located on the basis of its functional traits. The researchers focused on six traits that are readily available for a large number of taxa and that are central to determining a plant's ecological strategy: plant height, leaf area, leaf mass per area, nitrogen content per mass, stem mass per volume and seed mass. Their analysis, which incorporates these values from more than 45,000 species, is the first of its scope to explore relationships across seed, leaf, stem and whole-plant traits. This scale was possible only because of a database called TRY (ref. 7), which contains 5.6 million records of plant functional traits assembled over the past decade.

In principle, a given plant could occupy any point within this six-trait space. To assess how constrained plant species actually are within this space, the authors compared their observations with four null models representing different distributions of and correlations between traits. They found that, worldwide, plant species occupy only a small fraction of their potential trait space, and the observed pattern is driven largely by strong correlations between functional traits across species (Fig. 1). The researchers then conducted a principal component analysis and identified two primary dimensions in which plants vary globally: plant size, ranging from short species with small seeds to tall species with large seeds; and leaf strategy[6], ranging from 'acquisitive' species with low leaf mass per unit area and high leaf nitrogen content to 'conservative' species with high leaf mass per unit area and low nitrogen content.

It is difficult to evaluate the extent to which the constraints on plant form and function suggested by this analysis arise from biomechanical trade-offs, natural selection or competition. But this is where Kunstler and colleagues' study comes in. These researchers explored how three plant functional traits (leaf area per mass, plant height and wood density) predict the competitive interactions between forest tree species. Their data set is similarly impressive in scope to that of Díaz *et al.* — it includes three functional traits and trunk-diameter growth for more than 3 million trees from over 2,500 species in forest plots from 6 biomes. Taking advantage of natural variation in the density and identity of competitors surrounding a focal tree, the authors built a statistical model to quantify how a species' trait values predict its growth without competition, its resistance to competition and its ability to suppress the growth of neighbours.

The authors had good reason to expect that functional traits would predict competitive dynamics. Ecological theory holds that trait differences between species should cause these taxa to use the environment in different ways, resulting in a 'niche difference' that minimizes competition between species (Fig. 1a). Contrary to these expectations, however, Kunstler and colleagues found little to no evidence that trait differences minimize competition between trees across the six forest biomes. Instead, certain trait values tended to predict the competitive advantage of one species over others. Trees with high wood density, for example, tended to be most resistant to competition (Fig. 1b). These findings resonate with work[8,9] positing that trait differences should predict both the niche differences that stabilize species coexistence and the competitive imbalances that drive species exclusion.

If the three functional traits studied by Kunstler *et al.* predicted only competitive imbalances between forest trees, which traits explain their local coexistence? Although the authors point to trade-offs between high growth rate and competitive tolerance, their finding of greater competition within species than between species — a factor that also stabilizes species coexistence — must relate to traits other than those measured. This finding highlights the limitations of trait-based ecology. Although, in principle, all competitive dynamics must be explainable by plant traits, whether these are the functional traits that can be readily measured is an open question.

Answering this question, as well as related ones at the population and ecosystem levels, will require further integration of functional traits and mathematical models along the lines of Kunstler and colleagues' approach. Nonetheless, ecologists have a growing need to efficiently predict the nature of competition between plant species that do not co-occur today but will in the future as climate change causes species to migrate, and to migrate at different rates[10]. Trait-based approaches may be our only recourse. ■

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NEUROBIOLOGY

Pull out the stops for plasticity

The strength of synaptic connections between neurons needs to be variable, but not too much so. Evidence now indicates that regulation of such synaptic plasticity involves a complex cascade of feedback loops.

