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A transcriptomic axis predicts state modulation of cortical interneurons

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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 activity patterns in the living brain. We show that inhibitory subtypes in primary visual cortex (V1) have diverse correlates with brain state, but that this diversity is organized by a single factor: position along their main axis of transcriptomic variation. We combined in vivo 2-photon calcium imaging of mouse V1 with a novel transcriptomic method to identify mRNAs 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 across Subclasses, suppressing cells in the Sncg Subclass while driving cells in the other Subclasses. 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 have less axon in layer 1, narrower spikes, lower input resistance and weaker adaptation as determined in vitro and express more inhibitory cholinergic receptors. Subtypes firing more during arousal had the opposite properties. Thus, a simple principle may largely explain how diverse inhibitory V1 Subtypes shape state-dependent cortical processing.

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