Sense, memory, and decision-making in the somatosensory cortical network

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The brain constructs representations of objects and concepts based in sensory information combined with experience. This mental process, that we call perception, is the result of a chain of events consisting of phenomena such as detection, memory, discrimination, categorization and decision-making. Although the phenomenon of perception is not necessarily dependent on a given sensory modality (e.g. visual perception, auditory, tactile), single sensory models are indispensable for studying the neural mechanisms that generate it. The somatosensory system is a suitable model for studying the manner in which presentation of a single physical variable (e.g. vibration) triggers a perceptual process. Here, we discuss some recent studies in the somatosensory system that in our view, constitute a breakthrough to understanding decision making.

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Introduction

The somatosensory system has proved to be an elegant experimental model for studying the neural mechanisms that generate perceptual decision making [1]. For example, it has been useful to understand the way in which touch is represented in the primary afferents [2], and how is transformed into decision-making processes in the cerebral cortex [1]. Indeed, psychophysical detection and discrimination tasks have revealed essential information not only about the way in which the brain detects and brings sensory information into categories [3], but also the manner in which these sensory percepts are stored in memory [4–6] and transformed into decision signals that ultimately correlate with motor decision reports [7–9,10•]. The challenge now is to understand not only the capabilities of information processing by single neurons, but also, to reveal fundamental aspects of cell types differences within a network [11], and the mechanisms by which populations of neurons are functionally connected to generate perceptual decisions [1]. This review focuses on recent advances aimed to understanding perceptual decision processes using the somatosensory system as a model.

The detection problem

Detection of sensory stimuli is a basic function of the CNS. Successful detection not only allows analyzing the physical characteristics of stimuli such as location, intensity and duration; it also enables the brain to evaluate sensory information in the context of current and previous knowledge related to the stimulus. The behavioral relevance and the possible actions required can be evaluated upon detection. Detecting a stimulus is thus a cognitive process involving more than just the sensory systems. In addition to engaging a recognition process in which a current sensory stimulus is matched against short and long term memory, detection is also associated with sensory awareness, that is, the ability to subjectively perceive and report changes in the environment.

At the core of research efforts to understand how the brain elaborates sensory detection is the observation that repeated presentations of a weak sensory stimulus unpredictably fail or succeed to produce a sensory percept [3,12]. Given that the stimulus is physically the same, but the reported sensations vary, a sensory detection task constitutes a simple and elegant experimental design to address the mechanisms by which the brain analyzes sensory information and generates perception. The main idea behind these experiments is to identify variations in neuronal activity that correlate with variations in the subjects' behavioral reports. Where in the brain and what patterns of neuronal activity correlate with the subjects perceptual reports?

Primary sensory cortices are logical places to start this search. Seidemann and colleagues recently studied V1 activity in a contrast detection task and found that variability of V1 responses to the stimulus explains a small but statistically significant fraction of variability in behavioral choices that monkeys make about stimulus presence or absence [13]. Somewhat surprisingly, they also found that information contained in V1 neuronal responses could be used to generate detection curves that significantly outperform the monkeys' behavior on the detection task [14]. The finding of a primary visual cortex that is more

sensitive than the behavioral reports was recently confirmed in the mouse [15]. These observations suggest that upstream areas do not use an optimal decoding strategy, and indicate that we still do not understand the code the higher order areas use to extract information from the spiking activity of sensory neurons.

Information in the stimulus does not completely determine the behavioral output in a detection task. Support for this view was recently provided by Maunsell and colleagues. Studying the activity of V4 neurons, they demonstrate that trial by trial fluctuations in attention are largely responsible for variations in perceptual performance [16]. Furthermore, they demonstrated that attentional mechanisms can select the populations of neurons that contribute to the sensory information on which decisions are based [17]. They found that the decision-making circuit can vary the weight it assigns to neurons that contribute to the sensory evidence. These observations confirmed previous findings indicating that decisions are made from the relative activity of neurons preferring opposite directions of motion [18]; but see [19].

Using the somatosensory system as a model, de Lafuente and Romo recorded primary somatosensory (S1) cortical neurons in monkeys trained to report the presence or absence of a vibrotactile stimulus delivered to one fingertip [3]. These authors found that S1 neurons faithfully represented the stimulus amplitude, but they did not correlate with the monkeys' perceptual reports beyond chance levels. Thus, S1 neurons signaled the physical presence or absence of the stimulus, but they did not

inform whether the monkeys would fail or succeed to report stimulus presence.

