

- 5 Herman JP, Cullinan WE. Neurocircuitry of stress: central control of the hypothalamo-pituitary-adrenocortical axis. *Trends Neurosci* 1997; **20**: 78–84.
- 6 Iguchi A, Kunoh Y, Gotoh M, Miura H, Uemura K, Tamagawa T, Sakamoto N. Relative contribution of nervous system and hormones to CNS-mediated hyperglycemia is determined by the neurochemical specificity in the brain. *Physiol Behav.* 1991; **50**: 1019-1025.
- 7 Iguchi A, Uemura K, Kunoh Y, Miura H, Ishiguro T, Nonogaki K, Tamagawa T, Gotoh M, Sakamoto N. Hyperglycemia induced by hippocampal administration of neostigmine is suppressed by intrahypothalamic atropine. *Neuropharmacology* 1991; **30**: 1129-1131.
- 8 Iguchi A, Uemura K, Miura H, Ishiguro T, Nonogaki K, Tamagawa T, Goshima K, Sakamoto N. Mechanism of intrahippocampal neostigmine-induced hyperglycemia in fed rats. *Neuroendocrinology* 1992; **55**: 44-50.
- 9 Kaufer D, Friedman A, Seidman S, Soreq H. Acute stress facilitates long-lasting changes in cholinergic gene expression. *Nature* 1998; **393**: 373–377.
- 10 Levine S, Ursin H. What is stress? In: Brown MR, Koob GF, Rivier C, eds. *Stress: Neurobiology and Neuroendocrinology*. New York: Marcel Dekker, Inc. 1991: 1-23.
- 11 McEwen BS. The neurobiology of stress: from serendipity to clinical relevance. *Brain Res* 2000; **886**: 172-189.
- 12 Mizuno T, Kimura F. Attenuated stress response of hippocampal acetylcholine release and adrenocortical secretion in aged rats. *Neurosci Lett* 1997; **222**: 49–52.
- 13 Pacak K, Palkovits M. Stressor specificity of central neuroendocrine responses: Implications for stress-related disorders. *Endocr Rev* 2001; **22**: 502-548.
- 14 Paxinos G, Watson C. *The rat Brain in Stereotaxic Coordinates*, 2nd edn. San Diego, CA: Academic Press, 1986.
- 15 Pedersen WA, McCullers D, Culmsee C, Haughey NJ, Herman JP, Mattson MP. Corticotropin-Releasing Hormone protects neurons against insults relevant to the pathogenesis of Alzheimer's disease. *Neurobiology of Disease* 2001; **8**: 492-503.
- 16 Pignatelli D, Pinto P, Azevedo M, Magalhaes M. Acute stress effects on the adrenal cortex in the rat. A biochemical and immunohistochemical study. *Endocr Res* 1996; **22**: 445-451.
- 17 Senba E, Ueyama T. Stress-induced expression of immediate early genes in the brain and peripheral organs of the rat. *Neurosci Res* 1997; **29**: 183-207.
- 18 Tabata H, Kitamura T, Nagamats N. Comparison of effects of restraint, cage transportation, anesthesia, and repeated bleeding on plasma glucose levels between mice and rats. *Lab Animals* 1998; **32**: 143-148.
- 19 Tajima T, Endo H, Suzuki Y, Ikari H, Gotoh M, Iguchi A. Immobilization stress-induced increase of hippocampal acetylcholine and of plasma epinephrine, norepinephrine and glucose in rats. *Brain Res* 1995; **720**: 155–158.
- 20 Ueki A, Miwa C, Shinjo H, Kokai M, Morita Y. Synapse alteration in hippocampal CA3 field following entorhinal lesion. *J Neurol Sci* 1997; **151**: 1-5.

- 21 Umegaki H, Tamaya N, Shinkai T, Iguchi A. The metabolism of plasma glucose and catecholamines in Alzheimer's disease. *Exp Gerontol* 2000; **35**: 1373-2382.
- 22 Umegaki H, Zhu W, Nakamura A, Suzuki Y, Takada M, Endo H, Iguchi A. Involvement of the Entorhinal Cortex in the Stress Response to Immobilization, But not to Insulin-Induced Hyperglycemia. *J Neuroendocrinol* 2003; **15**: 237-241.
- 23 Zhu W, Umegaki H, Suzuki Y, Miura H, Iguchi A. Involvement of the bed nucleus of the stria terminalis in hippocampal cholinergic system-mediated activation of the hypothalamo-pituitary-adrenocortical axis in rats. *Brain Res* 2001; **916**: 101-106.
- 24 Zhu W, Umegaki H, Yoshimura J, Tamaya N, Suzuki Y, Miura H, Iguchi A. The elevation of plasma adrenocorticotrophic hormone and expression of c-Fos in hypothalamic paraventricular nucleus by microinjection of neostigmine into the hippocampus in rats: comparison with acute stress responses. *Brain Res* 2001; **892**: 391-395.

