fitted the neuronal activity during stimulus and delay analysis phases to an arbitrary linear function of both factors: intensity (all tested values) and decision ("yes" decision: hits and false alarms vs. "no" decision: misses and correct rejections). The firing rate (FR) can be formulated as $FR = a_0 + a_{int} \times INT + a_d \times D$, where a_{int} and a_d are the coefficients that quantify the firing rate dependence on intensity (INT) and decision (*D*), respectively. For the analysis of the rule cue phase (Fig. 5*C*), a sliding SLR analysis was calculated. Here, the dependence of firing rates on intensity (INT), decision (*D*), action (*A*), and rule cue (*R*) was assessed according to the equation $FR = a_0 + a_{int} \times INT + a_d \times D + a_a \times A + a_r \times R$ (*SI Materials and Methods*). We chose a significance level of 5% to determine which factors had a significant effect on the firing rates. Coefficients were included in the model if the *P* value for a predictor was below this level. Mulicollinearity did not affect the calculations (*SI Materials and Methods*).

Classification of Decision Cells into "Yes" and "No" Neurons. Neurons showing a significant effect of decision (SLR analysis) were classified according to the modulation strength of their firing rates during "yes" and "no" decisions. As a measure of the modulation strength (*M*), we used the mean absolute change of the firing rate (FR) in intervals of $t = 100$ ms, which were shifted in 10-ms steps $M = \frac{1}{n}\sum_{i=1}^{n}\left|\frac{\Delta FR_i}{\Delta t_i}\right|$. The starting point of the modulation analysis ($i = 1$) for both phases was advanced from the defined phase onset to a time point at which the firing rates for the "yes" and "no" decisions started to diverge significantly (see ROC analysis); the analysis ended ($i = n$) at the defined offset of the respective phase. The firing rate was convolved with a Gaussian kernel (bin width 150 ms; step 1 ms). If the modulation strength (*M*) was larger during "yes" decisions compared with the modulation strength during "no" decisions, the neuron was classified as a "yes" neuron. For stronger modulation during "no" decisions, the neuron was assigned to the "no" neuron class.

ROC Analysis. To analyze the representation of the abstract decision across time, we compared the discharge rates of salient hit trials to correct rejections and activity in hit trials to misses of threshold trials. Sliding ROC analysis was used to calculate choice probability indices, which estimated the strength of decision coding (*SI Materials and Methods*).

Response Latency. Latency calculations of neuronal responses were based on the sliding ROC analysis. No significant latency difference was found between cells coding only stimulus intensity (239 ms) and neurons coding the decision (194 ms) ($P > 0.05$, Wilcoxon test).

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Supporting Information

Merten and Nieder 10.1073/pnas.1121084109

SI Materials and Methods

Neurophysiological Recordings. We recorded single-cell activity from the lateral prefrontal cortex (PFC) (left hemisphere, around the principal sulcus) of both monkeys. The location of the recording sites and the placement of the recording chambers were reconstructed in stereotactic coordinates by using magnetic resonance images of individual monkey brains (Fig. 2*A*). Electrodes were inserted each recording day by using a grid with 1-mm spacing. Neurons were selected at random in every recording session; no attempt was made to preselect neurons according to response properties. Signal acquisition, amplification, filtering, digitalization, and spike sorting (offline) were accomplished by using the Plexon system (Plexon).

Stepwise Linear Regression (SLR) Analysis. Neuronal responses during the rule cue were analyzed in the period starting 200 ms before the rule cue onset and ending 300 ms after the rule cue onset. Sliding SLR analysis was calculated for analysis windows of 100-ms duration, slid in steps of 10 ms for the factors intensity (INT), decision (*D*), action (*A*), and rule cue (*R*). The number of neurons significantly encoding each factor in each analysis window was convolved with a Gaussian kernel (bin width 10 ms; step 1 ms) for the plot (Fig. 5*C*).

To test for the presence of multicollinearity, we calculated the variance inflation factor (VIF) $\mathrm{VIF} = 1/(1 - R^2)$, where R is the coefficient of the correlation of both explanatory variables decision and intensity. As a common rule of thumb VIF > 5 are used as cut off values for too high multicollinearity (1, 2). None of the VIF values calculated for every neuron exceeded the cutoff value.

Receiver Operating Characteristic (ROC) Analysis. To characterize how neurons represent the abstract decision across time, we applied sliding ROC analysis (3) to consecutive overlapping time windows of 300 ms moved in 50 ms steps across the trial. We compared the discharge rates of salient (≥2.4% visual contrast) hit trials to discharge rates of correct rejections. Further, hit trials of threshold stimuli (2.0%, 1.7%, 1.4%, and 1.1% of visual contrast) were compared to miss threshold trials. To exclude possible stimulus intensity biases in the analysis of four different intensities of hit or miss trials, equal numbers of trials of each stimulus intensity were included in the comparison for each cell.

To estimate the extent to which neuronal activity in both phases was influenced by the decision, we calculated the choice probability index (4) (area under the ROC curve). Values of 0.5 indicated chance-level discrimination; values >0.5 denoted neurons with higher firing rates for hits compared with misses or correct rejections; choice probability indices <0.5 signified cells with higher discharge rates for misses and correct rejections. We used bootstrapping to assess whether the indices were significantly different from 0.5. For this analysis, we constructed 1,000 resamples of the observed discharge rates, each of which was obtained by random sampling with replacement keeping the original number of trials for each condition. Then, we calculated the choice probability index for each resample, and compared the resulting distribution of the indices to the value of the original dataset. If 95% of the bootstrapped values were higher/lower than the original value, it was considered statistically significant ($P < 0.05$). Confidence intervals, depicted in Figs. 3 and 4, were calculated by using the bootstrap technique for each interval.

To calculate the response latency of the neurons, sliding ROC analysis with time windows of 50 ms slid by 1 ms was used. We defined the latency for each cell as the time after stimulus onset, but no later than 500 ms, for which the choice probability index exceeded for 50 consecutive windows the 95% threshold of the bootstrapped data. If no value could be determined, a default latency corresponding to the 75th percentile of the response latency distribution of a given recording was used (179 ms).

Population Analysis and Normalization. For the group analysis of each cell class, we normalized and averaged responses of all significantly selective cells. Normalized activity was calculated by subtracting the mean baseline activity and dividing by the SD of the baseline activity (300 ms period before stimulus onset). Spike density histograms for single neurons were averaged over trials and convolved with a Gaussian kernel (bin width 150 ms; step size 1 ms) for illustrative purposes only.

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Table S1. Number of neurons classified as "yes" and "no" decision neurons

	"Yes" neurons		"No" neurons	
	↑	↓	↑	↓
Stimulus phase	34	23	1	0
Delay phase	79	25	21	3

↑, increasing firing rate; ↓, decreasing firing rate.

Publication II

Comparison of abstract decision encoding in the monkey prefrontal cortex, the presupplementary and cingulate motor areas

Katharina Merten and Andreas Nieder

Department of Animal Physiology
Institute of Neurobiology
University of Tübingen, Germany

Comparison of abstract decision encoding in the monkey prefrontal cortex, the presupplementary and cingulate motor areas

Katharina Merten and Andreas Nieder

Animal Physiology, Institute of Neurobiology, University of Tübingen, 72076 Tübingen, Germany

Deciding between alternatives is a critical element of flexible behavior. Perceptual decisions are based on the evaluation of sensory information and have been studied extensively in an action-based framework. The processing of such intentional judgments involved the representation of sensory, cognitive, and motor variables simultaneously in the same neurons in various frontal and parietal brain regions. However, the processing of more complex decisions, which require abstract calculations and cannot be expressed in terms of motor actions, might be coordinated by an area operating at the top of the processing hierarchy, the prefrontal cortex (PFC). The involvement and interaction of various frontal cortex areas have not been studied for abstract decisions. We trained two monkeys to perform a visual detection task and applied a rule-cue to disentangle the processing of the abstract perceptual decision from motor preparation. We recorded the single-neuron activity during the formation of abstract decisions in the monkey pre-supplementary (preSMA) and the rostral part of the cingulate motor area (CMAr) and compared it to the mechanism previously found in the dorsolateral PFC neurons. We found that these areas, traditionally identified with motor planning, process the abstract decision independently of any motor preparatory activity by similar mechanisms as the PFC. Remarkably, the reliability of abstract decision coding in the preSMA was even significantly higher compared to PFC neurons. The processing mechanism of abstract decisions in the preSMA was different from how this area was shown to encode report-dependent decisions. Our findings emphasize that both preSMA and CMAr have abstract and cognitive encoding capacities for processes distinct from motor actions. The deployment of different encoding mechanisms for different task requirements in the preSMA demonstrates the high processing flexibility of this brain structure.

Introduction

Decisions are deliberative processes that allow for a choice between alternatives in a situation of uncertainty. Perceptual decisions are often studied in simple sensory-motor tasks; they evaluate ambiguous or noisy sensory information and transform it into categorical judgments to influence behavior. Such judgments cannot be explained alone by properties of early sensory areas neurons that reflect the physical properties of the stimulus (Mountcastle et al., 1969; de Lafuente and Romo, 2005). To determine the subjective judgment, processes that integrate the sensory information with internal goals, experiences, and expectations are required. Flexible and nuanced decisions are thus regarded as a hallmark of higher cognition.

Perceptual decision implementation has been addressed neurophysiologicaly in various cortical and subcortical structures and does not seem to be restricted to particular cognitive centers such as the prefrontal cortex (PFC) (Kim and Shadlen, 1999; Romo et al., 2004; Lemus et al., 2009; Hernández et al., 2010). Likewise, regions as the frontal eye field (Gold and Shadlen, 2003), the medial and ventral premotor cortices (Hernández et al., 2002; de Lafuente and Romo, 2005; 2006), the superior colliculus (Horwitz and Newsome, 1999; Gold and Shadlen, 2000), and the lateral intraparietal area (LIP) (Shadlen and Newsome, 2001; Roitman and Shadlen, 2002) have been implicated in decision formation. These studies thought of the perceptual decision as an intension to pursue a particular action associated with a percept (Gold and Shadlen, 2007; Shadlen et al., 2008). This might possibly be the reason why the decision related processing has been found in these brain areas involved in planning, preparation, and execution of motor actions.

However, if perceptual decisions are dissociated from action preparation the contributions of different brain areas to their formation are largely unclear. The region of paramount importance for the processing of such highly abstract computations is the PFC. In a recent study, we investigated the representation of abstract perceptual decisions in the PFC of rhesus monkeys (Merten and Nieder, 2012). In a rule-based visual detection task that allowed a clear dissociation of a decision about the presence or absence of a stimulus from motor preparation, we found a different way of detection decision processing as compared to previously reported action-based detection decisions (de Lafuente and Romo, 2005). In addition to the neurons actively modulating their discharges for 'yes, stimulus present' decisions, found for action-based detections, we found a second set of neurons actively modulating their responses for 'no' decisions. The appearance of 'no'-neurons is a hallmark of highly abstract calculations, because these responses are generated although this decision category lacks sensory input and is not triggered by motor preparations.

Our present work explores the encoding of abstract detection decisions in areas of the frontal cortex, which are traditionally identified with motor planning. Of particular interest is the presupplementary motor area (preSMA), because this area appears to be responsible for more abstract, cognitive, high-level motor functions (Tanji, 1994; Picard and Strick, 1996; Shima et al., 1996). Moreover, the rostral part of the cingulate motor area (CMAr) is a candidate to be involved in cognitive processing. Just as the preSMA, CMAr receives direct input from the PFC (Bates and Goldman-Rakic, 1993; Lu et al., 1994; Wang et al., 2005). Moreover, a recent study describes the involvement of this area in abstract rule processing (Vallentin et al., 2012). We apply the same detection protocol in the same rhesus monkeys to explore whether these structures translate decisions into abstract categories, similar to the PFC neurons. An alternative might be that these regions contribute to decision processing only on a stage when information about the motor action becomes available and the intension for an action is calculated.