The studies discussed above demonstrate that activity in sensory cortices do not completely determine the behavioral outcome on subjects performing detection tasks. Where are correlates of sensory detection found? de Lafuente and Romo observed that neurons in the premotor cortices of the frontal lobe correlated more closely with the behavioral reports about stimulus presence or absence [3]. Consistent with the view that perceptual decisions are represented in the frontal lobe, a recent investigation of prefrontal cortical (PFC) neurons found that there are distinct populations of neurons selectively encoding 'stimulus presence' and 'stimulus absence' decisions [20•].

A crucial question arising from these studies was whether these signals appear *de novo* in the premotor cortices or whether they could also be found in other cortical areas across the somatosensory processing hierarchy. To study this, de Lafuente and Romo recorded neuronal activity of several cortical areas including S1, secondary somatosensory cortex, areas 2 and 5; lateral, ventral and medial premotor cortices, as well as primary motor cortex [21]. They found that as the neuronal responses travel across this processing chain they increasingly correlate with the monkeys' perceptual reports (Figure 1). These results suggested that a detection process might be occurring on each cortical area and that the output of the previous node serves as the input to the next. Consistent with the view that each cortical area could be performing a detection operation, it was recently demonstrated that electrical

Figure 1
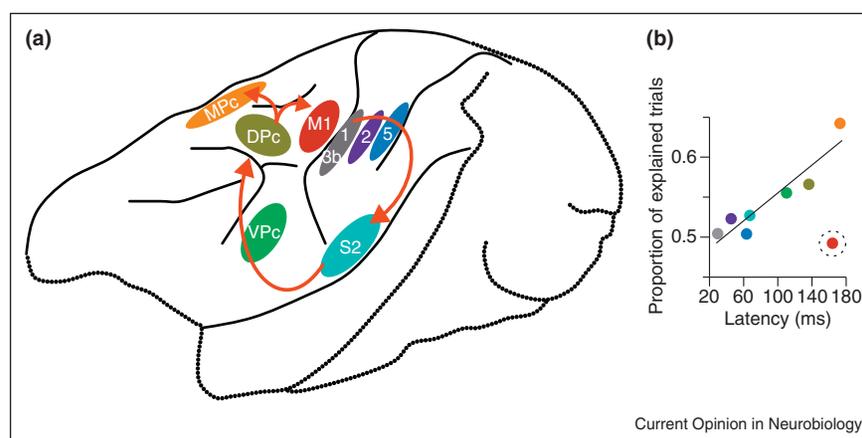
Flow of somatosensory information. **(A)** Cortical areas were recorded in a vibration detection task. The latency of response to the stimulus shows that vibrotactile information flows from sensory areas in the parietal cortex to premotor and motor areas in the frontal lobe. **(B)** The correlation between neuronal activity and behavioral responses increases in direct proportion to response latency (dot colors correspond to colored areas in **(A)**). With the exception of the primary motor cortex (broken circle), larger response latencies are correlated with increasing proportions of correctly predicted behavioral responses (ROC analysis (modified from [21])).

stimulation in a wide range of visual areas can successfully generate percepts that monkeys and humans are able to communicate in the context of a detection task [22,23].

Every time the brain makes a perceptual judgment, such as stimulus presence or stimulus absence, there is a degree of confidence associated with that decision [24,25]. Confidence allows estimating the gains and losses associated with our choices and permit us to modulate decision policies. However, although the all or none nature of frontal lobe responses faithfully reflect the outcome of perceptual decisions about the presence or absence of a sensory stimulus, they do not show modulations related to the level of confidence associated with decision making.

To gain insight into the neuronal mechanisms associated with the confidence of a decision, de Lafuente and Romo recorded from midbrain dopamine (DA) neurons while the monkeys performed the vibrotactile detection task [26,27]. They found that the activity of DA neurons was directly proportional to stimulus amplitude, but only on those trials in which the monkeys detected the stimulus presence. Instead of being all or none like MPC neurons, or having no modulation by choice like S1 neurons, DA activity was related to stimulus amplitude, but only on those trials in which the monkeys perceived the stimulus. Thus DA activity could be signaling the monkey's confidence in relation to the perceptual decision report. Consistent with these view, Nomoto et al. [28] found that DA neurons were activated with a latency that closely matched the time when decisions are reached after evaluating sensory stimuli. These dopamine signals predicted the expected magnitude of a reward to be obtained later at the end of the trial, responding with strong excitation for large future rewards, and with strong inhibition for small future rewards. Thus, the magnitude of these modulations with respect to basal activity represents a signal that could be related to decision confidence. Confidence is not only represented by dopamine neurons. Kepecs et al. [29] found that rat orbitofrontal neurons code stimulus uncertainty during a waiting period before decision outcome is revealed. These results are consistent with the interpretation that uncertainty signals could serve to alert other brain areas that future events could not be predicted from past ones and prepares the brain to assess an uncertain outcome.

