incoherent. However, coherent superpositions of molecular states can be produced using the light emitted by a laser. The ability to consistently generate these superpositions could improve the efficiency of the corresponding chemical processes and reduce the energy required to control such processes. It might even open up chemical-reaction mechanisms that are otherwise inaccessible[3,4].

Laser pulses are the main tool for manipulating molecules in this field. Improvements in the design of these pulses, such as increases in power and tunability, as well as the ability to reduce the duration of the pulses to attosecond (10^{-18} s) timescales, have enabled greater control of light-induced processes in molecules[5]. Since the pioneering work of Ahmed Zewail, who was awarded the 1999 Nobel Prize in Chemistry (see go.nature.com/2idzowq), laser pulses have been used to study quantum coherence in chemistry[6].

For example, quantum coherence has been used to enhance the rates of chemical reactions in biological systems at room temperature[7]. Such studies conclusively showed that quantum coherence can be partially preserved even in molecular systems open to the external environment[8].

These experimental advances call for accurate models of the quantum evolution of molecular systems. This is a challenging task for quantum-computing devices, although much progress has been made, thanks to the development of improved algorithms for simulating quantum dynamics[9,10].

Sparrow and colleagues engineered a quantum-computing device that is based on a single photonic chip. They used the quantum superposition of photons in the chip to carry quantum information and to model molecular systems. By adjusting the optical circuitry of the chip, the authors simulated a range of quantum dynamics associated with different molecules.

The authors began by simulating vibrational excitations in a variety of four-atom molecules. They then modelled energy transport in the chemical bond of a protein and the transfer of vibrational energy in liquid water. Finally, they tested an algorithm designed to identify quantum states that can lead to the break-up of ammonia. The results of these simulations were in almost perfect agreement with those obtained using ordinary computers.

The first quantum revolution occurred at the turn of the twentieth century, and provided us with the physical laws that govern reality. Sparrow and colleagues have now simulated the time evolution of a quantum superposition of molecular states with the aid of an experimental device that uses the quantum superposition of photons. Such a feat suggests that we could be entering a second quantum revolution, in which the physical laws of nature are used to develop innovative technologies.

Despite these promising prospects, it is not difficult to envisage the problems that follow-up studies will encounter. In this seminal work, the authors used rather simple molecular models, involving a limited number of mathematical terms. However, this number will increase exponentially when aiming to closely reproduce experimental conditions. Such an increase might dramatically enhance what the authors refer to as the "fundamental errors" in photonics, which include the loss of photons and the loss of quantum coherence.

Nevertheless, Sparrow and colleagues have demonstrated that simulations carried out by quantum-computing devices can be both reliable and efficient, by tackling problems that can be solved using well-established standard techniques. As the authors point out, slight improvements in their method could yield simulations that cannot be achieved using ordinary computers. ■

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IMMUNOLOGY

Gut molecules control brain inflammation

Metabolite molecules produced by the gut's microbes activate immune cells in the brain called microglia, which signal to astrocyte cells to mediate responses to inflammation in the central nervous system. SEE LETTER P.724

HARTMUT WEKERLE

Some immunologists regard the central nervous system (CNS) as a no-man's-land, avoided by immune cells and therefore uninteresting. But, in fact, the CNS has a vigorous immune potential that remains dormant in normal conditions but is awakened after injury. The switch that controls the brain's immune microenvironment involves non-neuronal cells called glia — not only microglia, which are sometimes called the immune cells of the CNS, but also multifunctional cells called astrocytes[1]. Rothhammer *et al.*[2] describe on page 724 how these two glial cell types communicate on a molecular level to influence inflammation in the CNS, and show that this interaction is controlled remotely by microbes that inhabit the gut.

