During his two years as a Lily's Fund research fellow, Antoine Madar has worked to better understand how a particular region of the brain affects both memory and epileptic seizures.

Our ability to remember events in our daily lives relies heavily on the hippocampus, a region of the brain that is also the starting point of many seizures. Indeed, the same characteristics that let the hippocampus recall memories make it vulnerable to seizures. To avoid this, a part of the hippocampus called the dentate gyrus filters excessive incoming signals. The breakdown of this gateway is a general feature of temporal lobe epilepsy.

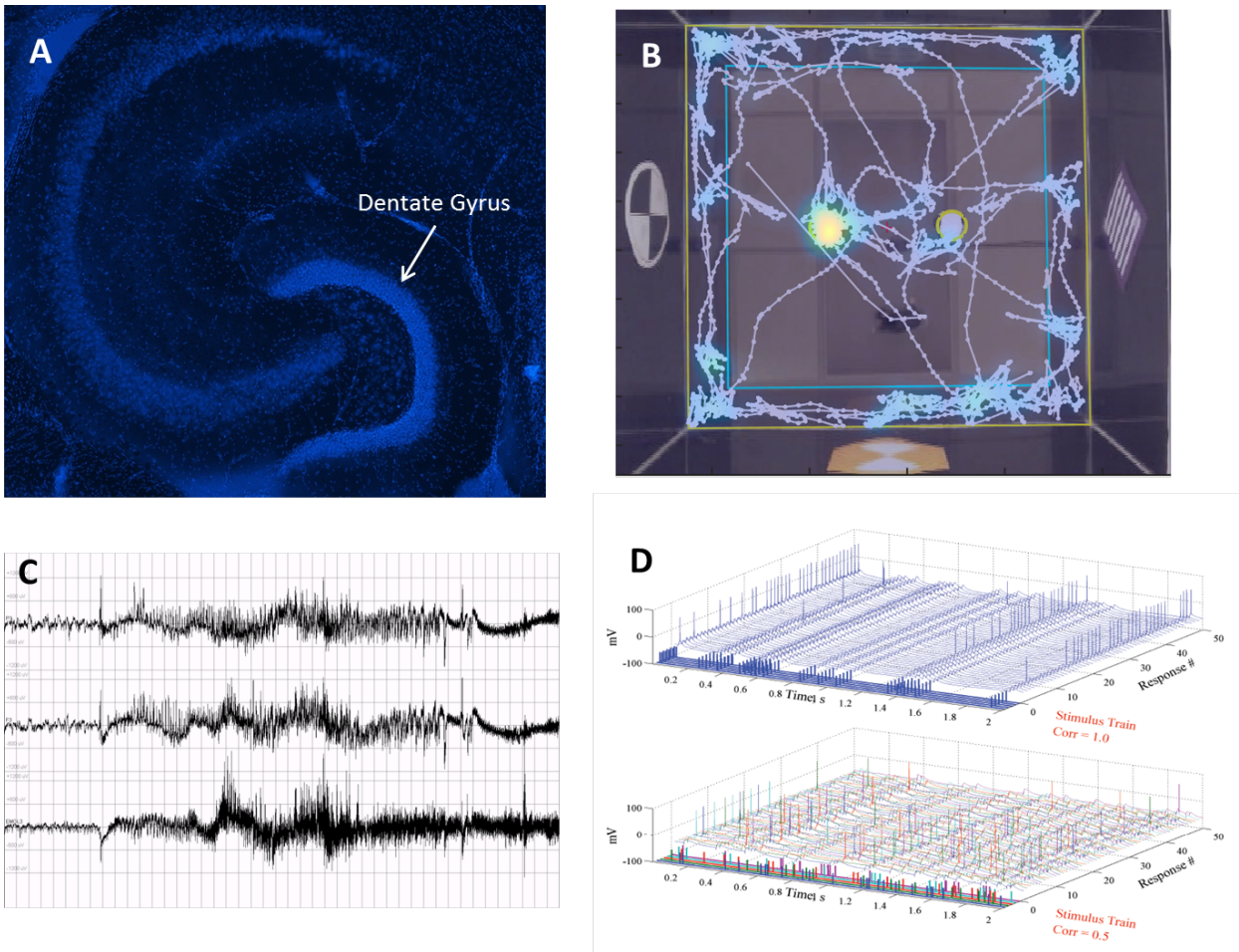
"We know the dentate gyrus supports our ability to not confuse memories of similar events, but it is still unclear how it is able to do this. The first part of my project focused on understanding how the filtering properties of the dentate gyrus relate to its ability to avoid confusion of memories. I tested the hypothesis that the filtering role of the dentate gyrus is to transform incoming neural signals that are similar to each other into output signals that are less similar to each other, a process called pattern separation," explains Antoine.

With his advisor Matt Jones and another previous student Laura Ewell, Antoine designed a novel experiment to measure pattern separation in brain slices from mice. They demonstrated for the first time that the dentate gyrus does, in fact, separate incoming neural signals at the level of single cells. This work is now complete and ready for publication. This refined understanding may help scientists design targeted treatments to restore normal filtering and pattern separation in the brain.

Antoine and his colleagues have started experiments to determine the effect of epilepsy on pattern separation and people's ability to distinguish present experiences from similar ones in the past.

"I hypothesize that the development of epilepsy leads to impairments of pattern separation and thus to an increase in memory confusion. We have developed new behavioral tests to measure the ability of mice to distinguish between similar memories, and we are starting to use the test on mice at different stages of development of temporal lobe epilepsy," says Antoine.

He hopes to establish the relationship between the advancement of epilepsy and impairments in pattern separation and memory. It is possible that pattern separation-related changes occur much earlier than more overt symptoms like seizures, and thus they could be used in the future as a tool for early diagnosis of seizure risk.



Legend: **A-** Picture of a slice of the hippocampus where cell nuclei are fluorescing in blue. By staining various types of neuronal features, we are assessing the extent of pathological changes in the microanatomy of the dentate gyrus of mice with epilepsy. **B-** The arena where behavioral tests take place, with visual cues on the walls seen from above. The trajectory of one animal is superimposed (colors correspond to time spent in one spot). **C-** Example of a seizure recorded in one of our mice (EEG traces on top, EMG trace on the bottom) **D-** Two examples of single neuron recordings allowing us to measure the amount of pattern separation performed by the dentate gyrus.

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