CHRISTINE E. GEE & THOMAS G. OERTNER

Learning is thought to manifest in the brain as physical changes that alter the strength of neuronal contact points called synapses. These contact points allow information to be transmitted from one neuron to another, and understanding the conditions that cause synapses to change strength (a phenomenon known as synaptic plasticity) has been a focus of neuroscience research for many years. Writing in *Nature Communications*, Tigaret *et al.*[1] challenge the prevailing idea that the local concentration of calcium ions (Ca^{2+}) is the key factor that determines whether a synapse becomes stronger or weaker after repetitive activation. They propose that plasticity involves an intracellular signalling cascade that overrides a safety mechanism. This suggests that the default state of the synapse is not to be plastic.

The main excitatory neurotransmitter in the mammalian brain is the molecule glutamate. Glutamate is released from the presynaptic neuron, and the postsynaptic neuron is excited when the molecule binds to and activates specialized receptor proteins, most of which are ion channels called ionotropic glutamate receptors. When activated, these channels open and positively charged ions enter the cell, depolarizing (reducing the voltage across) the cell membrane. In addition, glutamate receptors that are not ion channels, called metabotropic glutamate receptors, activate various intracellular signalling cascades. Their effect on synaptic transmission is generally slower than that of ionotropic receptors, but they are crucial for healthy brain function[2].

In the neuronal structure known as the dendritic spine, which forms a single synaptic contact, the initial depolarization caused by activation of ionotropic glutamate receptors

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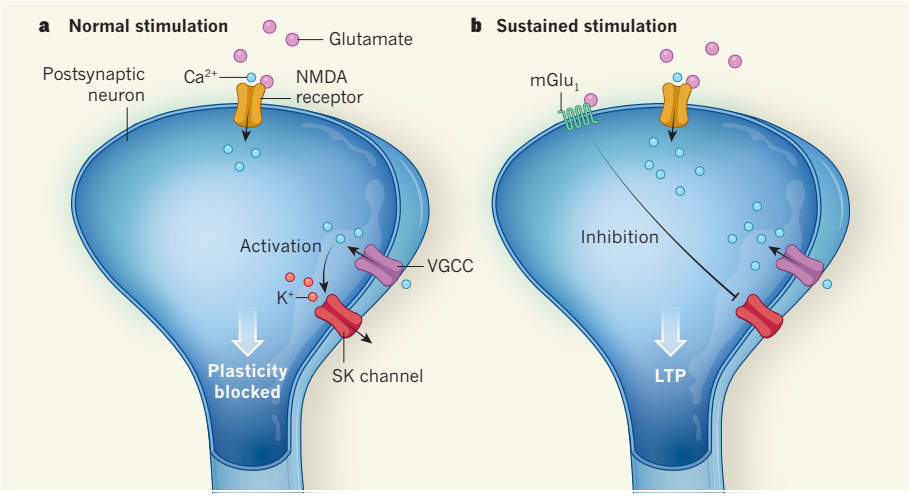

Figure 1 | The promotion of plasticity. **a**, The molecule glutamate is transmitted across the synaptic cleft between neurons to activate the postsynaptic neuron. When the voltage across the cell membrane decreases (depolarization), glutamate-bound NMDA-receptor proteins and voltage-gated calcium channels (VGCCs) open, allowing calcium ions (Ca^{2+}) to enter the cell. Under normal conditions, proteins called SK channels are activated by this Ca^{2+} influx. Potassium ions (K^+) flow out through SK channels, decreasing depolarization and preventing changes in synaptic strength, known as plasticity. **b**, Tigaret *et al.*[1] report that the metabotropic glutamate receptor protein $mGlu_1$ is activated by sustained glutamate signalling, and leads to inhibition of SK channels. This slow-acting inhibition enables prolonged depolarization and triggers strengthening of the synapse, known as long-term potentiation (LTP).

can be amplified by the opening of voltage-gated calcium channels, further depolarizing the spine. A special class of ionotropic glutamate receptors called NMDA receptors have a similar role — they open only when the neuron is already depolarized, forming a positive-feedback loop that increases Ca^{2+} influx and depolarization[3]. The activation of NMDA receptors is essential for many forms of long-lasting synaptic plasticity.