A decade ago, the group that performed the current study, along with another research group, discovered[3,4] an unexpected immunoregulatory role for a ligand-activated transcription factor called the aryl hydrocarbon receptor (AHR), which at the time was best known as a receptor for environmental toxins[5]. The two groups showed that AHR modulates the progression of experimental autoimmune encephalomyelitis (EAE) — an autoimmune disease in mice in which the immune system becomes overactive and attacks the CNS. EAE is often used a model of multiple sclerosis (MS). Initially, the groups focused on how AHR might affect EAE by regulating pathogenic and protective subsets of immune cells outside the CNS. But it later emerged that AHR is also strongly expressed in the CNS, particularly in microglia and astrocytes[6], raising the question of whether AHR in the CNS has a role in autoimmune diseases.

In the current study, Rothhammer *et al.* induced EAE in mice that had been genetically engineered so that AHR could be deleted in microglia (but not in other brain cells or immune cells) by a drug treatment. Elimination of microglial AHR substantially exacerbated EAE in the AHR-depleted mice, but left immune responses outside the CNS unaltered. This finding suggests that AHR activation in microglia inhibits inflammation in the CNS.

Microglia rarely act alone. Instead, they often team up with other cell types to respond to the stimuli that activate them. For example, after being activated, microglia can instruct certain astrocytes to attack local neurons[7]. Rothhammer and colleagues found that AHR-deficient microglia activated by EAE triggered exaggerated inflammatory responses in local astrocytes. Next, the authors used bioinformatics to analyse the gene-expression pathways altered in these glia. This analysis suggested that unexpected proteins signal from microglia to astrocytes.

The usual suspects in such cases are

pro-inflammatory signalling molecules, but Rothhammer *et al.* showed that AHR in microglia directly regulates the expression of genes that encode the proteins TGF-α and VEGF-B (Fig. 1) — neither of which has previously received much attention from neuroimmunologists. Subsequent detailed *in vitro* and *in vivo* analyses confirmed that TGF-α and VEGF-B regulate the pro-inflammatory reactivity of astrocytes. TGF-α dampens astrocyte inflammatory responses to EAE, and its expression in microglia is inhibited by AHR deletion. Conversely, VEGF-B enhances responses to EAE, and its expression is promoted by AHR deletion.

So, the activity of microglia and astrocytes is modulated by AHR during brain inflammation in autoimmune disease. But which signals might modulate microglial AHR? In addition to environmental toxins, AHR is bound by a broad range of molecules, including dietary derivatives[8]. In particular, food plants such as broccoli and other members of the cabbage family contain components that bind AHR either directly or after being processed into metabolite molecules, such as derivatives of tryptophan (Trp), by gut microbes[9]. Rothhammer *et al.* fed their mice diets either depleted or enriched in Trp. Trp depletion exacerbated EAE in wild-type mice, whereas enrichment ameliorated the effects of the disease. By contrast, neither diet had any effect on the progress of EAE in AHR-deficient animals, as might have been predicted — in these animals, Trp cannot bind to AHR to dampen immune responses.

To determine whether their work is likely to have implications for humans, the authors verified basic elements of their analyses in tissue samples from people with MS, in which an autoimmune attack drives glial inflammation, destruction of nerve processes and their insulating myelin sheaths, and ultimately scar formation[10]. The group found that AHR, TGF-α and VEGF-B were expressed in microglia-like cells in MS tissues. Levels of the proteins were higher in newly inflamed regions than in old scar tissue or unaffected surrounding tissue. This suggests (but does not prove) that TGF-α and VEGF-B have a role in the formation of MS scar tissue.

Rothhammer and colleagues' work sheds light on the complex regulation of inflammatory reactivity in the CNS and adds another facet to our understanding of the gut–brain connection. Robust regulation of inflammatory responsiveness is essential for proper CNS function. Deficient regulation, with unrestrained inflammatory episodes, leads to sickness, irreversible cell loss and scar formation[11], whereas compromised inflammatory reactivity can result in tumour formation and opportunistic infection[12]. The authors' findings are therefore likely to have implications beyond MS.

