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NEUROSCIENCE

Light moulds plastic brains

Stefan Thor

In tadpoles, the number of neurons expressing the neurotransmitter dopamine increases on exposure to light. Such plasticity might allow animals to physically match their brains' activity to environmental stimuli.

The nervous systems are known to adapt to environmental inputs. But such plasticity has been thought to involve modifications of neural circuits and communication between neurons via synaptic junctions — as in learning and memory — rather than alterations in the numbers of distinct classes of neurons. Dulcis and Spitzer¹ challenge this view, demonstrating that when the larvae of *Xenopus laevis* tadpoles are exposed to bright light, the number of dopamine-secreting — or dopaminergic — neurons in their brains increases, allowing them to adapt more rapidly to future exposures to light.

Anyone who has caught wild tadpoles from a pond has probably been surprised to see the captive animals turn pale after a couple of hours. This rapid change in pigmentation allows tadpoles to better blend in with their surroundings, reducing their risk of becoming prey. A distinct neural circuit controls this process. Specifically, light-induced signals from the eye are relayed to a brain region called the suprachiasmatic nucleus, which contains dopaminergic neurons. From there, signals pass onto another region containing neurons that secrete melanocyte-stimulating hormone to trigger pigment cells in the skin (Fig. 1a). This circuit works in an alternating manner such that, in response to light, positive inputs from the eye onto the suprachiasmatic nucleus trigger increased dopamine release. High dopamine levels then provide negative inputs to the hormone cells, resulting in reduced hormone secretion and so decreased pigmentation of the peripheral skin.

The pigmentation response is modulated by previous experience, because prolonged or repeated exposure to bright light results in tadpoles adapting more rapidly to subsequent exposures². Such changes in this response and its underlying circuitry have been studied extensively²⁻⁵, and were believed to primarily involve plasticity at the level of synaptic connections and signals passing through the circuit. Dulcis and Spitzer¹ reveal that, in fact, this adaptation involves a rapid increase in the number of dopaminergic neurons within the circuitry.

The speed of the response that these authors observe is remarkable — when exposed to only two hours of light, tadpoles that had been raised in the dark exhibited a doubling of dopaminergic neurons within the suprachiasmatic nucleus. What's more, the newly emerging dopaminergic neurons seem to contribute to the pigmentation process on subsequent exposures to light by reducing pigmentation more rapidly (Fig. 1b). The authors traced these neurons' axonal processes and found that they project onto the hormone-releasing neurons. They next ablated the baseline dopaminergic neurons using specific drugs to show that this treatment completely abolishes light adaptation. But when animals with ablated dopaminergic neurons were exposed to light on subsequent occasions, dopaminergic neurons that had appeared after drug treatment could restore light adaptation.

So where do these 'new' dopaminergic neurons come from? Do they result from a change in the type of neurotransmitter secreted by pre-existing neurons, or are they generated *de novo*? Earlier work revealed⁶⁻¹⁰ that the mammalian brain (even that of adult mammals) can generate additional

neurons in response to environmental cues. For instance, adult laboratory mice living in an enriched environment — large cages containing running wheels, nesting material and toys — have increased numbers of neurons in specific brain areas, particularly those crucial for spatial orientation¹⁰. Likewise, songbirds add and remove neurons to certain brain regions on a seasonal basis, a mechanism that acts to match brain anatomy to appropriate seasonal behaviour¹¹. In the case of light adaptation in tadpoles, however, Dulcis and Spitzer find no evidence for new cells being generated within the suprachiasmatic nucleus. Given the rapid appearance of the extra dopaminergic neurons, this observation was perhaps expected: it is unlikely that additional neurons could be generated *de novo* within the relatively short time frame of only two hours. Instead, it seems that pre-existing neurons expressing a different neurotransmitter now co-produce dopamine.

Dulcis and Spitzer's findings advance the idea that external sensory inputs modulate a specific response by regulating the population size of specific neuronal subtypes — those that are involved in controlling the physiological response to the input — in the brain. From a broader perspective, their observation that pre-existing neurons can switch on the expression of an additional type of neurotransmitter adds to the growing list of different ways in which brain plasticity can arise: weakening or strengthening of communication between neurons, formation of new connections, and the recent findings that additional neurons of certain types can be added to the system *de novo*. An issue that Dulcis and Spitzer do not address, however, is whether the particular type of brain plasticity they observe is limited to developing tadpoles, or whether it also applies to adult frogs — and mammals, for that matter.

Dysfunction of signalling cascades mediated by dopamine may be an essential element of seasonal affective disorder, also known as winter depression¹². So a way forward might

be patient analysis using positron emission tomography (PET), a technique that is routinely used to visualize dopaminergic cells¹³. Although PET images are of limited resolution, a dramatic increase in the number of dopamine neurons — possibly in response to seasonal changes in day length or diurnal changes in light intensity — could be detectable. If plasticity mediated by changes in the pattern of neurotransmitter production applies to humans, it is likely to open fresh avenues aimed at combating neurological diseases.

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Figure 1 | Plasticity in the tadpole pigmentation circuit. a, Tadpoles adjust their pigmentation in response to the surrounding light conditions using a neuronal circuit involving signals from the eye onto the dopaminergic neurons in the brain's suprachiasmatic nucleus (red). These neurons inhibit pigment-hormone release from melanocyte-stimulating cells (green). **b,** Dulcis and Spitzer¹ find that a longer exposure to light — about two hours — induces the generation of extra dopaminergic neurons in the suprachiasmatic nucleus of *Xenopus laevis* tadpole larvae. Return to darkness still allows for the darker pigmentation. Yet, on subsequent exposure to light, the presence of the new dopaminergic cells as well as the pre-existing ones triggers a more rapid reduction in pigmentation. Thus, in the developing tadpole, the extra dopaminergic neurons provide an adaptive advantage.