Methods

Behavioral protocol

Two rhesus monkeys (*Macaca mulatta*) were trained on a rule based visual detection task (Figure 1). In each randomly selected experimental trial the monkeys were required to report the presence or the absence of a stimulus dependent on a color cue, which instructed a particular motor response. The monkeys initiated a trial by grasping a lever and fixating a central fixation target for 500 ms. A brief stimulus (100 ms) appeared for in 50% of the trials. In the other half of the trials, the stimulus was absent. After the delay period (2700 ms), a color cue was presented. If the monkey correctly detected the presence of the stimulus a red square cue required the monkey to release the lever within 1000 ms to receive a fluid reward. A blue square instructed the monkey to keep holding the lever for 1200 ms. The rule applied in the inverse way if the absence of the stimulus was detected. During stimulus and delay periods, monkeys were required to keep their gaze within 1.75° of visual angle of the fixation target. Eye movements were monitored with an infrared eye-tracking system (ISCAN, Woburn, MA, USA). CORTEX program (NIMH) was used for experimental control and behavioral data acquisition.

Stimuli

The stimulus consisted of a grey object (4° of visual angle), whose shape was selected randomly from a set of three shapes: square, circle, hexagon for monkey H; cross, triangle, and rhomboid for monkey M. The area of the object was kept constant to maintain the visual contrast of the stimulus across different shapes. The stimulus was presented at nine levels of contrast close to the perception threshold (monkey H: 4.1 %, 3.2 %, 2.4 %, 2.0 %, 1.7 %, 1.4 %, 1.1 %, 0.7 %, 0.4 %; monkey M: 4.1 %, 3.2 %, 2.8 %, 2.4 %, 2.0 %, 1.7 %, 1.4 %, 1.1 %, 0.7 %), measured with a J16 Digital Photometer (Tektronix, Beaverton, OR, USA).

Neurophysiological recordings

All procedures involving animals were fulfilled the guidelines for animal experimentation approved by the local authorities, the Regierungspräsidium Tübingen, Germany. All the surgery procedures were carried out under aseptic conditions and under general anesthesia. We performed extracellular single-cell recordings simultaneously in the lateral prefrontal cortex (PFC), the presupplementary motor area (preSMA), and the rostral part of the cingulate motor area (CMAr). We used glass-coated tungsten microelectrodes of 1 MΩ impedance (Alpha Omega, Nazareth, Israel). Arrays of four to eight electrodes with 1 mm spacing were inserted during each recording session into the recording chambers. Neurons were selected at random in every recording session; no attempt was made to pre-select neurons according to response properties. Signal acquisition, amplification, filtering, digitalization, and were accomplished using the Plexon system (Plexon, Dallas, TX, USA). The placement of the recording chambers and the location of the recording sites were reconstructed in stereotactic coordinates using magnetic resonance images of individual monkey brains (Figure 2).

Data analysis

We sorted the spikes offline and studied the responses of all well-isolated neurons. We focused our analysis on two intervals during the decision period: the stimulus phase: a 300 ms period after stimulus onset shifted by the individual response latency of the cell and the (late) delay phase: a 1000 ms window starting 1900 ms after stimulus onset. Moreover, we analyzed the neuronal responses also during the motor phase: a 200 ms interval, which started 100 ms and ended 300 ms after rule-cue onset. Data analysis was performed using MATLAB (MathWorks, Natick, MA, USA).

Excluding non-abstract, object feature-selective neurons

A Kruskal-Wallis-test was used to analyze the selectivity of every neuron for the three different types of the presented objects, to ensure that the studied neuronsencoded abstract object properties irrespective of low-level visual features. For this test, hit trials of all intensities were grouped by object type. We found that only few neurons showed significantly different discharge rates for the object types: (PFC: 5 % during the stimulus and delay phase; preSMA: 4 % in both intervals of analysis; CMAr: 6 % during the stimulus phase and 5 % during the delay phase). These cells were excluded from the analysis.

Stepwise Linear Regression (SLR) analysis

To investigate the relationship of firing rate, monkey's choice, and stimulus intensity during the decision period, we used SLR (Draper and Smith, 1966). We fitted the neuronal activity measured for each single cell during the stimulus and delay phases to a linear function of both factors: intensity (all tested stimulus intensities) and decision ('yes' decision: hits and false alarms vs. 'no' decision: misses and correct rejections). The following equation describes this relationship: $FR = a_0 + a_{int} \times INT + a_d \times D$. The coefficients a_{int} and a_d quantify the dependence of the firing rate (FR) on intensity (INT) and decision (D).

For the analysis of the motor phase (Figure 9), the dependence of the firing rates was calculated using the factors intensity (INT), decision (D), motor action (A), and rule-cue (R) using the following equation: $FR = a_0 + a_{int} \times INT + a_d \times D + a_a \times A + a_r \times R$. We also carried out a sliding SLR analysis during the time of the rule-cue appearance and the motor phase. Analysis windows of 100 ms were slid in steps of 10 ms for all the four factors. The number of neurons and the SLR coefficients of neurons significantly encoding these factors in each analysis window were convolved with a Gaussian kernel (bin width 10 ms; step 1 ms) for the plot (Figure 9).

Coefficients were included in the model if the p-value for the predictor (decision outcome or the stimulus intensity) was below the significance level of 5 %. To test for the presence of multicollinearity we determined the correlation coefficient the explanatory variables decision and intensity (R) and calculated the variance inflation factor (VIF): $VIF = 1 / (1 - R^2)$. $VIF > 5$ were used as cut off values to detect too high multicollinearity (Kutner et al., 2004; O'Brien, 2007). The concern of multicollinearity did not apply to any of the calculated fits.

For the comparison of the SLR coefficients among each other and between areas, the coefficients were normalized. Normalized firing rates were used to determine the

coefficients (see Population analysis and normalization). The absolute coefficient values (a) were transformed to normalized values by $a_{norm} = tan^{-1}(a) / (\pi/2)$.

Classification of decision cells into 'yes' and 'no' neurons

Decision neurons were classified according to the modulation strength of their firing rates during 'yes' and 'no' decisions. We used the absolute mean change of the firing rate as a measure of the modulation strength (Merten and Nieder, 2012).

Receiver operating characteristic (ROC) analysis

ROC analysis was performed over both abstract decision analysis intervals (stimulus and delay phase). Sliding ROC analysis was applied to consecutive overlapping time-windows of 300 ms moved in 50 ms steps across the trial to characterize the temporal evolution of the abstract decision across time. We calculated the choice probability indices (area under the ROC curve) comparing the discharge rates of salient (≥ 2.4 % visual contrast) hit trials with discharge rates of correct rejections; and hit trials of threshold stimuli (2.0 %, 1.7 %, 1.4 %, 1.1 % of visual contrast) with miss threshold trials. To exclude stimulus intensity biases in the analysis of threshold trials, equal numbers of trials for each stimulus intensity were included in the comparison of hit and miss trials for each cell. Choice probability values of 0.5 indicated chance-level discrimination; values > 0.5 denoted neurons with higher firing rates for hits compared to misses or correct rejections; choice probability indices < 0.5 signified cells with higher discharge rates for misses and correct rejections. To calculate significance levels and confidence intervals we used the bootstrapping technique. We constructed 1000 resamples of the discharge distributions, each of which was obtained by random sampling of firing rates of both compared conditions with replacement keeping the original number of trials for each condition. We calculated the choice probability index for each resample and evaluated value of the original dataset compared to the distribution of the indices calculated for the resamples. If 95 % of the randomly generated distributions showed higher/lower choice probabilities than the original value; it was considered statistically significant ($p < 0.05$).

Response latency

Sliding ROC analysis (50 ms windows moved by 1 ms steps in a 500 ms window after stimulus onset) was used to calculate the response latency of the neurons. The latency was defined as the time for which the choice probability index exceeded for 50 consecutive windows the 95 % threshold of the bootstrapped data. If no value could be determined, a default latency corresponding to the 75th percentile of the response latency distribution of a given recording site was used (PFC: 179 ms; preSMA: 180 ms; CMAr: 225 ms).

Population analysis and normalization

Spike density histograms of significantly selective neurons assigned to a particular response class were normalized and averaged. Averaged firing rates of each cell were normalized by subtracting the mean baseline activity and dividing by the standard deviation of the baseline activity. Baseline activity was derived from a 300 ms period prior to stimulus onset. For illustrative purposes spike density histograms were convolved with a Gaussian kernel (bin width 150 ms, step size 1 ms).

Results

We recorded the activity of single neurons in the PFC, preSMA, and CMAr in two monkeys performing the rule-based detection task (Figure 1). The monkeys were presented with a visual stimulus at nine different stimulus intensity values; in half of the trials no stimulus was shown. Our experimental design assured that the monkeys could not prepare any motor response during the delay period, which followed the presentation of the visual stimulus. Only after the presentation of a rule cue the monkeys could prepare a particular motor action to report the presence or absence of the stimulus. The intensities of the stimuli were chosen close to the perceptual threshold to introduce uncertainty to the task. Thus the internal status of the animals determined whether the presented stimulus was detected (hit) or not (miss) or whether the absence of the stimulus was correctly reported (correct rejection) or erroneously indicated as a stimulus present trial (false alarm). Both monkeys reported in almost 100 % of the trials the presence of salient stimuli. In about 90 % of stimulus absent trials, the monkeys correctly rejected the presence of any stimulus; for stimuli close to the perceptual threshold animals were able to correctly detect the stimulus in a proportion of trials dependent on the intensity. The details of behavioral performance are presented in Merten and Nieder (2012).

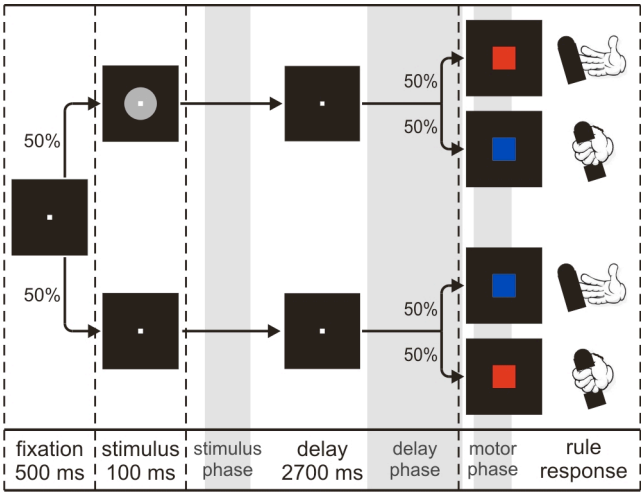

Figure 1. Rule-based detection task. To start a trial the monkeys grasped a lever and maintained fixation. In 50 % of the trials, the monkeys were presented with a grey object, whose intensity varied in nine levels, centered around the perceptual threshold. In the other 50 % of the trials, no stimulus was shown. During the delay period the animals decided about the presence or absence of the stimulus. After the delay, a color cue (50 % red, 50 % blue) appeared to instruct the appropriate response to a particular decision. After the presentation of a stimulus, a red square cue required the monkeys to release the lever within 1000 ms to receive a fluid reward, wheras a blue cue demanded the monkey to keep holding the lever for another 1200 ms. The rule applied in the inverse way in stimulus absent trials. The protocol ensures, that no motor response preparation could take place during the delay period. The grey areas mark the periods of data analysis: stimulus and delay phase during the decision period and the motor phase, after the rule-cue onset.

Types of neurons processing the abstract deciosion

We recorded randomly selected neurons in the lateral PFC around the principal sulcus; in the preSMA, largly rostral to the arcuate genu; and in the CMAr, which is buried in the cingulate sulcus spanning both banks of the sulcus rostral to the arcuate genu (PFC: 708 neurons; preSMA: 520 neurons; CMAr: 149 neurons). The placement of electrodes, depicted in Figure 2, was reconstructed using MR images and depth estimation (PFC: monkey H: 2-4.8 mm, monkey M: 2-5.8 mm; preSMA: monkey H: 2-5.6 mm, monkey M: 2-5 mm; CMAr: monkey H: 10-11 mm, monkey M: 7-13 mm).

