compounds, which requires first grasping the nature of the charge-density-wave phase from which it emerges.

The observation of time-reversal symmetry breaking is essential to our efforts to describe exotic and rare types of superconductivity. In particular, Mielke and colleagues' work provides a key ingredient for developing a model to describe the vanadium antimony kagome systems. Among the crucial questions to be addressed is the relative importance of the reorganization of electrons compared with the vibration and displacement of the atoms in the lattice. Although much of the theory of charge density waves relies on these atomic displacements, the very existence of a loop-current phase implies that the electrons have a central role, which is also in line with Nie and colleagues' findings.

A robust model must also reconcile the presence of time-reversal-symmetry breaking with superconductivity. This, in itself, is an exciting prospect for the broader field of topological superconductivity, in which the Cooper pairs take on the topological properties of the electronic wavefunctions. As well as being fascinating, topological superconductors might have future applications in quantum computing. The results of these two studies clearly bring fresh insight into symmetry breaking in kagome superconductors, and this will no doubt motivate further research into these intriguing materials.

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The authors declare no competing interests.

Neuroimmune interactions

Neurons in the brain recall gut inflammation

David Brea & Henrique Veiga-Fernandes

The nervous and immune systems interact in a bidirectional manner. It emerges that inflammation in the body activates brain cells that, when later reactivated, can trigger a recapitulation of the inflammatory response.

Interactions between the nervous and the immune systems have been a topic of great interest over the past few decades. Neuronal signals can affect immune functions, and immune cells can modulate the activity of neurons in the brain and spinal cord, or in the rest of the body (known as the periphery), in health and disease[1,2]. Writing in *Cell*, Koren *et al.*[3] demonstrate that inflammation in the abdominal cavity results in the stimulation of certain neurons in a brain area called the insular cortex, or the insula. Artificial reactivation of these 'immune-imprinted' neurons is sufficient to generate organ-specific recall of inflammatory responses that resemble the initial inflammatory episode.

Using a model of inflammatory bowel disease (in which a chemical called DSS is given to mice in their drinking water to induce intestinal inflammation), the authors investigated whether intestinal inflammation leads to the activation of certain brain areas. To do this, they used mice genetically engineered to express a fluorescent marker molecule in active (but not inactive) neurons when the animals were treated with the drug tamoxifen. The authors compared the fluorescent labelling in the brains of tamoxifen-treated mice given DSS with that in the brains of control mice, which were treated with tamoxifen but not with DSS. Neurons activated during episodes of bowel inflammation were identified in the insula, a region in the cerebral cortex that is involved in sensory processing and motor control (Fig. 1a).

The authors injected an engineered virus into the insula of the genetically engineered mice so that the neurons that were activated during bowel inflammation could be specifically reactivated by treating the animals with a small molecule called

From the archive

The discovery of a key defence response, and a collection of items from an inventor that highlights advances in photography.

100 years ago

Life of Elie Metchnikoff, 1845–1916. By Olga Metchnikoff — It was at Messina ... that what Metchnikoff regarded as the great event of his scientific life occurred. It is described by him in his own words as follows: — "One day, when the whole family had gone to a circus, I remained alone with my microscope, observing the life in the mobile cells of a transparent starfish larva, when a new thought suddenly flashed across my brain. It struck me that similar cells might serve in the defence of the organism against intruders. I felt so excited that I began striding up and down the room ... [I]f my supposition was true, a splinter introduced into the body of a starfish larva ... should soon be surrounded by mobile cells ... I fetched some rose-thorns and introduced them under the skin of some beautiful starfish larvae ... I was too excited to sleep that night in the expectation of the result of my experiment, and very early the next morning I ascertained that it had fully succeeded. That experiment formed the basis of the phagocyte theory".

From *Nature* 9 February 1922

150 years ago

I trust you will kindly allow me space for a few lines on the subject of some rare specimens connected with the History of Photography, now in the possession of Madame Nièpce de St. Victor, whose husband it will be remembered was the first to employ glass, and a transparent medium (albumen) for the purposes of photography, thus discovering, to a great extent, the process of Photography as it exists at the present day. The first glass negative, or rather *cliché*, Madame Nièpce possesses, as likewise prints executed in 1848. Nièpce de St. Victor was ... one of those who have worked hard to secure natural colours in the camera, some very perfect specimens — photographs of coloured dolls — which prove distinctly that the solution of the problem is not impossible, as many believe, are also included in the Nièpce collection.

