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A transcriptomic axis predicts state modulation of cortical interneurons

Speaker

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Abstract

Transcriptomics has revealed that cortical inhibitory neurons exhibit a great diversity of fine molecular subtypes, but it is not known whether these subtypes have correspondingly diverse patterns of activity in the living brain. Here we show that inhibitory subtypes in primary visual cortex (V1) have diverse correlates with brain state, which are organized by a single factor: position along the main axis of transcriptomic variation. We combined in vivo two-photon calcium imaging of mouse V1 with a transcriptomic method to identify mRNA for 72 selected genes in ex vivo slices. We classified inhibitory neurons imaged in layers 1–3 into a three-level hierarchy of 5 subclasses, 11 types and 35 subtypes using previously defined transcriptomic clusters. Responses to visual stimuli differed significantly only between subclasses, with cells in the *Sncg* subclass uniformly suppressed, and cells in the other subclasses predominantly excited. Modulation by brain state differed at all hierarchical levels but could be largely predicted from the first transcriptomic principal component, which also predicted correlations with simultaneously recorded cells. Inhibitory subtypes that fired more in resting, oscillatory brain states had a smaller fraction of their axonal projections in layer 1, narrower spikes, lower input resistance and weaker adaptation as determined in vitro, and expressed more inhibitory cholinergic receptors. Subtypes that fired more during arousal had the opposite properties. Thus, a simple principle may largely explain how diverse inhibitory V1 subtypes shape state-dependent cortical processing.