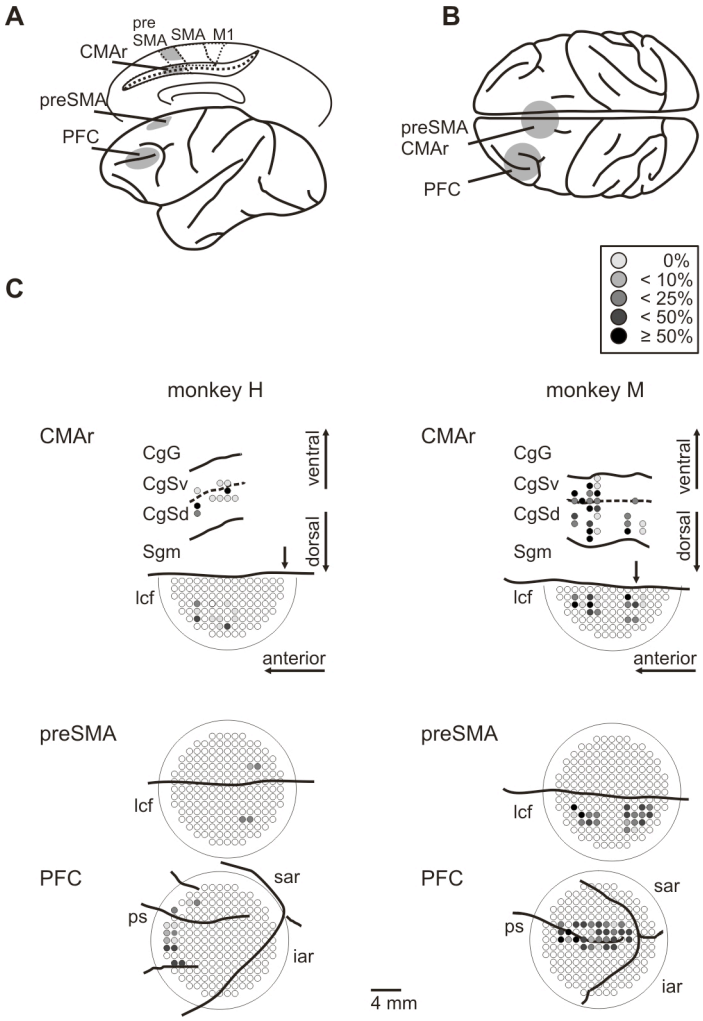

Figure 2. Recording sites. (A) Medial and lateral view of the monkey brain showing the recording sites in the lateral prefrontal cortex (*PFC*), pre-supplementary motor area (*preSMA*), and the cingulate motor area (*CMAr*). *SMA*, supplementary motor area; *M1*, primary motor cortex. (B) Locations of the two recording chambers indicated on a top view of a monkey brain (grey area). (C) The circular panels show the precise recording sites inside each recording chamber for both monkeys. The proportion of decision neurons at individual recording sites is coded on a grey scale. The locations and the density of the CMAr decision neurons are depicted on the surface to indicate their location within the recording chamber. They have also been projected to an unfolded reconstruction of the medial wall. The medial wall is reflected upward from the midline (*lcf*) so that it appears upside down. Solid lines indicate the boundaries of the lower and upper lips of the cingulate sulcus; a dashed line depicts the fundus. The arrow shows the level of the genu of the arcuate sulcus; *ps*, principal sulcus; *iar*, inferior arcuate sulcus; *sar*, superior arcuate sulcus; *lcf*, longitudinal cerebral fissure; *CgG*, cingulate gyrus; *CgSv*, ventral bank of the cingulate sulcus; *CgSd*, dorsal bank of the cingulate sulcus; *Sgm*, medial superior frontal gyrus.

For all three areas we compared the coding of the abstract perceptual detection during the early decision phase (stimulus phase) and during the late decision processing, when any motor preparation was still excluded (delay phase, compare Figure 1). We were interested to investigate how the activity of the neurons was influenced by the subjective decision about the stimulus presence ('yes' decision) or absence ('no' decision) and whether and how strongly the activity was modulated by the physical properties of the presented stimulus. We applied stepwise linear regression analysis (SLR) to access the impact of both factors on the firing rates of hit and false alarm trials ('yes' decision) compared for all stimulus intensities to correct rejections and miss trials ('no' decision). We found that the abstract decision was processed by all three recorded areas: 58/708 (8 %) of the neurons in the PFC, 69/520 (13 %) in the preSMA, and 16/149 (11 %) in the CMAr significantly encoded the monkey's judgment about the stimulus presence or absence during the stimulus phase ($p < 0.05$, SLR analysis, Figure 3A). Significantly more cells represented the decision in the preSMA compared to the PFC ($p < 0.05$, Fisher's exact test, Bonferroni corrected).

During the delay phase, we recorded 128/708 (18 %) abstract decision selective neurons in the PFC, 113/520 (21 %) in the preSMA, and 27/149 (18 %) in the CMAr ($p < 0.05$, SLR analysis, Figure 3B). The proportions were not significantly different for the three areas ($p > 0.05$, Fisher's exact test). These neurons were termed 'decision neurons'.

Stimulus intensity was encoded by 96/708 (14 %) of the cells in the PFC, 58/520 (11 %) in the preSMA, and 24/149 (16 %) in the CMAr during the stimulus phase; and by 106/708 (15 %) in the PFC, 73/520 (14 %) in the preSMA, and 24/149 (16 %) in the CMAr during the delay phase ($p < 0.05$, SLR analysis, Figure 3). No differences of the proportions of intensity coding cells were found between the three areas during the stimulus and delay phase ($p > 0.05$, Fisher's exact test). Few cells were modulated by both factors stimulus intensity and decision during both decision analysis phases in all areas (1 - 3 %, compare Figure 3).

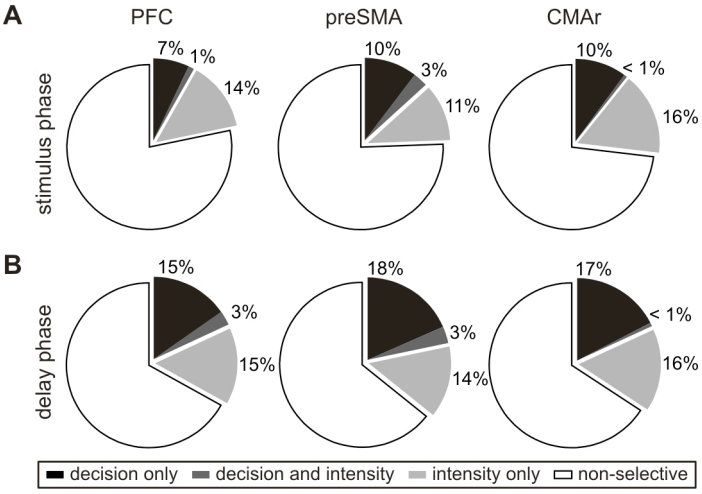

Figure 3. Proportions of selective cells in the decision period. The pie charts show frequency distributions of neurons coding stimulus intensity and / or decision in the prefrontal cortex (PFC), presupplementary motor area (preSMA), and cingulate motor area (CMAr) during the stimulus (A) and delay phase (B).

Classes of neurons encoding the abstract decision

We identified different types of decision neurons according to the active modulation of their discharge rates during 'yes' and 'no' decisions. This approach assured that exciting as well as suppressive effects could be detected as the dominant influence of a particular stimulus. The selectivity of a neuron was defined by the condition, which elicited the stronger modulation of the neuron's firing rate. Neurons modulating (increasing or decreasing) their activity more strongly for 'yes' decisions were termed 'yes' neurons, cells modulating their activity more strongly to 'no' decisions were called 'no' neurons.

During the stimulus phase, virtually all decision neurons in all three areas PFC, preSMA, and CMAr were classified as 'yes' neurons. Figure 4A depicts single cells that increased their firing rates for 'yes' decisions (during hit trials, when a salient stimulus was present), whereas the activity for 'no' decisions (correct rejections in stimulus absent trials) remained at baseline level. This activity is compared to the discharges in trials when a near-threshold stimulus was presented, and the animal decided that the stimulus was present in about half of the trials, but missed the stimulus in other half of

trials. Neuronal responses for threshold trials closely resembled the responses for the decisions in salient trials and, therefore, correlated significantly with the monkey's judgment.

Some cells encoded the decision for a short period after stimulus presentation (e.g. Figure 4A, the PFC neuron), other cells maintained high levels of activity for 'yes' decisions throughout the delay period (e.g. Figure 4A, the preSMA neuron). Neurons in Figure 4B show a transient suppression of their firing rates for 'yes' decisions. Few cells (see Table 1) were erroneously classified as 'no' neurons during the stimulus phase. The averaged responses of such cells recorded in the preSMA are displayed in Figure 6; they clearly show a stronger decrease of activity for 'yes' decisions compared to the increase of activity for 'no' decisions. These cells were excluded from further analysis. Overall, decisions in the stimulus phase were processed by active 'yes' neurons in the PFC, preSMA, and CMAr.

Interestingly, in all three areas additionally to the population of 'yes' cells (Figure 5C), a population of 'no' cells emerged during the delay phase (Figure 5D). 'Yes' neurons, just as in the stimulus phase, increased (Figure 4C) or decreased (not shown) their discharge rates more strongly for 'yes' decisions in salient and threshold trials. However, the newly emerging category of 'no' neurons modulated their firing rates more strongly for 'no' decisions (Figure 5D), i.e., during correct rejections, when no stimulus appeared and during miss trials whenever a physical stimulus remained undetected.

The identified cell classes and the respective numbers of cells are summarized in Table 1. Averaged responses of decision neurons averaged for each cell class and each frontal cortex area are depicted in Figure 5. The population analysis includes the activity of the decision neurons during false alarm trials. In a similar way as during hit trials, the false alarm firing rates were increased (Figure 5A) or decreased (Figure 5B) during the stimulus phase; and increased (Figure 5C) or remained at baseline level (Figure 5D) in the delay phase during this erroneous 'yes' decisions.

Table 1: Classification of 'yes' and 'no' decision cells

	Stimulus Phase				Delay Phase			
	'yes' neurons		'no' neurons		'yes' neurons		'no' neurons	
	↑	↓	↑	↓	↑	↓	↑	↓
PFC	34	23	1	0	79	25	21	3
preSMA	32	29	8	0	65	18	25	5
CMAr	4	11	1	0	13	7	7	0

↑ increasing firing rate; ↓ decreasing firing rate

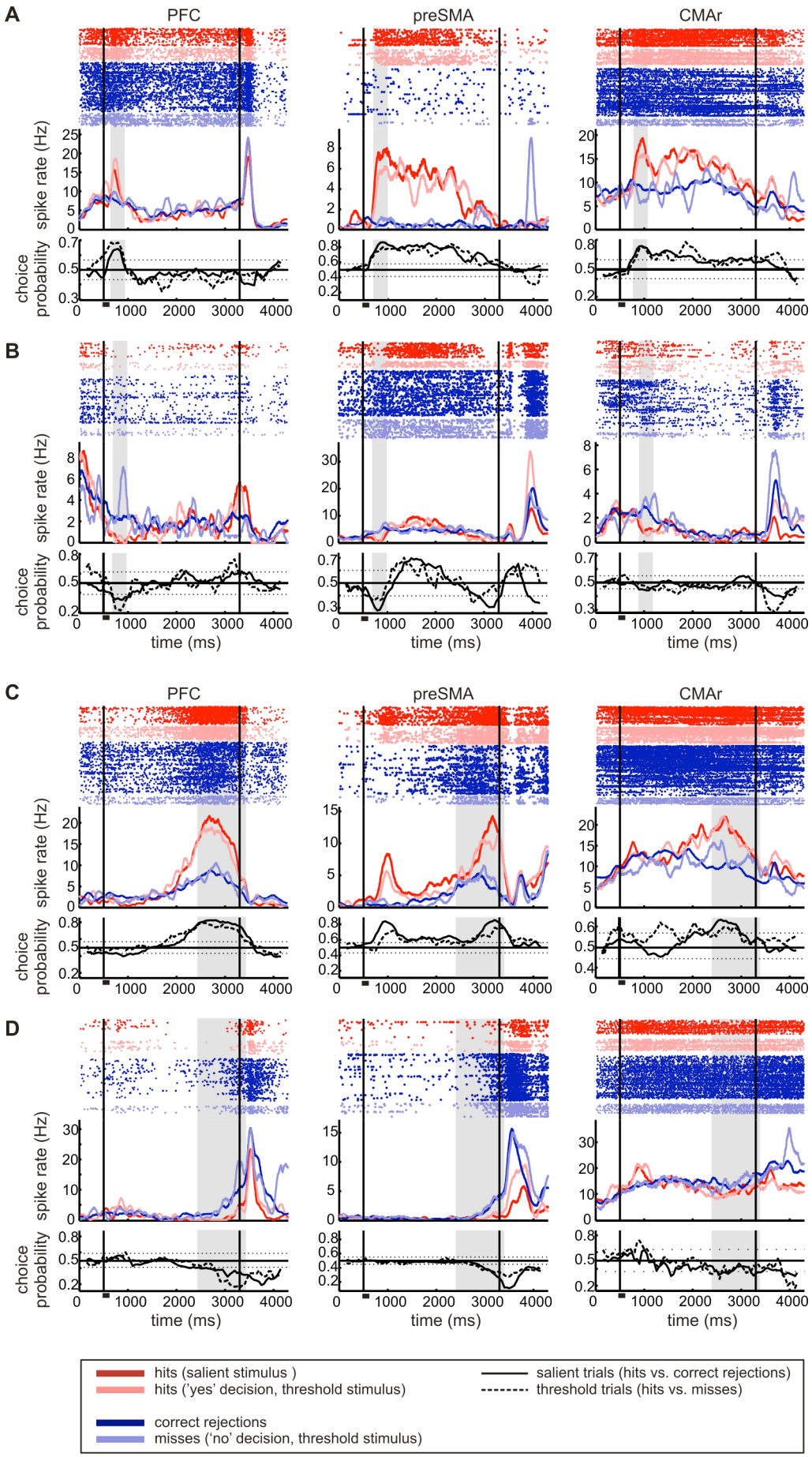
A
PFC
preSMA
CMAr
spike rate (Hz)
choice probability
B
time (ms)
C
D
hits (salient stimulus)
hits ('yes' decision, threshold stimulus)
correct rejections
misses ('no' decision, threshold stimulus)
salient trials (hits vs. correct rejections)
threshold trials (hits vs. misses)

