Cell-type specific dopaminergic modulation of information transfer in cortical neurons

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Summary: Neurons in the sensory cortices form representations of the world by processing information coming from the periphery, a process that involves giving complex, non-linear spike responses to incoming stimuli. The responses of excitatory pyramidal cells and inhibitory interneurons in cortical networks are shaped by each neuron's place in the network (connectivity of the network) and its biophysical properties (ion channel expression, Azarfar et al. 2018), which are modulated by top-down neuromodulatory input.

Rodents' somatosensory 'barrel' cortex (S1) is responsible for processing sensory input coming from the whiskers. Layer 2/3 (L2/3) of S1 integrates input coming from surrounding cortical columns via horizontal connections, long-range neocortical inputs via L1 and (neuromodulatory) information originating elsewhere in the brain, thereby integrating top-down and bottom-up information. Dopamine modulates such sensory representations (Gittelman et al. 2013).

We study the effects of D1 receptor (D1R) activation on neural computations of inhibitory and excitatory neurons in L2/3 of barrel cortex. Using a recently developed ex-vivo method (Zeldenrust et al. 2017), we estimate the information transfer and fit computational models to a large number of in vitro recordings (Lantyer et al., 2018). We show that D1R activation results in cell-type specific regulation: while D1R activation hyperpolarizes the spike-threshold and increases the firing rate in inhibitory neurons, it inhibits stimulus-evoked spiking in excitatory neurons. This results in an increase in information transfer in inhibitory, but not excitatory neurons. These differences in neural responses are accompanied by faster decision-making on a behavioural level: in a gap-crossing task (Celikel & Sakmann, 2007), mice show a decrease in latency and amount of information needed to cross with D1R activation. We hypothesize that D1R modulation improves the integration of tactile evidence to reach a perceptual decision by modulating the cell-type specific gain modulation to enhance inhibitory neurons' contribution to sensory coding.

Mutual information and neural properties: We investigate the single neural computation by estimating the mutual information between input and spike train using a recently developed ex-vivo method (Zeldenrust et al. 2017). This frozen-noise (FN) stimulation protocol (Fig 1A) involved somatic injection of the current that is the output of an artificial neural network of 1000 neurons, each firing Poisson spike trains in response to a binary 'hidden state', which represents the presence or absence of an external stimulus. Using this protocol, we can directly quantify neuronal information transfer (Fig 1F-I) and at the same time assess and compare other neural properties, such as its optimal filter and the spike threshold (Fig 1C,D). We explicitly fitted models to each recording in the dataset, to investigate both generic principles of computation and neural variability (Marder & Taylor, 2011).

Behaviour: We trained animals on the spontaneous gap-crossing task (Fig 2A,B). On this task animals locate a tactile target, an elevated platform, while standing on another platform located beyond a gap. We implanted animals with a guide cannula and trained animals to criteria (two consecutive sessions with 5+ trials during which animals contacted the target only using their whiskers before successful object localization). After animals reached the criteria, animals received either D1 agonist (SKF38393) or vehicle (Ringer's solution) for 30 trials/drug condition.

Results: Inhibitory and excitatory neurons in L2/3 of mouse barrel cortex process information differently: excitatory neurons show strong threshold adaptation and fire at low rates (Fig 1E), resulting in strong information compression (Fig 1F&I), and are diverse in their response properties. Inhibitory neurons show threshold behaviour that favours fast spiking (Fig 1B-E), resulting in broadband information transfer, and are uniform in their response. Upon D1R activation, inhibitory neurons decrease their spike threshold and increase their firing rate (Fig 1C-I), resulting in an increase in transferred information. Excitatory neurons show a more variable response: most excitatory neurons decrease their firing rate and information transfer, but a large minority shows an increase.

