cells that display different transcriptomes are of two different types or are two states of the same cell type. Tasic *et al.*[4] take a first step in this direction. Using retrograde tracing followed by single-cell RNA-seq analysis, they show that, as predicted, neurons labeled from the ipsilateral visual thalamus largely group with the deep-layer clusters expressing corticothalamic and corticofugal projection neuron markers. In contrast, single neurons retrogradely labeled from the contralateral visual cortex fall in the clusters with molecular signatures of cortico-cortical projection neurons. This validates the fidelity of the Cre lines in labeling neuronal classes and the analysis pipeline used to assign cells to specific neuronal identities. Most importantly, the authors demonstrate that, among GABAergic neurons, two of the less well-characterized clusters, the Ndnf^{+} types[7], have morphological and electrophysiological traits of L1 neurogliaform cells. These neurons could also be subdivided into two groups on the basis of distinct electrophysiological traits; it would be interesting to see whether these electrophysiologically distinct groups correspond to the two Ndnf+ cell clusters defined by single-cell transcriptome analysis. For now, these efforts represent initial steps in the right direction of a long journey to elucidate the functional significance of the transcriptional cell types defined by single-cell RNA-seq.

Beyond the existing data set, potential applications of the pipeline developed in this study for analyzing complex molecular identities would be of wide interest. Although requiring heroic efforts and resources, expansion of the current analysis to encompass more genetic lines and cortical areas could lead to a molecular atlas of the mouse cortex with unprecedented resolution and depth. The same pipeline would also be useful for elucidating the developmental origin (timing and mechanisms) of neuronal diversity in the embryonic and juvenile cerebral cortex. Looking forward, similar analyses applied to mouse models of neurodegenerative and psychiatric diseases could help pinpoint affected cell types and mechanisms of pathogenesis.

Mapping the human brain transcriptome at single-cell resolution is of course a highly sought-after goal. The Allen Brain Institute has laid the groundwork with the Adult Human Brain Atlas[8,9], and single-cell RNA-seq has already been successfully applied to human fetal brain[5,10]. Although genetic labeling is impossible in this context, new techniques for purifying neuronal populations using endogenous markers have recently been shown to be compatible with single-cell RNA-seq[11]. These recent advances, combined with the methods and the data analysis tools developed by Tasic *et al.*[4], could bring the single-cell transcriptomic atlas of the human brain within our reach.

COMPETING FINANCIAL INTERESTS
The authors declare no competing financial interests.

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Rapid control of olfaction

The serotonergic raphe nuclei have been implicated in regulating neural circuits that produce nearly all types of behavior, including cognitive, motor and social, and are strongly linked to slower timescale changes in mood and mental health. However, increasing evidence suggests that the raphe nuclei are capable of broadcasting phasic, temporally precise signals that regulate information processing on fast, subsecond timescales. Projections from the raphe nuclei terminate throughout the brain and influence neural processing even in early sensory areas. On page 271, Kapoor and colleagues demonstrate that phasic raphe nuclei activation leads to rapid changes in odor coding in the olfactory system. As depicted in the image of the tortoise and the hare (right), these data support the emerging notion that the raphe nuclei affect information processing at multiple timescales.

The olfactory bulb processes incoming odor signals, performing operations that include normalization and contrast enhancement, before sending information to downstream regions via mitral and tufted cell axons. Using two-photon imaging of mitral and tufted cells *in vivo*, the authors show that activation of raphe nuclei triggers distinct changes in these olfactory bulb output channels. Raphe stimulation sensitized tufted cells, generally enhancing odor-driven activity. On the other hand, it led to bidirectional modulation of mitral cell responses, which improved pattern separation of similar odors. The distinct effects on tufted versus mitral cells provide strong clues to functional differences between the two olfactory bulb output channels. Although the authors did not examine behavioral consequences in this study, it is tempting to speculate that these effects would simultaneously improve odor detection and discrimination.

Through an elegant series of *in vitro* electrophysiology, optogenetics and pharmacology experiments, the authors next dissected the cellular and synaptic mechanisms underlying the rapid changes in odor coding. They found that raphe activation exerted both excitatory and inhibitory influences on mitral and tufted cells through dual release of glutamate and serotonin, respectively. Notably, the inhibitory effects of raphe activation were polysynaptic, suggesting that serotonin may exert its direct influence on GABAergic microcircuits in the bulb.

In summary, the authors demonstrated that raphe nuclei activation regulates early olfactory information processing on a subsecond timescale through dual release of glutamate and serotonin in the olfactory bulb. Beyond the olfactory bulb, the raphe nuclei exert control over widely distributed brain networks. It will be critical for future work to examine how these rapid changes in sensory processing are coordinated with modulation of other brain networks, including regions involved in affect and reward processing.

Sasha Devore