Figure 4. Example decision neurons in the PFC, preSMA, and CMAr. Decision neurons correlated with the subjective decision of the monkey about the presence or absence of the stimulus. During the stimulus phase (analysis window highlighted by the grey shaded area), 'yes' neurons encoded the decision by increasing (A) or decreasing (B) their firing rates for 'stimulus present' reports of the monkey. During the delay phase, decision is encoded by active 'yes' (C) and 'no' (D) neurons increasing their firing rates for 'yes' (stimulus present) or 'no' (stimulus absent) decisions, respectively. Top panels of each plot depict dot raster plots; middle panels represent the corresponding spike density histograms averaged and smoothed with a Gaussian kernel for illustration. The vertical black lines indicate the presentation of the stimulus (at 500 ms) and the rule cue (3300 ms). Stimulus duration is marked by a small horizontal bar underneath the x-axis of each plot. Bottom panels show the individual neurons' choice probability indices as a function of time. Dotted lines mark significance levels.

Temporal response characteristics

For all decision cells, we calculated the choice probability indices (ROC analysis, (Green and Swets, 1966; Britten et al., 1996)) to quantify the predictability of the monkey's decision throughout the trial. The bottom panels of Figure 4 represent the comparison of choice probabilities calculated for 'yes' decisions in salient hit trials versus 'no' decisions in stimulus-absent trials (correct rejections) as well as for 'yes' (hits) versus 'no' (misses) decisions in threshold trials. Indices derived from threshold trials closely mirrored indices of salient trials; values above chance level indicated the intervals during which these neurons' discharges reliably predicted the monkey's decision ($p < 0.05$, ROC analysis, bootstrapping). This effect was also present on the neuronal population level (Figure 5).

Response latencies

To further analyze the response characteristics of the neurons actively participating in the task, we computed the latency of the neuronal response selectivity after the onset of the stimulus. There was no difference in the response latency between neurons encoding the intensity of the stimulus (250 ms) and neurons encoding the monkey's subjective decision (231 ms) ($p > 0.05$ Mann-Whitney U test). We found comparable response latencies (intensity and decision coding neurons together) in all thee recorded areas: 234 ms in the PFC, 255 ms in the preSMA, and 280 ms in the CMAr ($p > 0.05$, Kruskal-Wallis test).

Strength of decision encoding

We compared the PFC, preSMA, and CMAr areas in their selectivity strength for the abstract decision. Two types of measurements were used for this evaluation. First, we compared the decision SLR coefficients of decision neurons across the three areas (a_d, Figure 7A). Moreover, we related the strength of the decision processing of these brain areas to the encoding strength of stimulus intensity, by intensity selective neurons (a_{int}, Figure 7B). We calculated a three-way ANOVA for these SLR coefficients with the following factors: neurons coding intensity or decision only, stimulus or delay analysis phase, and recording area. This analysis showed a significant effect of recording area (PFC: $a_d = 0.22$; preSMA $a_d = 0.27$; CMAr $a_d = 0.24$; $p < 0.05$, ANOVA). Post-hoc tests revealed that preSMA showed significantly higher decision encoding strength than PFC ($p < 0.01$, Wilcoxon test, Bonferroni corrected). No differences of decision encoding strength were found between the analysis phases ($p > 0.05$, ANOVA). In all three areas the encoding strength of the abstract decision ($a_d = 0.24$) was significantly larger compared to the encoding strength of stimulus intensity ($a_{int} = 0.04$; $p < 0.05$, ANOVA).

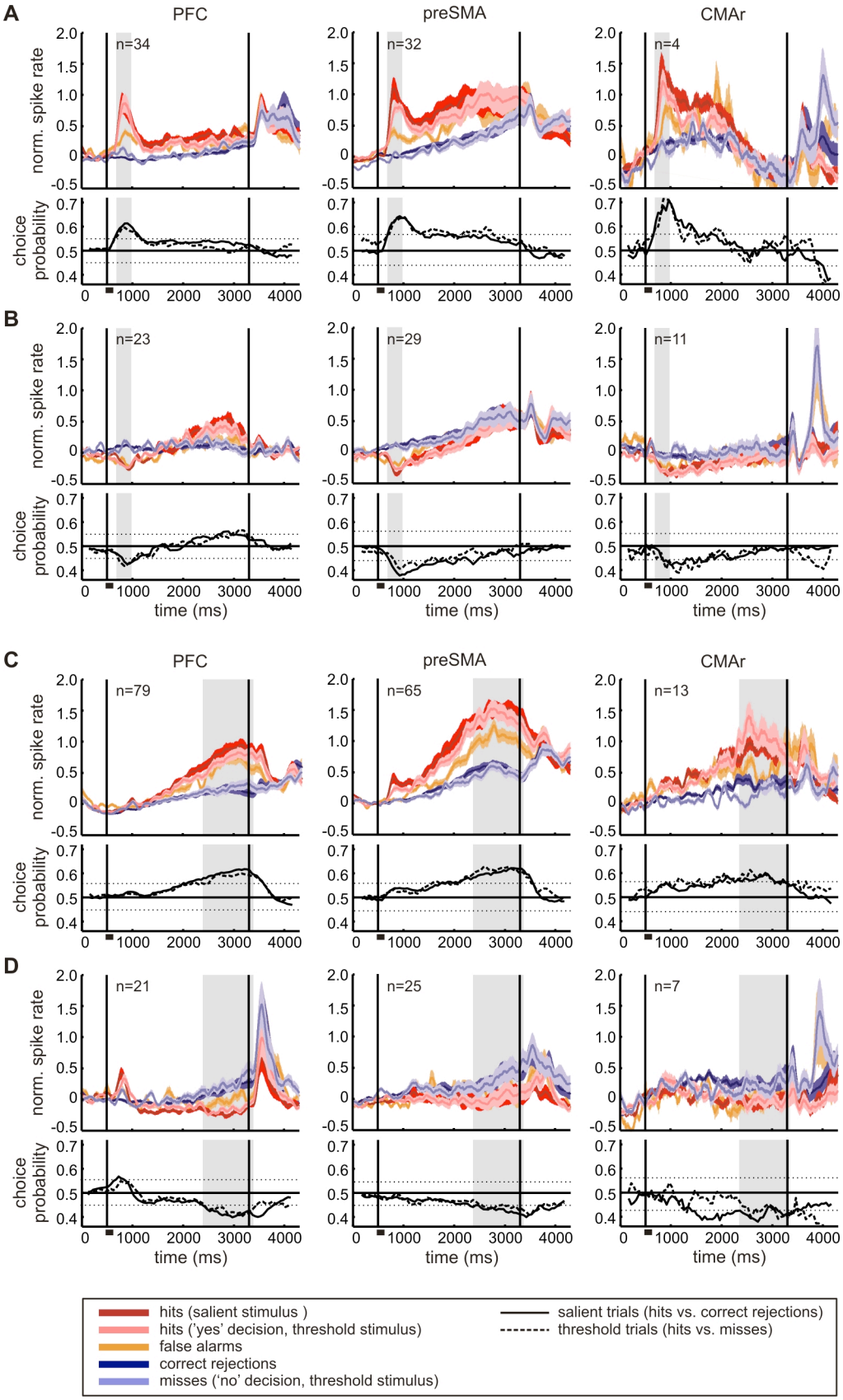

Figure 5. Decision neurons averaged across different response classes and recording areas. (A, B) Normalized, averaged responses and choice probability indices of neurons in the PFC, preSMA, and CMAr coding the 'yes' decision during the sample phase. (C, D) Averages of neuron classes increasing their activity for 'yes' decisions (C) or for 'no' decisions (D) during the delay phase. Shaded regions indicate s.e.m, n, number of neurons. Same layout as in Figure 4.

As a second measurement of the encoding strength, we used the choice probability indices derived from salient and threshold trials for all recording areas during the stimulus and delay phase, respectively. A three-way ANOVA with factors (salient/threshold scaled choice probability, *sc*) × (stimulus/delay phase) × (recording area) showed a significant effect of the recording area PFC: sc = 0.11; preSMA *sc* = 0.14; CMAr *sc* = 0.14; $p < 0.05$). Post-hoc tests revealed that preSMA showed significantly higher decision encoding strength than PFC ($p < 0.01$, Wilcoxon test, Bonferroni corrected) and significantly higher choice probabilities than CMAr ($p < 0.05$, Wilcoxon test, Bonferroni corrected).

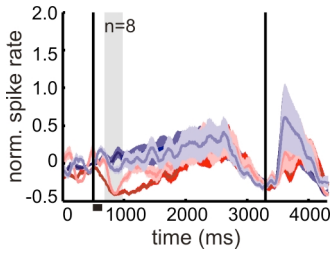

Figure 6. Averaged responses of misclassified decision cells. Normalized and averaged responses of eight preSMA neurons coding the decision during the stimulus phase, which erroneously were classified as 'no' cells. The response characteristics of the average (as well as single cells, not shown) are equivalent to cells decreasing their firing rates during 'yes' responses (see Figure 5B, same layout as in Figure 5).

To access the strength of the influence of stimulus intensity on the encoding of abstract decisions, we plotted the mean choice probability indices of the salient hit trials and correct rejections trials against the indices of the threshold hit trials and miss trials (Figure 8). Regression lines provided a good fit to the indices. The fitted slopes slightly deviated from 1, indicating lower choice probability values for threshold trials and, therefore, a weak impact of stimulus intensity on decision coding. Yet, no significant effect of the factor salient/threshold choice probability was found ($p > 0.05$, ANOVA).

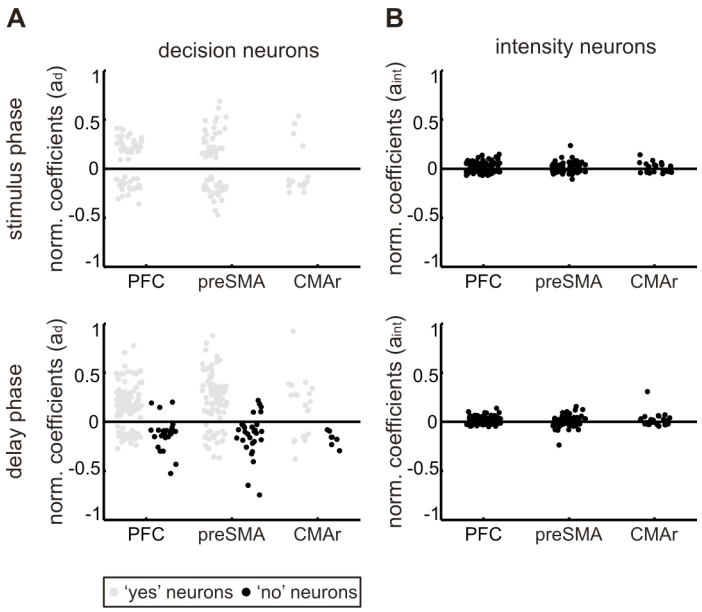

Figure 7. Strength of decision and intensity encoding across the recorded areas. Stepwise linear regression (SLR) coefficients quantify the dependence of (A) the activity of decision neurons on monkey's subjective decision about the presence or absence of the stimulus (a_d). Decision coefficients are separated for 'yes' and 'no' decision neurons. This encoding strength is compared to (B) the dependence of the firing rates of intensity neurons on stimulus intensity (a_{int}). Normalized coefficients are plotted across all recorded brain areas and both decision phases. Points are randomly shifted along the horizontal axis for clarity.