A key question remains unanswered, however, and it lies at the core of most sensory research: is activity in upper brain areas also responsible for perception/awareness or does it only reflects higher cognitive processes such as decision making? The answer to this question is the subject of current research. In the light of current evidence, we argue that the processes by which the brain evaluates sensory information and generates

sensory awareness might be undistinguishable and probably occur in the same neuronal circuits (Figure 2).
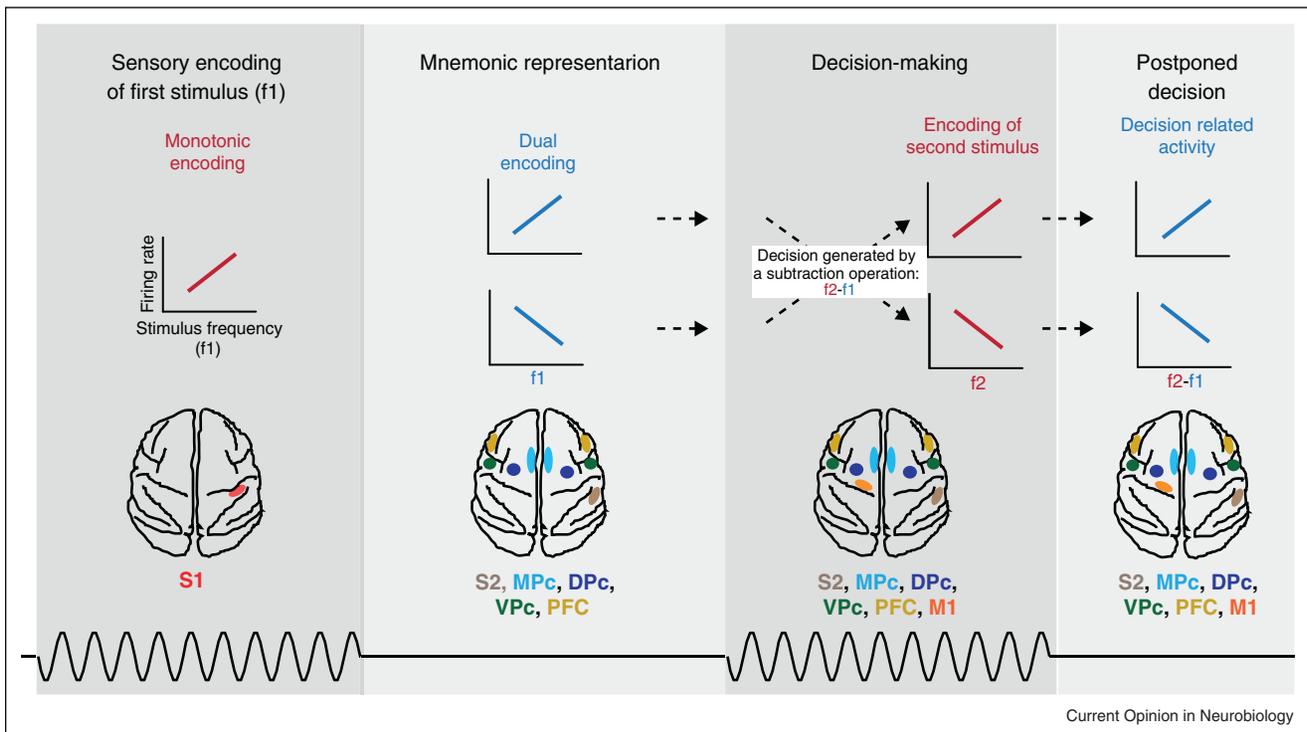
The discrimination problem

Sensory information stored in neural circuits (i.e. memories), constitute templates used to fit incoming sensory signals into a category (e.g. high, slow, long, dim, etc.). Interestingly, a perceived category may jump to its opposite category given the variability in the neural representation of the sensory input. Thus, information constituting each category is coded within the neural activity at different instances of the brain. This representation shifts gradually the correlation with the pure sensory signal, to a behavioral response. But, how and where are these circuits formed and how sensory information transforms into perception and decision making?

Recently, Pei et al. [30] showed that this basic coding, which can be observed separately in primary afferents, is integrated by single neurons in S1, in combined signals of slow and fast adaptation. The authors also showed that this process is used by neurons of area 1, for encoding information about the orientation of an object, similar to visual area MT [31].

