Perforant pathway

The perforant path or perforant pathway, provides a connectional route from the entorhinal cortex to all fields of the hippocampal formation, including the dentate gyrus, all CA fields (including CA1), and the subiculum.

Though it arises mainly from entorhinal layers II and III, the perforant path comprises a smaller component that originates in deep layers V and VI. There is a major dichotomy with respect to the laminar origin and related terminal distribution: neurons in layer II (and possibly layer VI) project to the dentate gyrus and CA3, whereas layer III (and possibly layer V) cells project to CA1 and the subiculum via the temporoammonic pathway.

In addition to playing a role in spatial memory learning generally, the temporoammonic branch (TA-CA1) of the perforant path mediates spatial memory consolidation.

The temporoammonic pathway has also been implicated in stress-based animal models of depression.

It may also play a role in temporal lobe seizures.

The perforant pathway projection from layer II of the entorhinal cortex to the hippocampal dentate gyrus is especially important for long term memory formation, and is preferentially vulnerable to developing a degenerative tauopathy early in Alzheimer disease (AD) that may spread over time trans-synaptically.

Despite the importance of the perforant pathway to the clinical onset and progression of AD, a therapeutic has not been identified yet that protects it from tau-mediated toxicity.