From *Nature* 8 February 1872

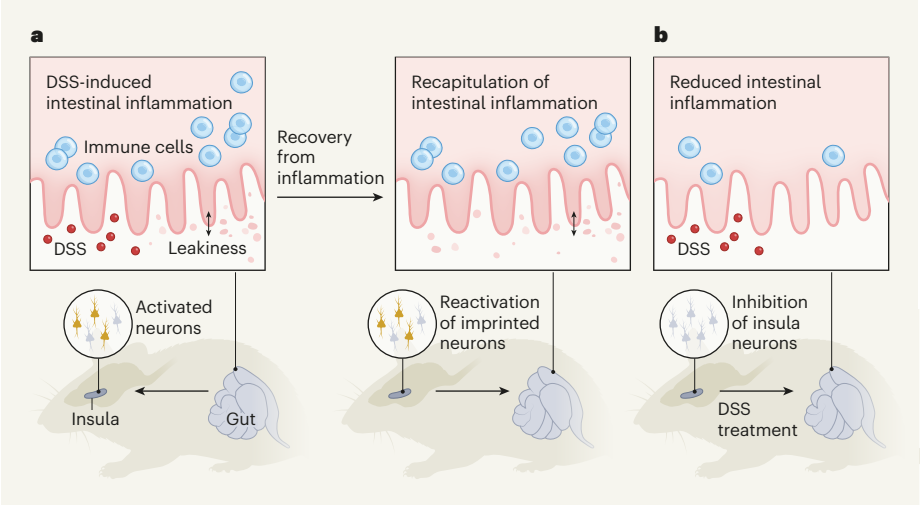

Figure 1 | The brain recalls inflammatory episodes. Treating mice with the chemical DSS in their drinking water leads to intestinal inflammation, characterized by an increase in pro-inflammatory immune cells and leakiness in the gut wall. **a**, Koren *et al.*[3] reveal that, in mice treated with DSS, the episode of intestinal inflammation activates neurons in a brain region called the insular cortex, or the insula. Artificial reactivation of these same 'immune-imprinted' neurons after the intestinal inflammation has resolved triggers a recapitulation of the inflammatory response in the gut, suggesting these neurons encode the immune system's response. **b**, The authors then showed that artificial inhibition of neurons in the insula in mice could reduce some of the signs of inflammation caused by DSS.

clozapine-*N*-oxide (CNO). When the mice had recovered from the episode of bowel inflammation, CNO-induced reactivation of these 'captured' insula neurons was sufficient to trigger an intestinal response that was reminiscent of the initial bowel inflammation (for example, in terms of the types of immune cell observed in the gut tissue).

To establish whether this recapitulated immune response was the result of activating the immune-imprinted neurons, and not a consequence of the general activation of the insula, the authors activated this region in mice that had not had an episode of bowel inflammation. In this experiment, no signs of intestinal inflammation were observed, confirming that the previously activated set of insula neurons, rather than the insula generally, specifically encoded the immune response.

The authors report similar neuronal encoding of the immune response during inflammation of another abdominal tissue called the peritoneum (the membrane that lines the abdominal cavity), which can be induced by injection of a microbial cell-wall component called zymosan. Moreover, after the zymosan-induced peritoneal inflammation had resolved, artificial activation of the captured insula neurons with CNO resulted in peritoneal inflammation that was reminiscent of the initial inflammatory reaction. The fact that the recall inflammatory responses were restricted to the peritoneum suggests that the captured insula neurons encode anatomical information about the inflammatory response. Together, these observations indicate that reactivation of immune-imprinted neurons in the brain is sufficient to induce and recapitulate inflammatory responses at specific sites in the body.

Next, to shed light on the anatomical basis for communication between the insula and the intestine, the authors used a cell-labelling strategy that enables the identification of neuronal circuits that connect peripheral neurons to brain areas involved in complex processing. They injected a virus encoding a fluorescent protein into the mouse intestine. This virus infected and fluorescently labelled the neurons innervating the intestine. It propagated along these neurons and across the synaptic connections with their partners in the circuit, and thus labelled the neural pathway from the intestine to the insula.

Finally, Koren *et al.* tested whether inhibiting neurons in the insula affects the course of intestinal inflammation. To this end, they injected a different engineered virus into the insula in mice that enabled the activity of neurons in this region to be inhibited by treating the animals with CNO. Inhibition of insula neurons during an episode of DSS-induced intestinal inflammation reduced some signs of inflammation, indicating that inhibition of this brain area can attenuate intestinal inflammatory responses (Fig. 1b).

Over the past decade, several studies[1,2,4–8] have explored the effect of bidirectional interactions between the nervous system and the immune system on communication between organs — especially between the brain and other organs, such as the intestine and lungs[9]. Koren and colleagues' study builds on previous knowledge that peripheral immune responses can be encoded by certain brain areas. For example, previous work has shown that responses of the innate branch of the immune system leave traces in the brain[10]. In mice, immune challenges in the periphery led to long-term activation of microglia (the immune cells of the brain), and persistent microglial activation altered the progression of neurodegenerative disease in mouse models[9].

Koren and co-workers have now shown that the stimulation of immune-imprinted neurons in the brain can induce inflammatory responses in particular peripheral organs. It is tempting to speculate that an animal's immune status can be dynamically encoded and recapitulated by the brain, fine-tuning the course of immune responses and associated diseases.

The authors' study opens up fresh approaches in the field of neuroimmunology and raises many questions. Although the authors describe the neuronal pathway connecting the insula to the intestine, it remains unclear exactly how communication between these two sites occurs. How are sensory neurons and the autonomic nervous system (a part of the nervous system that regulates organ function) involved in this brain–body communication? Does the immune system signal to neurons in the insula by releasing soluble factors? Do brain-derived neuronal signals control immune cells directly, or indirectly, through other cell types in the intestine? Are immune responses that occur in other organs, such as the lungs or the skin, encoded by distinct sets of neurons in the insula, or in other brain regions?

Koren and colleagues' study serves to highlight the importance to biomedical research of investigating the interactions between the nervous and immune systems. Together with previous work[2,8], it unravels biological underpinnings of these interactions that might be relevant to designing therapeutic approaches to many diseases, including cancer and inflammatory, neurological and metabolic disorders.

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The authors declare no competing interests.
This article was published online on 10 January 2022.