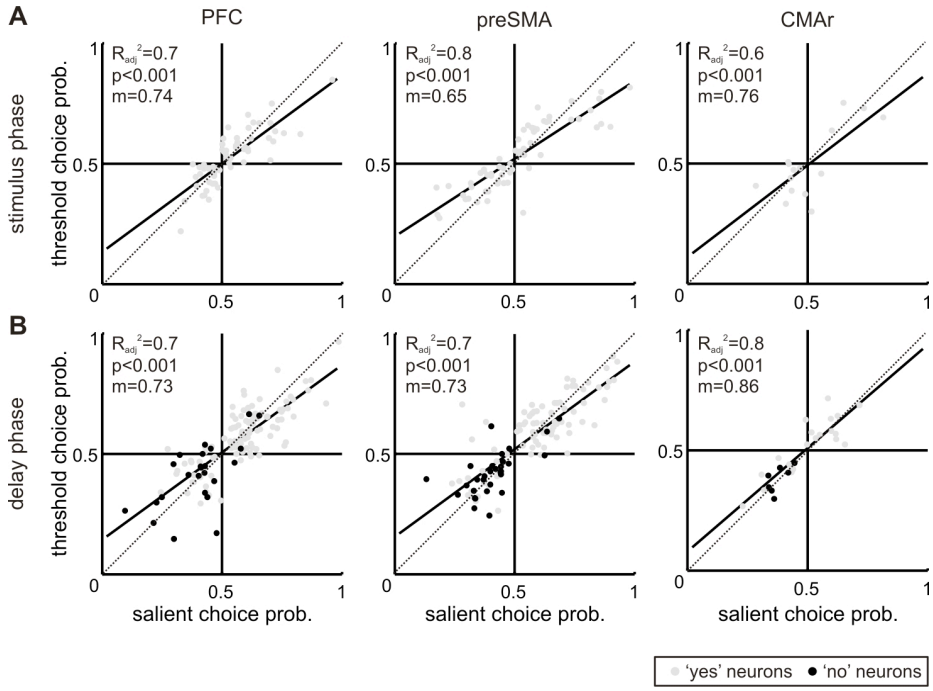

Figure 8. Comparison of choice probability indices for salient and threshold trials. Choice probability indices of the salient trials are plotted against indices of threshold trials for significant decision cells (stimulus phase (A); delay phase (B)) for all recorded brain areas. Grey points depict values of 'yes' neurons; black points mark 'no' neurons. Choice probability indices > 0.5 mark cells increasing their firing rates for the type of decision they encode. Neurons decreasing the firing rate to encode the decision have choice probability indices < 0.5. The dotted diagonal depicts the line of equality on which all points would fall if the cells differentiated equally well between salient hits / correct rejections and threshold hits / misses. The continuous black line represents the regression line. Inserts show goodness of fit estimation (R_{adj}^2) and the associated p-values for H_0: $R_{adj}^2=0$; m, slope of the linear fit.

Encoding during the motor phase

To access the encoding properties of PFC, preSMA, and CMAr during the motor phase (compare Figure 1), we analyzed the selectivity of these areas for the factors decision, stimulus intensity, rule cue, and the instructed motor action using SLR analysis. The proportions of neurons selective for these factors are summarized in Table 2. Even during the motor phase after the motor action was instructed, neurons in all three areas maintain the representation of the decision. Comparable proportions of neurons encoding the decision ($p > 0.05$, Fisher's exact test) and their SLR coefficients ($p > 0.05$, Wilcoxon test) were found for all three areas. The representation of the motor action showed significant differences. The fractions of neurons encoding the motor action significantly exceeded the fraction of PFC motor coding cells in the preSMA ($p < 0.01$, Fisher's exact test, Bonferroni corrected) and the CMAr ($p < 0.05$, Fisher's exact test, Bonferroni corrected). Additionally, the SLR coefficients were significantly higher in preSMA compared to PFC neurons ($p < 0.05$, Wilcoxon test, Bonferroni corrected).

Table 2: Proportions of neurons encoding task factors during the motor phase

	Decision	Intensity	Action	Rule-cue
PFC	17 %	13 %	16 %	11 %
preSMA	15 %	16 %	31 %	15 %
CMAr	13 %	11 %	30 %	11 %

A sliding SLR analysis illustrates the time course of the encoding of the different factors (proportions of selective neurons, Figure 9A; SLR coefficients, Figure 9B). Only after a latency of 100 ms after the rule-cue onset, the neurons started to encode the color of the rule-cue and most dominantly the motor response. Although comparably high proportion of neurons represents the intensity of the stimulus during the motor phase in all three areas (see Table 2), their SLR coefficients are negligibly small (Figure 9B).

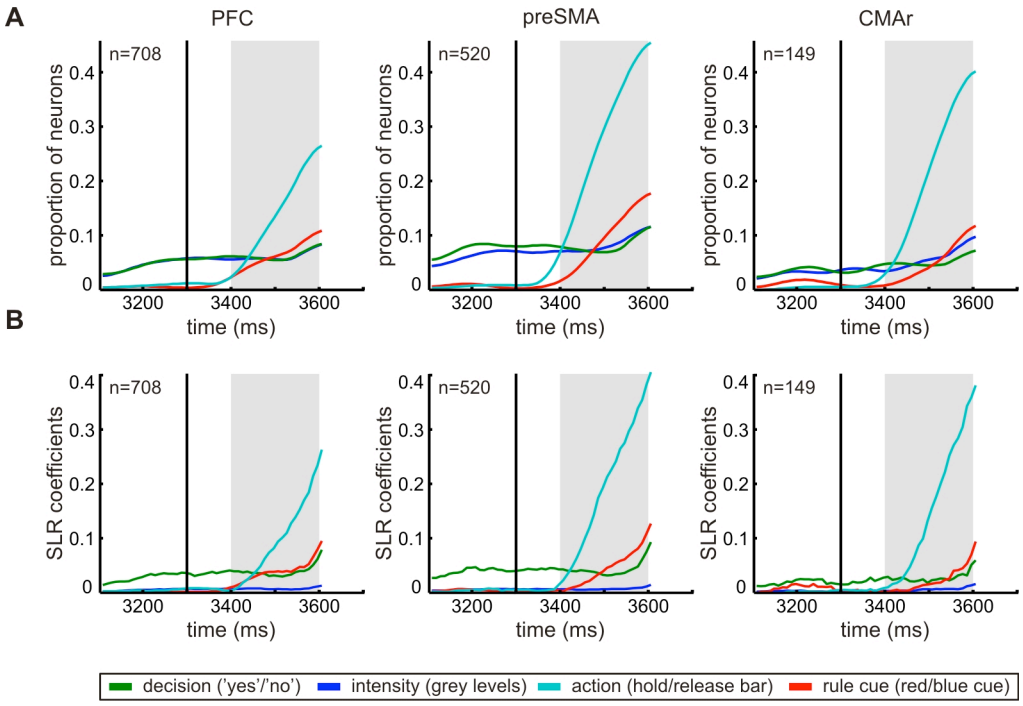

Figure 9. Neuronal responses during the motor phase. (A) Proportions of neurons in each recorded area significantly selective for the factors decision, stimulus intensity, motor response, and rule cue and (B) encoding strength of these factors across time during the motor phase. The vertical black line at 3,300 ms depicts the onset of the rule cue that instructs the action. The grey area highlights the analysis window of the motor phase, which starts 100 ms after the onset of the rule cue and lasts for 200 ms, which is the average time, after when monkeys performed an action in instructed release trials. No selectivity for the rule cue or motor action was present during the previous delay phase (until 100 ms after rule onset).

Differences between the PFC, preSMA, and CMAr

A summary of the differences between the studied brain structures is presented in Figure 10. A higher proportion of decision encoding neurons was identified during the early decision phase in the preSMA than in the PFC; the fraction of action encoding cells during the motor phase is higher in the preSMA and the CMAr compared to the PFC

(Figure 10A). The encoding strength for the motor action was also significantly larger in the preSMA than in the PFC (Figure 10B). Both SLR and ROC analyses identified the preSMA as a more reliable encoder of the abstract decision compared to the PFC (Figure 10B,C). Additionally, the choice probabilities of the preSMA were also significantly larger compared to the CMAr (Figure 10C).

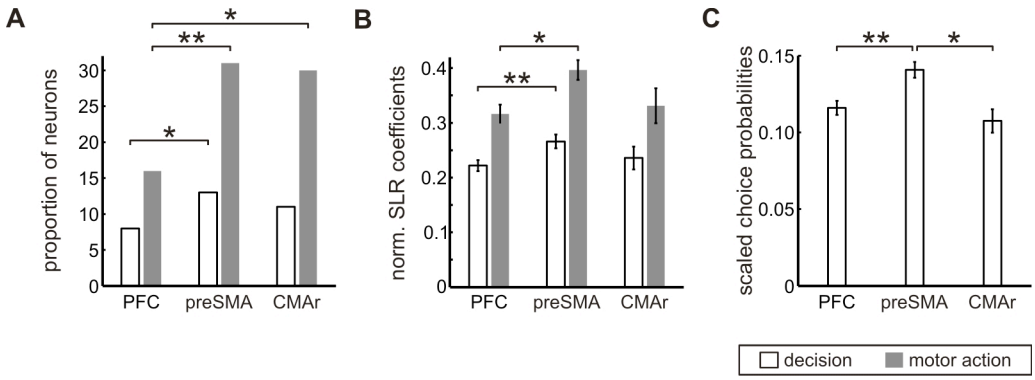

Figure 10. Differences between PFC, preSMA, and CMAr. Comparisons of quantity and quality of decision and action encoding during the decision and motor phases, respectively, for all three studied brain structures. (A) Proportions of neurons significantly encoding the decision during the early decision phase compared to the proportions of neurons encoding the motor report during the motor phase. (B) Comparison of normalized stepwise linear regression (SLR) coefficients for the factors decision during the decision phase and motor action during the motor phase. (C) Scaled choice probability indices for decision derived during the decision phase. Asterisks indicate significant differences (* $p < 0.05$; ** $p < 0.01$, Bonferroni corrected).

Discussion

In the present study, we investigated the representation of abstract detection decisions in the areas preSMA and CMAr and compared it to the encoding of such decisions in the PFC. Both areas, traditionally associated with the planning of motor activities, represented the abstract decision about the stimulus presence or absence by a similar mechanism as the PFC (Merten and Nieder, 2012), even before any motor action instruction became available. Notably, the overall strength of abstract decision encoding was even stronger in the preSMA than in the PFC. During the motor phase, after the instruction of the motor action, preSMA and CMAr still continued to encode the decision with similar selectivity as the PFC, in spite of the more pronounced representation of the upcoming motor action.

Functional connectivity of the PFC, preSMA, and CMAr

The PFC has been identified as the most important cortical structure for the representation of cognitive control and highly abstract processes (Miller, 2000; Miller and Cohen, 2001; Fuster, 2008). The PFC is thought to interpret the sensory data and recruit brain areas and circuits which generate motor commands to execute a response (Heekeren et al., 2008; Shadlen et al., 2008). Both areas, preSMA and CMAr, are reciprocally interconnected with the PFC (Bates and Goldman-Rakic, 1993; Lu et al., 1994; Wang et al., 2005). This extensive cortico-cortical connectivity provides great

possibilities for communication between cognitive and motor systems. The preSMA and CMAr have been shown to play important roles in the convergence of sensory information and linking it to action (Hernández et al., 2002; Romo and Salinas, 2003; Hoshi et al., 2005; Hoshi and Tanji, 2006). However, the capacity of these brain structures to encode abstract processes, not linked to action, has not been investigated so far.