However, positive-feedback loops are inherently dangerous for neurons — too much depolarization and Ca^{2+} can be toxic, eventually triggering cell death. To prevent this from happening, spines have a safety mechanism in the form of calcium-activated, potassium-conducting SK channels[4]. When intracellular Ca^{2+} reaches a critical concentration, SK channels open, allowing positively charged potassium ions to exit the cell and so preventing further depolarization (Fig. 1a). This SK mechanism stops the positive-feedback loop, blocking further Ca^{2+} influx. But a side effect is that the synaptic strength becomes difficult to change[5].

Tigaret *et al.* describe a plasticity-enabling mechanism that inhibits SK channels in individual spines. They found that repeated sequential activation of pre- and postsynaptic neurons in slices of rat brains induced synaptic strengthening, also known as long-term potentiation (LTP). In addition to NMDA-receptor activation, LTP induction required the activity of group 1 metabotropic glutamate receptors ($mGlu_1$). The authors show that activation of $mGlu_1$ triggers a slow-acting mechanism that inhibits SK channels, allowing for sustained depolarization and enhanced Ca^{2+} entry into the spine (Fig. 1b).

The authors used a strong induction protocol (300 paired activations in 1 minute) to allow the relatively slow metabotropic process to take effect and enable LTP. This might seem unusual — after all, we don't need to be presented with information 300 times before learning a new association. Why was such a strong protocol required?

In an intact brain, specific neuromodulator chemicals such as dopamine and acetylcholine are released when the animal is in an aroused state: for example, when it learns that a certain sound predicts a frightening event. These substances modulate glutamate-activated synapses and have been shown to promote synaptic plasticity by blocking SK channels[5,6]. The timing window for successful induction of LTP has been shown[7] to change radically in the presence of neuromodulators. Thus, it seems that there is not just one rule for how synapses change during learning, but a whole set that are tailored to various occasions such as different mental states. This makes sense from a systems perspective — synaptic potentiation is gated not only by timing, but also by the brain's reward system. From an experimental point of view, the lack of neuromodulatory inputs, which is an inherent limitation of brain-slice experiments, might explain why a strong protocol was required. Functional imaging of single synapses in live, active animals is not yet possible.

The mechanism highlighted by Tigaret and colleagues is not the only way in which synapses can be strengthened. Enzymes called Src tyrosine kinases (which add phosphate groups to proteins) can directly enhance NMDA-receptor function[8]. This pathway has been shown to cause LTP in the same type of synapse as that analysed in the current study[9]. The activity of various metabotropic receptors, including $mGlu_1$, can increase glutamate-mediated responses through this pathway[10]. It will be interesting to investigate whether the $mGlu_1$-triggered blockade of SK channels identified by Tigaret *et al.* acts together with direct NMDA-receptor phosphorylation to enable LTP, or whether one mechanism is dominant under specific conditions, depending, for instance, on cell type or the age of the animal.

This study also confirms[11] that, contrary to general thinking, it is not possible to predict the direction and magnitude of synaptic plasticity by simply analysing levels of Ca^{2+} in dendritic spines. For example, a pair of presynaptic stimulations triggered a very strong Ca^{2+} influx into the spine, but no plasticity whatsoever. But before Ca^{2+} is discarded as the key state variable, we must consider that successful induction of long-term plasticity relies on the interplay of local synaptic Ca^{2+} signals with Ca^{2+} signals in the cell body (soma) of the neuron. Indeed, the authors emphasize the importance of postsynaptic electrical activity and the activation of voltage-gated calcium channels for LTP. These processes are not restricted to the active spine; they increase Ca^{2+} levels throughout the neuron. Thus, it might be possible to predict the future strength of a synapse from simultaneous Ca^{2+} measurements in the spine and soma. This is certainly not an easy experiment, but sophisticated 3D scanning microscopes could be used to analyse compartmentalized Ca^{2+} signalling in individual neurons — and perhaps one day in intact animals during learning. ■

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