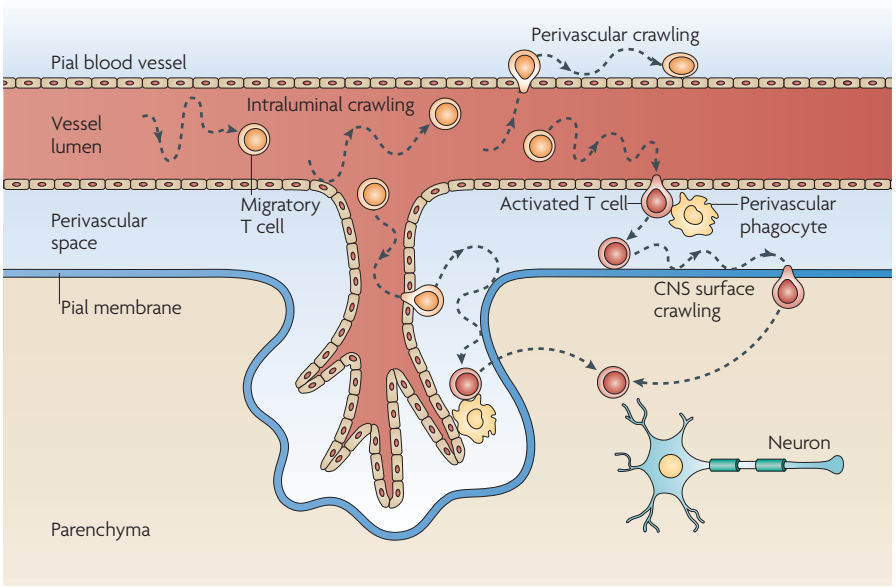
T CELLS

Crawling into the brain

A study involving real-time imaging of effector T cells provides new insight into how autoreactive T cells interact with cerebral structures and access the central nervous system (CNS) to cause autoimmune disease.

Flügel and colleagues induced experimental autoimmune encephalomyelitis in rats with intravenous injection of effector T cells specific for the CNS antigen myelin basic protein (MBP). The fate of the T cells was followed for 3–4 days after transfer, until the onset of disease, using a fluorescent marker. The first T cells appeared in the CNS 1–2 days after transfer, in the pial blood vessels of the subarachnoid areas. The intraluminal T cells tended to crawl (for an average of 15 minutes) on the inner vascular surface, most often against the blood flow. By day 2, an increasing number of the MBP-specific T cells had migrated out of the pial vessels and begun to crawl — first on the outer surface of the vessels and then on the underlying leptomeningeal (pial) membrane. With the onset of the first clinical symptoms (day 3) the T cells could be found invading the spinal cord parenchyma, and a day later (coinciding with the peak of disease) they became dispersed throughout the white and grey spinal cord matter.



Interestingly, effector T cells specific for non-brain antigens (such as ovalbumin (OVA)) showed a similar accumulation and behaviour in the leptomeninges but rarely entered the CNS parenchyma, suggesting the involvement of antigen-specific processes for CNS infiltration. Consistent with this idea, MBP-specific T cells transgressing the pial vascular wall encountered perivascular phagocytes that could present myelin antigens, leading to T cell activation. The finding that OVA-specific T cells could invade deeply into the CNS parenchyma and could form productive contacts with phagocytes if the phagocytes expressed OVA further supports the idea that CNS invasion is triggered following the recognition of antigen.

So, effector T cells undergo a series of crawling steps as they traverse the leptomeningeal vessels and membranes of the CNS, scanning for their cognate antigen presented by local phagocytes to receive the necessary trigger for access to the CNS and induction of disease.

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ORIGINAL RESEARCH PAPER Bartholomäus, I. *et al.* Effector T cell interactions with meningeal vascular structures in nascent autoimmune CNS lesions. *Nature* 14 Oct 2009 (doi:10.1038/nature08478)