In more detail, the CMAr has prominent projections to the primary motor cortex (Bates and Goldman-Rakic, 1993; He et al., 1995; Dum and Strick, 2002) and to the corticospinal system (Hutchins et al., 1988; He et al., 1995). Stimulation studies underpin the involvement of this area in the initiation and execution of arm movements (Shima et al., 1991; Procyk et al., 2000). Further, the activity of the CMAr is influenced by emotional and motivational states as it receives projections from the limbic system (Amaral and Price, 1984; Morecraft and Van Hoesen, 1998) and thalamic nuclei (Vogt et al., 1987; Vogt and Gabriel, 1993). The anterior cingulate cortex is the main target area of the mesocortical dopamine system (Lewis, 1992; Vogt and Gabriel, 1993), this implicates CMAr in error detection (Gemba et al., 1986; Ito et al., 2003) and converting reward value into action (Shima and Tanji, 1998).

The area preSMA has sparse projections to the corticospinal system (Dum and Strick, 1991; Luppino et al., 1994), no projections to the primary motor cortex, yet it has extensive connections to the non-primary motor structures, as the CMAr (Luppino et al., 1993). This connectivity is responsible for more abstract, the so-called high level motor functions like the sequential organization of multiple movements (Shima and Tanji, 2000; Nakajima et al., 2009), updating of motor plans (Shima et al., 1996), or switching from automatic to controlled action (Isoda and Hikosaka, 2007).

Our study demonstrates the involvement of both areas also in the processing of abstract decisions, which could not be formulated as motor intensions. This emphasizes the strong role of premotor areas in cognitive control; and seems inconsistent with the proposed function of PFC to process abstract calculations exclusively.

Processing of abstract decisions in the PFC, preSMA, and CMAr

Using a rule-cue to separate the motor action from the processing of sensory information, we addressed the decision process as an abstract process. Similar to the previously reported abstract decision processing mechanism in the PFC (Merten and Nieder, 2012), we found single neurons in the preSMA and CMAr encoding the perceptual report of the animal, before the motor action was specified. Same classes of decision neurons were involved: during the stimulus phase, neurons modulated their firing rates for 'yes' decisions only; however, during the late delay phase, additionally, the abstract category of 'no' decisions was represented actively by a group of neurons.

The fraction of the neurons in the preSMA and the strength of encoding of abstract decisions were even stronger compared to the PFC. A stronger selectivity of this area has also been proposed for the processing of abstract numerical rules (Vallentin et al., 2012) compared to the selectivity of PFC neurons. After the presentation of the rule-cue, preSMA and CMAr continued to encode the decision to the same extent as the PFC. During the motor phase, proportionally more neurons represented the instructed

motor-action in the two areas than the PFC. Moreover, the neurons in the preSMA showed stronger selectivity for motor actions than PCC neurons. Overall, our finding of abstract perceptual decisions representation in the preSMA and CMAr expands the previously reported competence of these areas in intentional decisions to more abstract processes, which must be calculated independent of motor aspects and are only relevant for motor actions in later task phases.

Detections in the abstract and report dependent frameworks

The involvement of preSMA in detection decisions has been previously studied in the intentional framework on the single-cell level (de Lafuente and Romo, 2005; 2006). In this framework, only one decision category, stimulus present, was encoded actively by 'yes' neurons; no active encoding of stimulus absent decisions was found. This finding demonstrates the flexibility of the preSMA to deploy a particular processing mechanism for decisions dependent on whether an abstract decision is enforced or whether the decision can be expressed in terms of motor preparation.

Information processing in the brain

We did not find differences in the latencies of decision encoding for PFC, preSMA, and CMAr. One might argue that the abstract decision could also be computed in parallel in different brain areas, similar to decisions studied in action-based framework (Cisek and Kalaska, 2010). Alternatively, the failure to identify differences in the latencies of the responses might constitute a resolution problem, given a limited number of neurons and notoriously difficult latency estimates in association cortices, because the projections between PFC and preSMA are direct involving only one synapse (Wang et al., 2005). A serial processing mechanism of information would be required for the accomplishment of complex operations. First, the brain would construct an internal representation of the stimuli, then use this information for cognitive, context-dependent computations in a nonmovement-related framework; and finally construct and execute an action plan. Serial processing is prerequisite for solving of situations, which require several steps of cognitive computation before any motor action can be carried out.

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Publication III

A neuronal network model of abstract detections: modeling of active 'yes' and 'no' neurons

Katharina Merten and Andreas Nieder

Department of Animal Physiology
Institute of Neurobiology
University of Tübingen, Germany

A neuronal network model of abstract detections: modeling of active 'yes' and 'no' neurons

Katharina Merten and Andreas Nieder

Animal Physiology, Institute of Neurobiology, University of Tübingen, 72076 Tübingen, Germany

Detections of sensory stimuli belong to the most elemental perceptual experiences. Recently, we explored the representation of abstract visual detections, which are independent of the motor report about the decision, in electrophysiological experiments in rhesus monkeys. We found that single frontal cortex neurons encoded the subjective judgment of the monkeys about the stimulus. In addition to neurons found previously in a motor-based framework, which actively encoded the 'yes-stimulus present' decision, we identified a second type of neurons that actively encoded the 'no-stimulus absent' decision. Here, we propose a computational neuronal network model for the processing of abstract detection decisions that specifically seeks to explain the emergence and function of active 'no' neurons. Our model output corresponds well with the behavioral and the neuronal single-cell data of real experiments; it generates all experimentally observed classes of decision neurons and captures the characteristics of their responses. Moreover, we address the question of the origin of threshold values that are typically used to evaluate neuronal responses to produce a decision. We suggest that the activity of real neurons encoding stimulus intensity might be well suited to provide such threshold values. Our computational results provide new insights into the mechanism of decision-making supporting the idea that abstract perceptual 'yes'/'no' decisions are translated into categorical judgments and extend our physiological findings.

Introduction

Detections of sensory stimuli belong to the simplest perceptual experiences and are prerequisite for further cognitive processing; yet they present great challenges to scientists studying the underlying decision process. Signal Detection Theory (SDT) provides a successful formalism to address the detection mechanisms in the presence of uncertainty. It determines how a single observation of noisy evidence can be converted into a choice (Green and Swets, 1966). When the sensory evidence includes a signal, the magnitude of the evidence is different from a state in which the stimulus was absent. SDT helps to decide which of the states (stimulus present or stimulus absent) gave rise to the observation of this evidence. Similarly, in the framework of a diffusion model (Gold and Shadlen, 2002), sensory evidence is accumulated over time and if a signal were present, the decision variable, which is based on sensory evidence, would be biased in favor of the 'stimulus present' and against the 'stimulus absent' state. If the decision variable exceeds a criterion, the decision outcome is 'yes', otherwise 'no' (Gold and Shadlen, 2007). These models describe accurately the phenomenon, but it is difficult to assign biophysical and physiological meaning to the model parameters (Deco and Romo, 2008).

A biologically plausible model was suggested by Deco and colleagues (Deco et al., 2007) who simulated the detection decision as a dynamical bistability phenomenon. This model was based on the neurophysiological findings of de Lafuente and Romo (2005), who found neurons in the monkey medial premotor cortex that reflected the subjective experience of the stimulus presence during a mechanical vibration detection experiment. The neurons actively encoded the 'yes' decision; the 'no' decision was represented as a default decision in a report-dependent protocol. The proposed model is based on an excitatory population, which is selective to the stimulus and yields a 'yes' decision in a high activation state; additionally a second population encodes the default 'no' response as a constant bias. Both populations inhibit each other recurrently. The fluctuation-driven computation causes a probabilistic transition between the two bistable states, corresponding to the 'yes' or 'no' decision.

However, this processing mechanism appears to be best suited when the decision is made in a movement-related framework. In a recent study, we have excluded motor preparatory activity from the processing of detection decisions. We found that the representation of such abstract decisions, involves active 'no' neurons in in the prefrontal cortex (PFC), the pre-supplementary motor areas (preSMA), and the rostral part of the cingulate motor area (CMAr) of rhesus monkeys (Merten and Nieder, 2012; submitted).

The emergence of active 'no' neurons is of particular interest because the sensory evidence leading to the 'stimulus absent' decision involves only noise and lacks any presence of a signal. In this work, we propose a computational network model that describes possible connectivity and information flow during abstract decision-making that leads to active 'no' neurons.

Methods

Analysis of the neuronal responses and normalization

Firing rate-intensity functions were calculated for decision neurons classified according to their response type (see Merten and Nieder, 2012). Firig rates were averaged during the stimulus phase, a 300 ms interval after stimulus onset shifted by the individual response latency of the cell, and the delay phase, a 1000 ms window starting 1900 ms after stimulus onset. For the population analysis decision neurons recorded in PFC, preSMA, and CMAr were pooled. Activity of each cell was normalized by subtracting the cell's mean activity and dividing by the standard deviation of the baseline activity (300 ms prior to the stimulus onset).

Network model architecture

We developed a feedforward network model with two processing layers (stimulus phase and delay phase) that uses firing rates as in- and output values (Figure 2). The firing rate of the sensory evidence, the input to the network r_s, is linearly dependent on the stimulus intensity c and additional noise $r_0 \in N\,(0,\sigma)$:

$$r_s = c + r_0 .$$

All computational units of the two processing layers (N1-N6) have the same characteristics. They sum up their input and generate an output by a linear transition function. The input to the computational units is dependent on the firing rate of the driving unit in the previous layer r_{inp}. For the stimulus phase computational units (N1, N2) input comes from the sensory evidence (r_s); the delay phase computational units (N3-N6) use the output of the stimulus phase as input firing rates: r_{out_exc} or r_{out_inh} respectively. Every computational unit is modulated in two ways. First, to model the decision, the input firing rate is processed via a threshold neuron (T1-T3) that uses a step function as a transition function to provide an output r_{th_out} only if the input firing rate reaches a threshold criterion r_{cr}:

$$r_{th\_out} = f(r_{inp}) = \begin{cases} r_{th} \ , \ r_{inp} > r_{cr} \\ 0 \ , \ otherwise \end{cases}$$

Second, to model the influence of stimulus intensity, the firing rate of every computational unit is modulated proportionally to the input firing rate independently of the threshold. It is necessary to use both modulation paths because the responses of the real data neurons to the decisions, which are not actively encoded by these neurons ('no' response of a 'yes' coding neuron or the 'yes' response of the 'no' neuron) are still modulated by stimulus intensity. Dependent on whether the connections of the modulation between units are excitatory or inhibitory, units either increase r_{out_exc} ($r_{N1,}$ $r_{N3,}$ r_{N5}) or decrease r_{out_inh} ($r_{N2,}$ $r_{N4,}$ r_{N6}) their activity. The input firing rates are added to a baseline noise of the unit r_0 and weighted according to the type of the connection by: w_{exc} for excitatory or w_{inh} for inhibitory connections:

$$r_{out\_exc} = (r_{0\,+} r_{th\_out} + r_{inp}) \cdot w_{exc},$$
$$r_{out\_inh} = (r_{0\,+} r_{th\_out} + r_{inp}) \cdot w_{inh}.$$

Modeling of the threshold criterion (r_{cr}) and the psychometric function

The value of the threshold criterion r_{cr} is drawn from a distribution, which covers the range of the input firing rates (r_s or $r_{N1,}$, r_{N2}) evaluated by this criterion. On each trial, the input firing rate is compared to the randomly selected criterion (Figure 3A). This comparison determines the decision outcome and thus whether the threshold neuron will increase its firing rate on that particular trial or not. The decision rule is to choose 'yes' if the input firing rate exceeds the criterion, otherwise the 'no' decision applies. Dependent on the stimulus condition (c = 0, stimulus absent; or c > 0, stimulus present) 'yes' decisions were classified in false alarms or hits; 'no' decisions in correct rejections or misses. The probability density function of the criterion firing rates determines the shape of the resulting psychometric curve (proportion of 'yes' responses for different stimulus intensities).

To model the exact psychometric curve acquired in the real experiments (Merten and Nieder, 2012; submitted), the real psychometric function can serve as the cumulative distribution function that determines the probability density function of the criterion values. The real performance data were fitted by a sigmoidal function and revealed the small bias the animals developed towards 'yes' responses whenever the stimulus was not visible. To illustrate the shape of the resulting threshold distribution, we fitted two sigmoidal functions to the real data $y(c)$: the ideal sigmoid performance curve and the curve accounting for the 'yes' decisions in trials when the stimulus was not visible to the monkeys (Figure 3B):

$$f(c) = \frac{y(0)}{1+e^{-\frac{c-m}{s}}} + y(4) - \frac{y(4)}{1+e^{-\frac{c-m}{s}}},$$

whereas the values m = 1.8 and s = 0.3 were estimated. The resulting probability density functions of the criterion are depicted in Figure 3C. The area under the bias-curve represents the probability of the criterion being zero. The criterion r_{cr} is randomly selected for T1, T2, and T3 from the resulting distribution (black curve) and is weighted by t_1, t_2, or t_3 to adapt to the range of the firing rates generated by the model (r_s or r_{N1}, r_{N2}).

