

Immunolesioning Hippocampal Inhibitory Interneurons

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hoping to use this approach in the hippocampus. However, we discovered in pilot experiments that SP-SAP, when injected directly into the hippocampal parenchyma, did not diffuse sufficiently far from the injection site to destroy interneurons in an area large enough for our purposes. Fortunately, ATS had just developed a conjugate using a peptidase-resistant SP analog (SSP-SAP), which we obtained and tested while we conducted an anatomical study designed to determine exactly which hippocampal interneurons constitutively express SPRs, and should therefore be vulnerable to SSP-SAP. That study demonstrated that most inhibitory neurons of all hippocampal subregions expressed SPRs, and that no excitatory principal cells or glia were SPR-positive.³

We found that 10 nl of a solution containing less than 1 ng of SSP-SAP was capable of selectively eliminating all SPR-positive neurons within a 2-mm diameter sphere of tissue. The survival of SPR-negative elements within the

SPR depletion zone was remarkable and included excitatory neurons, glia, myelinated fibers, and a number of afferent fiber systems originating outside the hippocampus. Selective loss of SPR-positive inhibitory interneurons was associated with a highly focal disinhibition and hyperexcitability⁴ that was clearly not caused by a global neurological insult that invariably causes a myriad of non-specific pathologies.



Our results indicate that epileptiform behavior is intrinsic to the hippocampal network and does not require the principal cell loss or synaptic reorganization that other models of network hyperexcitability exhibit as a result of less specific neurological injuries. At the least, our results clearly

indicate that SSP-SAP will be an extremely useful tool for a wide variety of studies in the hippocampus and other SPR-positive brain regions.

References

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2. Acsády L, Katona I, Gulyas AI, Shigemoto R, Freund TF (1997) Immunostaining for substance P receptor labels GABAergic cells with distinct termination patterns in the hippocampus. *J Comp Neurol* 378:320-336.
3. Sloviter RS, Ali-Akbarian L, Horvath KD, Menkens KA (2001) Substance P receptor expression by inhibitory interneurons of the rat hippocampus: enhanced detection using improved immunocytochemical methods for the preservation and colocalization of GABA and other neuronal markers. *J Comp Neurol* 430:283-305, 2001.
4. Martin JL, Sloviter RS (2001) Focal inhibitory interneuron loss and principal cell hyperexcitability in the rat hippocampus after microinjection of a neurotoxic conjugate of saporin and a peptidase-resistant analog of Substance P. *J Comp Neurol* 436:127-152.

Targeting Ticklers

Excerpts from "The Ultimate Scientific Dictionary"

Butyl: An unpleasant-sounding word denoting an unpleasant-smelling alcohol.

Chemical: A substance that: 1. An organic chemist turns into a foul odor; 2. an analytical chemist turns into a procedure; 3. a physical chemist turns into a straight line; 4. a biochemist turns into a helix; 5. a chemical engineer turns into a profit.

First Order Reaction: The reaction that occurs first, not always the one desired. For example, the formation of brown gunk in an organic prep.

Natural Product: A substance that earns organic chemists fame and glory when they manage to synthesize it with great difficulty, while Nature gets no credit for making it with great ease.

Research: (Irregular noun) That which I do for the benefit of humanity, you do for the money, he does to hog all the glory.

Scientific Method: The widely held philosophy that a theory can never be proved, only disproved, and that all attempts to explain anything are therefore futile.

Targeting Teaser Winners

Congratulations to the puzzle solvers from our last newsletter. Each winner receives \$100 credit towards research product purchases from Advanced Targeting Systems.

The solution to the puzzle was:

Jumbles: ACADEMIC QUALITY MIXER LITER TRYPSIN

Answer: How the technician felt after a full day of stock solution preparation --- LIKE A "MULTI-MEDIA" EXPERT!

WINNERS: Dr. Chien Li, The Salk Institute * Bob Speth, WSU * Pelin Chen, OR Primate Res Ctr * Teri Milner, Weill Med College, Cornell University * Kristen Phend, Univ of North Carolina * Gina Broadnax, Ohio State University * Reema Shafi, Ohio State University * Christopher Nelsen/Michelle Rivera, Ohio State University

