brain may be seeking extra cues to infer a potential change point. One possibility is that the brain may misinterpret the auditory cue switch as indicating the change-point occurrence, despite instructions, as the brain may be predisposed to integrate co-occurring events as though they are semantically congruent[14]; that is, the pupil dilation observed following the auditory cue switch may be a consequence of an activated locus coeruleus norepinephrine system, but the pupil diameter itself may not control task-related prediction or learning. Another possible route is that the auditory cue switch directly dilates the pupil, which is used by the brain to infer an appropriate cognitive state, such as the level of uncertainty critical for determining learning rate. This would be analogous to the manner in which levels of arousal and other physiological measures, such as physical configuration of the face[15], can be used by the brain to infer an appropriate emotional state. In Nassar *et al.*'s study[4], the pupil diameter would be used by the brain to infer an appropriate level of uncertainty and therefore learning rate. One potential method to tease these two hypotheses apart would be to repeat the auditory cue switch experiment while administering an agent that constantly dilates the pupil for the duration of the experiment. The first hypothesis would predict a persistence of the auditory cue switch effect, whereas the second would not.

Nassar *et al.*'s findings[4] about pupil dilation reflecting computational variables that are important for driving learning in a changing world are very timely and exciting. Not only do they provide firmer evidence than ever before that various forms of uncertainty, possibly mediated by cholinergic and noradrenergic modulatory systems, drive learning, as predicted by theoretical models[1,3], but they also suggest a potentially cheap, easy and noninvasive tool for diagnosing cognitive dysfunctions that involve impairments in probabilistic inference and response to changing environments, such as those associated with Alzheimer's disease and Parkinson's disease[12]. More work is needed to establish a clear picture of how the dynamics of pupil diameter specifically relate to activations in various neuromodulatory systems, as well as the route by which task-irrelevant pupil dilation can influence central cognitive processes.

COMPETING FINANCIAL INTERESTS
The author declares no competing financial interests.

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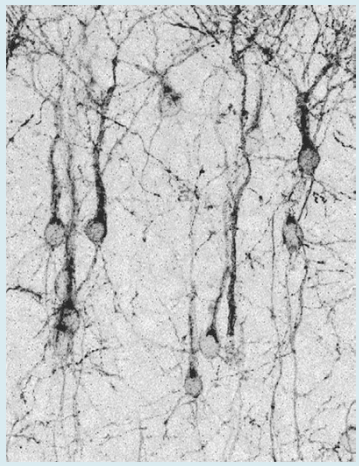
Getting to the root of basal dendrite formation



Cortical pyramidal neurons, named for the shape of their cell bodies, also have prominent dendritic arbors that are critical for their functionality. These neurons are fairly unique in that they possess two distinct dendritic branches, the apical and the basal. However, the mechanisms that drive dendritic tree formation are poorly understood and it is, as yet, unclear whether there are specific mechanisms mediating the formation of each branch. On p. 1022, Calderon de Anda and colleagues provide evidence suggesting that *TAOK2*, a known autism spectrum disorder (ASD) susceptibility gene, is important for basal, but not apical, dendrite formation in the neocortex.

Although TAOK2 has only recently been associated with ASD in humans, it is not a mystery molecule to neuroscientists. TAOK2 is known to modulate gene transcription via its activation of several MAP kinase pathways, including c-Jun amino-terminal kinase (JNK), and has been implicated in the modulation of actin and microtubule dynamics. Here the authors show that the time course of TAOK2 expression is consistent with a role for it in neuronal differentiation.

To investigate the role of TAOK2 in development, the authors interfered with TAOK2 by *in utero* electroporation of small hairpin RNAs (shRNAs). Both knockdown and overexpression of TAOK2 disrupted neuronal differentiation, specifically by affecting the complexity of the basal dendritic arbor.

Recent work has suggested that basal dendritic arborization is controlled by the Sema3A-Npn1/PlexinA4 signaling cascade, so the authors asked whether TAOK2 might exert its effects by interacting with this pathway. Indeed, they found that TAOK2 interacts with the Npn1 receptor and that Sema3A signaling activates TAOK2 kinase activity. Disrupting Npn1, either by transgenic manipulation or shRNA interference, resulted in reduced branching and growth of basal dendrites from cortical neurons. This effect could be rescued *in vitro* and partially restored *in vivo* by TAOK2 overexpression, confirming a functional link between Npn1 and TAOK2. Exploring more of this signaling pathway, the authors found that activation of the MAP kinase JNK by Sema3A-TAOK2 signaling is essential for the formation of the basal dendrites.

Taken together, these results implicate the Npn1-Sema3A signaling pathway in basal dendrite formation and branching via a TAOK2- and JNK-dependent pathway. Given that most of the synaptic contacts onto pyramidal cells are along the basal dendrite arbor, disruption of this structure might be expected to substantially influence the activity of these important neurons. Thus, these findings suggest one way in which disruption of the ASD-associated TAOK2 could have far reaching effects on cortical function and, given previous work reporting under-connectivity in ASD patients, could potentially provide a hint into ASD disease pathology.

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