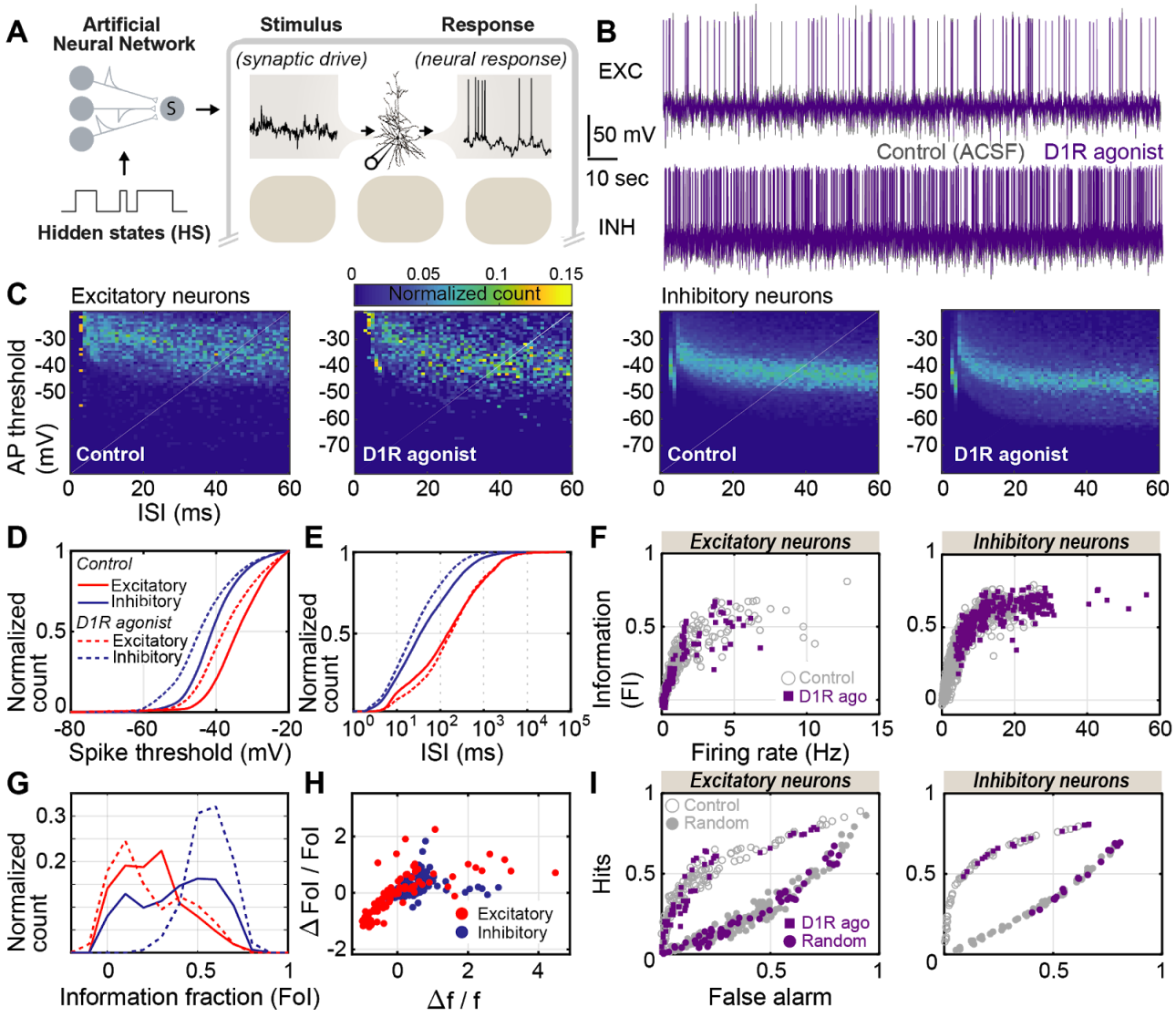

Figure 1: Ex-vivo 'frozen noise' recordings capture information transfer.

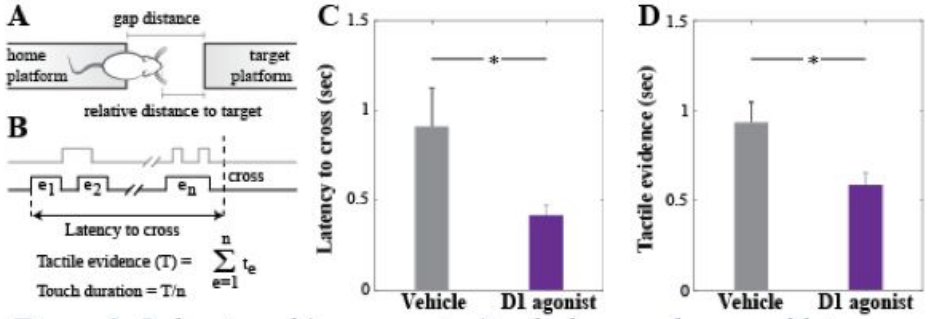

Figure 2: Behavioural 'gap-crossing'-task shows a decreased latency and tactile evidence needed

The pharmacological activation of the D1R in S1 in freely behaving animals results in faster integration of sensory information (Fig 2C,D). The mechanism underlying this behavioral improvement might be the bidirectional control of neuronal excitability by D1R activation.

In conclusion, we show that dopamine is a potent regulator of cellular and behavioral information processing in (somatosensory) cortex.

References

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