Previously, several codes for representing tactile information (i.e. frequency) were tested in behaving monkeys [32]. Again, the authors found that firing rate of S1 neurons coded the stimulus frequency and correlated with the monkeys' psychophysical performance. The same neural code was observed in trigeminal ganglion neurons of rats during the discrimination of frequencies applied to rats' whiskers [33•]. In the same spirit, behavioral experiments were designed to quantify the interaction between frequency and amplitude while rats discriminated pair of frequencies [34], finding an actual integration of both the frequency and amplitude. But even more, recordings in somatosensory cortex of rats, suggest that single units are capable to represent in a firing rate code other stimulus features such as, identity, intensity and time [35,36]. It has been also shown that within the vibrissae system of rats, single neurons code information about object identity and location [36,37]. Finally, the evolution and integration of information of mechanical information that generates the representation of an object, proved to be similar in rats and humans [38].

Behavior is crucial for modeling sensory circuitry activity [39]. In fact, active touch is crucial for generating behavior [40]. For instance, studies across different animal species show that the behavioral relevance (i.e. achievements of goals for survival), depend on contexts created by sensory information coded by interneurons [41]. Blind humans, for example, have a better capacity to detect tactile information than sighted subjects [42]. But to understand the value of sensory information in the generation of perception and decision making, Romo and colleagues

Figure 2

Discrimination process across cortical areas. Determining which of two stimuli has the higher vibration frequency engages multiple cortical areas on the parietal and frontal lobes. After a delay period (postponed decision), monkeys had to press one of two push buttons to communicate which vibrotactile stimuli (f1 or f2) had the higher frequency. Diagrams of the macaque brain depict cortical areas with task-related activity. The primary somatosensory cortex (S1) encodes f1 only through positive monotonic responses. This sensory information is distributed to other cortical areas and transformed in such a way that opposite representations (dual encoding) arise in secondary somatosensory cortex (S2), MPC, dorsal premotor cortex (DPC), ventral premotor cortex (VPC) and prefrontal cortex (PFC). Dual representations of the first stimulus (f1) are encoded during the delay period (mnemonic representation) by the sustained activity of cortical areas on the frontal lobe. After the delay period, the frequency of the second stimulus (f2) is encoded in all recorded areas of the frontal and parietal lobes. Importantly, neurons with decision-related activity (i.e. reflecting the comparison of f1 and f2) emerge in frontal and parietal cortical areas reflecting the difference in frequency between the two stimuli. This decision related activity could arise by subtracting the firing rates of neurons encoding f1 and f2 with opposite tuning. Note that with the exception of S1, neurons with opposite tuning are observed across all recorded areas (modified from [10•]).

designed a behavioral task where monkeys were trained to discriminate the frequency of two vibratory stimuli applied consecutively to one fingertip. To solve this task, monkeys had to decide whether the frequency of the second stimulus (f2) was higher or lower than the memory of the frequency of the first stimulus (f1). They found that the tactile information was stored in the working memory, by neurons of several cortical areas, whose firing rate was a parametric function of the mechanical input [10•]. The decision signal resulting from the comparison of tactile frequencies correlated with the motor decision reports. Nevertheless, in order to dissect the motor component from the decision signal, they added a delay to their task where the monkeys had to hold in the working memory the decision signal until a motor cue was presented. As expected, they found information correlated with the decision signal that was coded in the firing rate of neurons of several areas, and it was different from the categorical all or none motor signal. But surprisingly, they also found memory traces of the sensory components f1

and f2 [43]. In other words, sensory information was active even after the presentation of the stimuli (f1 and f2) and after a decision was taken. This finding could only be interpreted as a brain mechanism that allows a constant evaluation of information previous to a motor act, so new decisions can be achieved in order to improve behavior.

Conclusion

The facility to experiment with different physical attributes alone or in combination, make the somatosensory system a suitable model to study the neural mechanisms associated with perceptual processes, but this should not be different in other sensory modalities [44]. This model has been essential for understanding the processes ranging from detection to decision making. However, many questions remain open about the way with which different brain areas process sensory information to generate a percept. For example, recent studies have challenged the long standing concept that sensory cortices are unimodal [45–49], but see Lemus *et al.* [50••]. Also, an essential

problem is to search the most basic cellular mechanisms of these cognitive functions. This could be achieved using techniques such as two-photon microscopy that have yielded data about the different types of neurons active during perceptual tasks [51,52], or functional connectivity between areas [53•,54]. In turn, optogenetic studies promise to be fundamental for understanding the mechanisms of information flow at cellular level [55]. These new experimental approaches will surely help to describe the basic cellular architecture underlying perceptual decision making together with neural computational modeling.

Acknowledgements

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