The performance of the model is shown in Figure 3D. The psychometric function is based on the averaged proportion of the network's 'yes' decisions of the delay phase processing layer (N3-6). That is the proportion of trials in which the firing rate of the stimulus layer units N1 exceeded the criterion T2; and proportion of trials in which N2 remained below T3.

Modeling parameter

To generate the model data, we ran the simulation 3.000 times, for all stimulus intensity values. Following equations were applied to calculate the responses of the model neurons:

$$r_{N1} = \left(r_0 + r_{th\_out} + r_s\right) \cdot w_{exc},$$

$$r_{N2} = \left(r_0 + r_{th\_out} + r_s\right) \cdot w_{inh} \qquad with \qquad r_{th\_out} = \begin{cases} r_{th}, & r_s > \left(r_{cr} \cdot t_1\right) \\ 0, & otherwise \end{cases};$$

$$r_{N3} = \left(r_0 + r_{th\_out} + r_{N1}\right) \cdot w_{exc},$$

$$r_{N4} = \left(r_0 + r_{th\_out} + r_{N1}\right) \cdot w_{inh} \qquad with \qquad r_{th\_out} = \begin{cases} r_{th}, & r_{N1} > \left(r_{cr} \cdot t_2\right) \\ 0, & otherwise \end{cases};$$

$$r_{N5} = \left(r_0 + r_{th\_out} + r_{N2}\right) \cdot w_{exc},$$

$$r_{N6} = \left(r_0 + r_{th\_out} + r_{N2}\right) \cdot w_{inh} \qquad with \qquad r_{th\_out} = \begin{cases} r_{th}, & r_{N2} > \left(r_{cr} \cdot t_3\right) \\ 0, & otherwise \end{cases}.$$

We estimated this model with the following parameters:

σ = 0.2	t_1 = 4.0	w_{exc} = 0.15
r_{th} = 2.4	t_2 = 1.2	w_{inh} = -0.05
	t_3 = -0.3	

Testing the model with recorded neuronal data

The stimulus phase was used as input layer, in which real recorded neurons encoding the decision during the stimulus phase (Figure 1E) were applied to the model (N1: normalized firing rates of decision neurons increasing their firing rates for 'yes' decisions in randomly selected trials; N2: discharge rates of neurons decreasing their activity for 'yes' decisions). The threshold criterion values (T2, T3) used to evaluate the stimulus phase responses were derived from neurons that were significantly modulated by stimulus intensity, but not by decision outcome during the stimulus phase. Firing rates of cells increasing their responses with stimulus intensity were used as criterion

values in T2 (Figure 5A) and discharge rates of neurons decreasing their responses with increasing stimulus intensity in T3 (Figure 5B). Dependent on the stimulus intensity of a particular trial, a threshold criterion r_{cr} was chosen from normalized firing rates during the stimulus phase of randomly selected trials of the corresponding neurons. Furthermore, to exclude extreme neuronal responses, we only used discharges within ± four standard errors of the mean of the respective stimulus intensities.

To estimate the suitability of the intensity modulated cells for providing threshold values, we calculated the proportion of correct classifications of stimulus phase decision cells' responses into 'yes' or 'no' responses by the criterion. We considered a trial as a correct classification if the randomly selected criterion T2 was below the N1 firing rate of a randomly selected hit/false alarm trial, or above a correct rejection/miss trial. Similarly, the criterion selected for T3 had to be below the N2 firing rate of correct rejections/miss trials and had to exceed the discharges of hits/ false alarms to count as a correct classification. We found that 76 % of the criteria values derived from stimulus intensity modulated cells led to correct classifications of stimulus phase firing rates as 'yes' or 'no'.

Results

Physiological findings

In a rule-based detection task, the animals decided about the presence or the absence of a visual stimulus (Figure 1A). To introduce uncertainty, the stimuli were presented at nine grey levels close to the perceptual threshold of the animals. A rule-cue determined the appropriate motor response for the particular decision and assured that no motor action could be prepared during the decision period. Decision outcomes were classified into hits or false alarms, for 'yes' decisions when the stimulus was present or absent, respectively; and as misses or correct rejections for erroneous or correct 'no' decisions (Figure 1B).

We found single neurons in the PFC, preSMA, and CMAr whose spiking activity co-varied with the monkeys' subjective judgment about the stimulus presence or absence (Merten and Nieder, 2012; submitted). Here, we plot the firing rates of the different classes of decision neurons as functions of stimulus intensity. During the early decision phase (stimulus phase, immediately after stimulus presentation, Figure 1A), we found two classes of decision neurons (Figure 1C, example neurons; Figure 1E, averaged responses). One class of neurons actively increased the firing rates for 'yes' decisions (hits and false alarms, N1). The other class decreased the discharge rates for 'yes' decisions (N2). During the late decision phase (delay phase, before the rule-cue is presented, Figure 1A) both the 'yes' decision as well as the 'no' decision were encoded actively (Figure 1D, example neurons; Figure 1F averaged responses). Four classes of neurons were identified: 'yes' neurons increasing (N3) or decreasing (N4) their discharges during 'yes' decisions; and 'no' neurons increasing (N5) or decreasing (N6) their discharges actively during 'no' decisions (correct rejections and misses). Moreover, the firing rate-intensity functions revealed a weak additional modulation of all decision neurons by the intensity of the stimulus.

The emergence of 'no' neurons indicates that activity during the delay phase is not a pure reflection of memory of the decision made during the stimulus phase. This activity might rather result from a transformation and further processing of stimulus phase information. The unexpected finding that 'no' decision neurons were also modulated by stimulus intensity further supports this assumption.

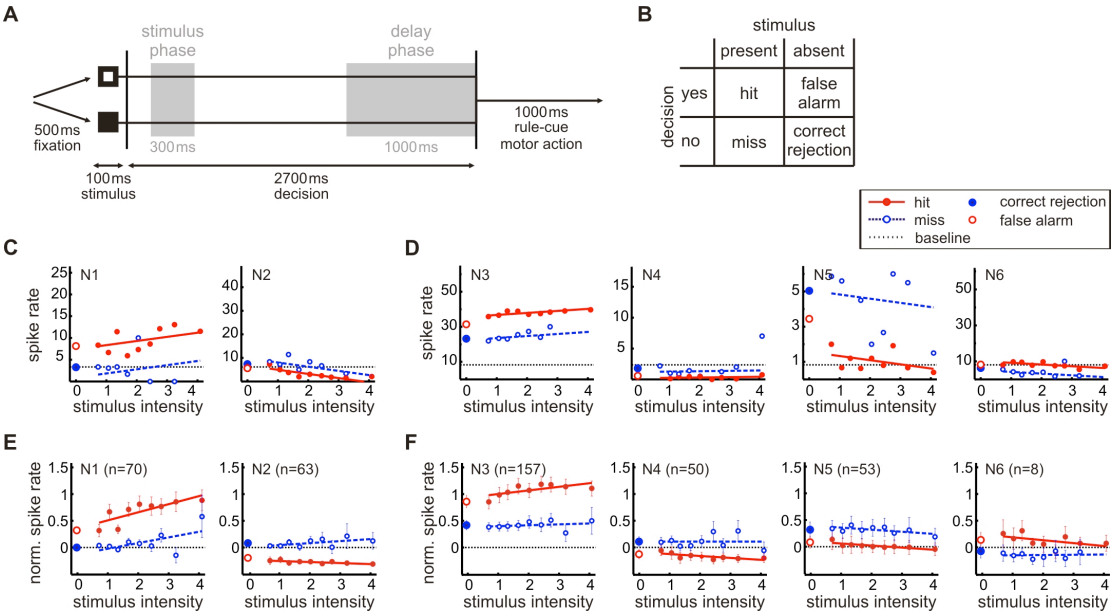

Figure 1. **Visual detection protocol and response classes of decision neurons**. (A) Trials began when the monkeys grasped a lever and fixated on the central fixation target for 500 ms. In 50 % of the trials a stimulus was presented for 100 ms (intensity varied in nine levels, centered around the perceptual threshold). In the other 50% of the trials, no stimulus was shown. Decision about the presence or absence of the stimulus was made during a 2700 ms decision time; gray shades highlight the two analysis periods for the decision neurons: the stimulus and the delay phase. After the decision phase, a rule cue informed the monkeys about the appropriate motor response to report the decision and, thus, separated the processing of the abstract decision from motor preparation. (B) Decision outcomes according to signal detection theory. Two stimulus conditions (stimulus present or absent) and two possible decisions ('yes, stimulus present' and 'no, stimulus absent') classify the behavioral outcomes. (C,D) Firing rate-intensity functions of example decision neurons. Two classes of decision neurons encode the 'yes' decision during the stimulus phase (C); two classes of 'yes' and two classes of 'no' neurons represent the decision during the delay phase (D). Stimulus intensity is presented as % visual contrast. For the stimulus intensity 0, no stimulus was presented; this condition contains about 50 % of the all trials. (E,F) Mean normalized population responses of each class of decision cells during stimulus (E) and delay (F) phases. n, number of neurons. Bars represent s.e.m.

Network model

To test the hypothesis that the coding mechanism of abstract detection decisions implies two processing steps, which give rise to active 'no' neurons during the delay phase, we constructed a feedforward network model consisting of two processing layers (Figure 2). As network input layer we used sensory evidence modeled by firing rates linearly increasing with stimulus intensity. The decision outcome for units in the stimulus phase (N1, N2) was calculated based on the comparison of the input firing rate r_s and a criterion r_{cr} (Figure 3A) (Kim and Shadlen, 1999; Kepecs et al., 2008). Additionally, the response of these units was linearly influenced by the input (to account

for the weak modulation of decision neurons by stimulus intensity). The connections between the computational units were either excitatory or inhibitory. The output of the stimulus phase units was subsequently used both linearly and nonlinearly (via a threshold neuron) as input for the delay phase computations (N3-N6). The proportion of the network's 'yes' decisions in the delay phase was used to generate the psychometric function (see Methods). The resulting performance of the model (Figure 3D) closely resembled the behavioral function of the monkeys (Figure 3B).

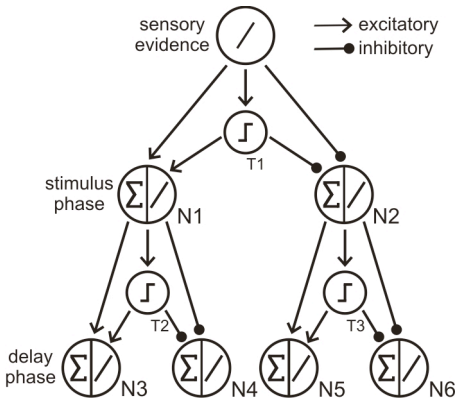

Figure 2. Schematic network model architecture. The sensory evidence constitutes the input to the network and is processed in two layers: stimulus phase and delay phase. The connections between computational units (N1-N6) are either excitatory or inhibitory. The projections are realized either directly, influencing the following layer linearly, or via a threshold neuron (T1-T3) providing a constant output only if a threshold criterion is reached. The computational units in each layer sum up the input and provide linear output.

The architecture of the model implies two possible classes of decision coding responses during the stimulus phase (Figure 4A): units increasing (N1) or decreasing (N2) their activity relative to the baseline for 'yes' decisions. During the delay phase, four types of possible response profiles arise (Figure 4B): units coding the 'yes' decision by elevating (N3) or decreasing their responses (N4) and units coding the 'no' decision by increasing (N5) or reducing their firing for the 'no' decision (N6). The characteristics of the modeling results for the rate-intensity functions closely resembled the experimental data in terms of decision representation and the corresponding modulation by stimulus intensity.