The interactions between the gut, microglia and astrocytes outlined by Rothhammer *et al.* are not the only mechanisms that safeguard inflammatory responses in the brain[13]. It will be of interest to examine how other regulators of the CNS immune microenvironment modulate the newly identified signalling pathway. These factors include the cells associated with the cerebral blood vessels, as well as active neurons. Indeed, pharmacological silencing of neurons leads to the activation of neighbouring microglia[14].

That the behaviour of microglia can be controlled remotely by intestinal products is intriguing, although not without precedent. A flurry of observations previously linked the CNS to the gut and its microbial contents. Neuronal pathways, hormones, microbial molecules and metabolites are all involved in signalling between these regions[15]. Specifically, short-chain fatty acids produced by gut bacteria can modulate microglia cells[16], and tryptophan metabolites act directly on astrocytes[6]. Nonetheless, the current findings broaden our understanding of the gut–brain connection. The authors speculate that this pathway might support the repair of injured neural cells.

"That the behaviour of microglia can be controlled remotely by intestinal products is intriguing."

As Rothhammer and colleagues point out, their experimental observations might lead to new therapeutic approaches to quelling unwanted CNS inflammation, and possibly to supporting neuronal repair. First, enhancement of TGF-α and blockade of VEGF-B might reduce CNS inflammation to an acceptable, non-toxic level. Second, clinical CNS inflammation could be dampened indirectly by means of the gut. Dietary protocols that promote anti-inflammatory regulation could be a promising non-invasive approach to treating brain inflammation. It is to be hoped that diets that have been proposed as effective medications for diseases such as MS, but whose effectiveness has yet to be formally proved[17], will now be re-examined. ■

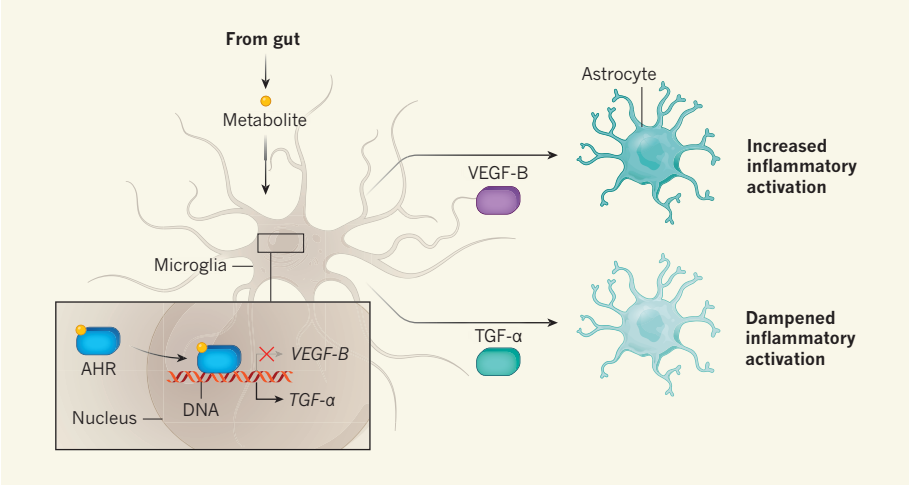

Figure 1 | Long-distance regulation of immune cells in the brain. Gut bacteria process the dietary component tryptophan to produce metabolite molecules that enter the central nervous system (CNS). In the brain, these metabolites act as ligands for the aryl hydrocarbon receptor (AHR) — a transcription factor expressed in cells called microglia and astrocytes that mediate responses to inflammation in the CNS. Rothhammer *et al.*[2] report that, when activated in microglia, AHR binds to the genes that encode the proteins VEGF-B and TGF-α, inhibiting the expression of the former and promoting that of the latter. Any VEGF-B released from microglia enhances the responsiveness of astrocytes to CNS inflammation. By contrast, TGF-α dampens astrocyte responsiveness.

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