Verification of the model with recorded data

Our model critically depends on appropriate threshold criterion values that classify the input, leading to 'yes' and 'no' decisions. During the stimulus phase, we found neurons varying their responses linearly dependent on the intensity of the stimulus, but not encoding the decision: one population increasing (Figure 5A), another decreasing (Figure 5B) their discharges. These neurons could possibly provide the important function of generation of criterion values. We tested this idea by feeding experimental data into our neuronal network. The computational units N1 and N2 in the model architecture were replaced by firing rates of decision neurons recorded during the stimulus phase (Figure 1E). The threshold values T2 and T3 were obtained from the responses of neurons coding the stimulus intensity during the stimulus phase (Figure 5). The evaluation of the experimental responses of decision neurons by stimulus intensity coding neurons resulted in responses profiles of the output layer (N3-N6, Figure 4C).

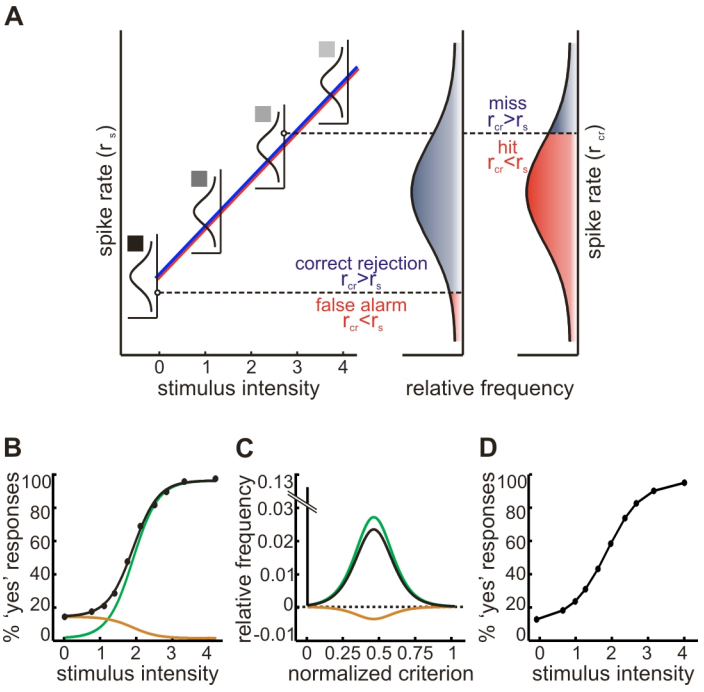

Figure 3. Modeling of the threshold criterion and performance of the model. (A) In each trial, the strength of the sensory evidence r_s and a threshold criterion r_{cr} are drawn from their respective distributions of firing rates. The decision outcome is calculated by comparing the firing rates: in the stimulus absent trials $r_{cr} > r_s$ leads to a correct rejection and $r_{cr} < r_s$ to false alarms, whereas in stimulus present trials $r_{cr} < r_s$ is considered a hit trial, and $r_{cr} > r_s$ a miss. (B) The black line is the sigmoidal fit of the proportion of monkeys' 'yes' responses in the real experiment as a function of stimulus intensity. This fit results from a sum of two sigmoidal functions: The first component is the ideal sigmoidal performance curve of an unbiased performance (green line). The orange function represents the proportion of additionnal 'yes' responses the monkeys give in trials when the stimulus was not visible. (C) The green line depicts the shape of the probability density function, which would result from the ideal psychometric curve. The orange distribution is the probability of 'yes' responses given when the stimulus was not visible. The black distribution is the criterion probability density function resulting from the sum of the green and the orange functions that is used to model the threshold criterion r_{cr}. The probability of the criterion being zero corresponds to the area enclosed by the orange curve. (D) Psychometric function of model computations.

These firing rate-intensity response profiles mirrored the recorded rate-intensity functions of real decision neurons in the delay phase (Figure 1D,F). In fact, 76 % of the generated responses were correctly classified by the threshold criterion as 'yes' or 'no' responses, in agreement with the monkeys' decisions given in stimulus phase trials (see Methods for details).

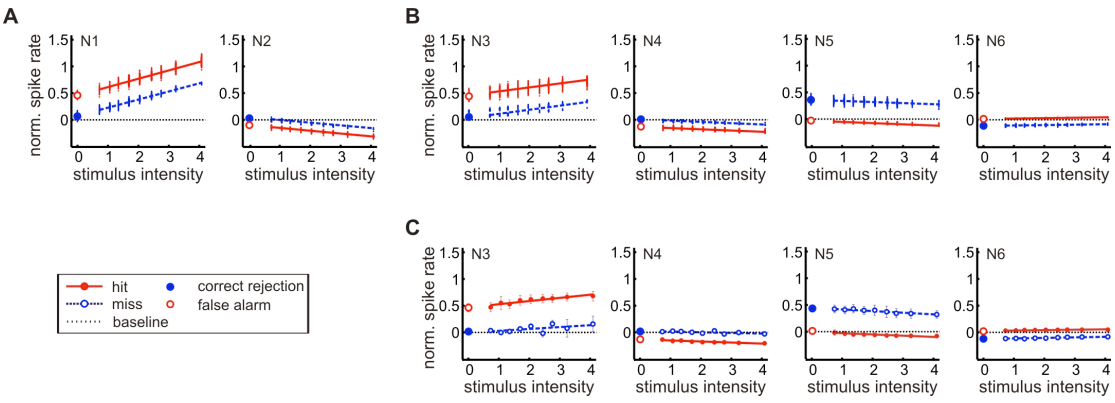

Figure 4. Stimulus intensity modulated neurons used as criterion values. Discharge rates of neurons varying with stimulus intensity normalized and pooled for PFC, preSMA, and CMAr. (A) Neurons increasing firing rates; (B) decreasing firing rates during the stimulus phase. Bars represent s.e.m. Dotted like represents the baseline.

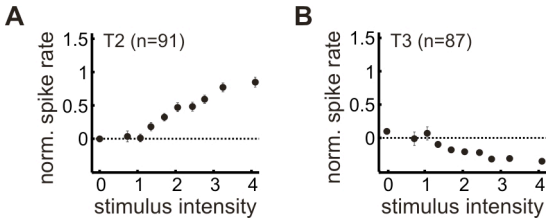

Figure 5. Abstract decision coding in a network model. Firing rates generated by the model as functions of stimulus intensity and decision outcome for the stimulus phase (A) and delay phase (B). The small dots depict the calculated firing rate for a particular trial and are colored according to the determined decision (red - 'yes'; blue - 'no' decisions). A linear slope fits means of stimulus present trials. (C) Delay phase responses generated by the model using real neuronal data recorded during stimulus phase.

Discussion

We implemented a computational network that generates the experimentally observed classes of decision neurons and captures the characteristics of decision and stimulus intensity coding by frontal cortex neurons. The proposed network implies a two-stage processing mechanism of abstract detection decisions. Activity of an early decision stage, the stimulus phase, is further processed in a second active processing step, the late delay phase. In our network, neurons coding the 'yes' decision during the delay phase result from activity of neurons encoding the 'yes' decision by increasing their firing rates during the stimulus phase; active delay phase 'no' neurons are driven by neurons decreasing their activity for 'yes' decisions during the stimulus phase. To model the decision, neuronal responses of the stimulus phase were evaluated by a criterion. If the criterion was reached, a subsequent delay phase computational unit increased its firing rate. We implemented the responses of real recorded stimulus phase decision neurons as responses of the stimulus phase model layer and evaluated these responses by criterion values obtained from real recorded neurons, which encoded the intensity of the stimulus only. These calculations suggest that the activity of intensity coding neurons is well suited to provide criterion values to deduce decisions.

Models of perceptual decisions

A remarkably successful modeling of the decision-making process is achieved in a sequential analysis framework, which relies on the accumulation of sensory evidence. Here, the decision is based on a sequence of observations, which are converted into a decision variable until a predefined decision boundary is reached. Two important representatives are the diffusion model (Gold and Shadlen, 2002), according to which evidence is accumulated to support either the one alternative or another; and the race model (Logan and Cowan, 1984; Reddi et al., 2003), in which the evidence supporting the various alternatives is accumulated for each alternative independently to fixed boundaries. The advantage of the sequential analysis approach is that it assumes that the decision has two parts: the actual decision about the alternatives and another about when to stop the decision process (Gold and Shadlen, 2007; Deco and Romo, 2008). Therefore, these models explain very well the behavioral data: the generation of correct and error responses, the reaction times and the trade-off between speed and accuracy of a response (Smith and Ratcliff, 2004). Neurons in the monkey parietal areas have been shown to accumulate sensory evidence during perceptual decisions with a positive relationship between activation strength and the amount of accumulated evidence (Platt

and Glimcher, 1999; Shadlen and Newsome, 2001; Yang and Shadlen, 2007). On the other hand, a magnetoencephalography study of sequential decision making of humans revealed an inverse relationship of the amount of activity in the parietal areas to the amount of the previously accumulated evidence, meaning that when a large amount of evidence was accumulated, new sensory evidence had a lower impact on brain activity (de Lange et al., 2010).

Our simple network model did not involve accumulation of evidence and treated the detection decision analogous to a categorization problem. The main concern of our task design was to separate the decision from its motor report. Therefore, we cannot access the reaction times corresponding to the decisions for different stimulus intensities. The neuronal responses during the stimulus phase appear to be categorically dependent on the decision and stereotype for all stimulus intensities (Merten and Nieder, 2012). We also did not find differences between latencies of neuronal response onset after salient stimulus presentations and stimuli with lower intensity presented close to the perceptual threshold. One possible explanation might be the nature of the stimulus in our experiment. A flash of an object is a momentary, single event, which does not provide a plausible foundation for the accumulation of sensory evidence. Another explanation might be that the recorded frontal cortex neurons represent the decision outcome of an abstract decision and not the decision variable developing in time.

Another class of computational models, the biophysical microscopic models, which seek to satisfy biological plausibility of the modeling parameters, has also been developed to model decision processes (Wang, 2002; Machens et al., 2005; Wong and Wang, 2006). Such models construct and simulate neuronal computations relying on large numbers of neurons and synapses carefully connected to a neuronal network attempting to find the connectivity structure from which the measured neuronal correlates emerged. Nevertheless, the dynamics can be reduced to a one-dimensional diffusion model (Roxin and Ledberg, 2008) and, thus, establish a solid foundation for diffusion models. Biophysical microscopic models typically involve two coupled groups of neurons. Each group is driven by an input proportional to the sensory evidence for the respective decision alternative. The mutually inhibiting connections lead to a competition between the groups, with one group winning this competition at the expense of the other. Because of the lack of the signal in the stimulus absent condition, the 'no' neurons population encodes the default 'no' response as a constant bias in biologically related detection models (Deco et al., 2007).

In our abstract detection decision protocol (Merten and Nieder, 2012), we found this way of decision representation during the early decision phase, the stimulus phase. However, during the late delay phase, decision was represented by active 'yes' and active 'no' decision neurons, very similar to discrimination decisions. Our network model is the first attempt to explain the origin of the 'no' neurons. Of course, it would be of great interest to expand our simple network to populations of neurons and construct a biophysical microscopic model to investigate the biological plausibility of our suggested connections and interactions between neurons.

In this work, we explored the possibility of generation of active 'no' responses in the local circuits of the frontal cortex. Alternatively, it is possible that much more distant brain areas are involved in this process. A recent study reports high activity of midbrain

dopamine (DA) neurons in high uncertainty conditions (de Lafuente and Romo, 2011). This uncertainty arises internally during the evaluation of sensory stimuli presented close to the perceptual threshold, because these stimuli remain often undetected. For the subject performing the task, there is no chance to distinguish between true absence of a stimulus from a presence of an undetected stimulus. Thus, stimulus-absent events carry high levels of uncertainty. The high levels of DA activity during these stimulus-absent events might possibly serve as a trigger for the active 'no' decision responses we measured in the frontal cortex.

Threshold used in decision models

Little is known about the threshold mechanism used in decision models applied to classify the neuronal choices. There is even no consensus about the origin of the nonlinearity: in the standard view this computation is done by a neuron receiving linear weighted inputs from other neurons, and the sum is then passed through a static nonlinearity; alternatively, it has been proposed that synaptic computations might provide this nonlinearity (Zador, 2000). The neurons we recorded in frontal cortex that were only modulated by stimulus intensity provided a good estimate of the threshold values. This finding is in agreement with the idea that the threshold is an intrinsic property of a single neuronal circuit converting the decision variable into a final choice (Wang, 2002; Machens et al., 2005; Wong and Wang, 2006). It remains to be determined whether this processing of abstract decisions is generated locally in the subnetworks of a particular brain area, or through a reciprocal loop between different connected areas.

Acknowledgments

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