### Figure legends

#### Figure 1.

(A): Schematic representation of a bilateral entorhinal cortex lesion.

Photomicrographs of coronal sections through the entorhinal cortex stained with Cresyl violet illustrating the extent of damage:

(B) Vehicle injection into the entorhinal cortex. (C) Enlarged view of that shown in (B).

(D) Ibotenic acid injection into the entorhinal cortex. (E) Enlarged view of that shown in (D).

The section was sampled from the injection sites where the maximal amount of cell damage was observed.

**Scale bar: (B) and (D) = 0.25 mm; (C) and (E) = 0.06mm.**

#### Figure 2.

Plasma ACTH and blood glucose concentrations in rats microinjected by neostigmine into the hippocampus.

(A) Blood glucose concentrations. Repeated ANOVA showed that entorhinal-lesioned rats had significantly lower concentrations than unlesioned rats ( $p < 0.0001$ )

■, Group 1: unlesioned neostigmine-injected (n=6); ◆, Group 2: unlesioned saline-injected (n=5); ▲, Group 3: lesioned neostigmine-injected (n=11); ●, Group 4: sham-operated, neostigmine-injected (n=6).

(B) Plasma ACTH concentrations. Repeated ANOVA showed no significant difference between entorhinal lesioned rats and rats who had saline injected into the entorhinal cortex.

■, Group 1 unlesioned neostigmine-injected (n=6); ◆, Group 2: unlesioned saline-injected (n=5); ▲, Group 3: lesioned neostigmine-injected (n=6); ●, Group 4: sham-operated, neostigmine-injected (n=5).

**FIGURE 1**

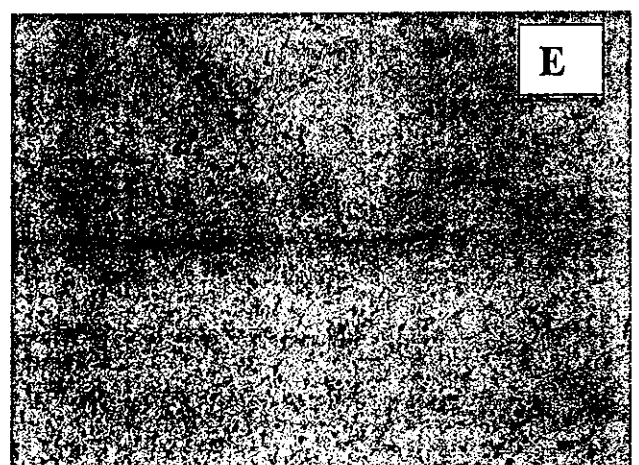
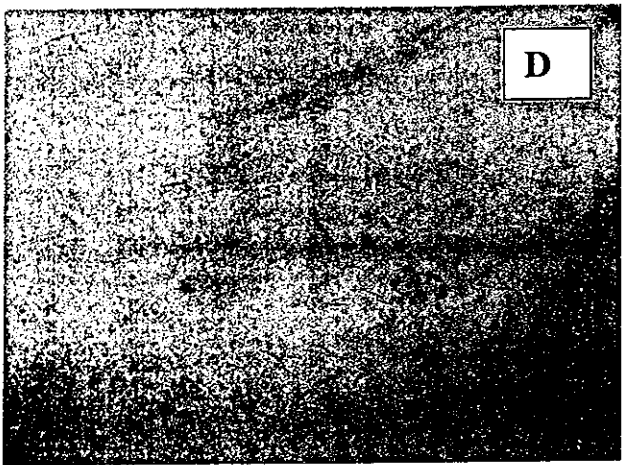
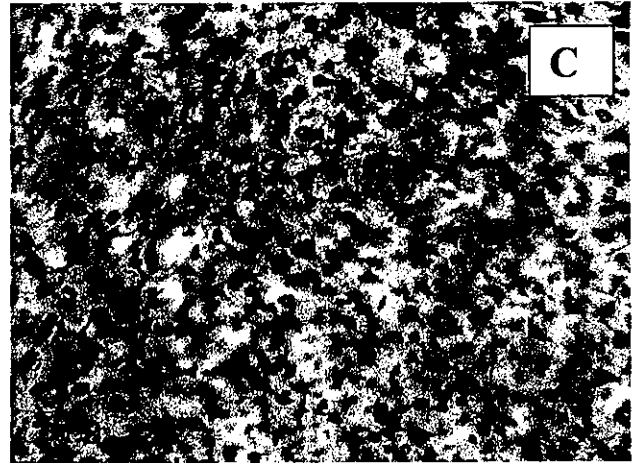
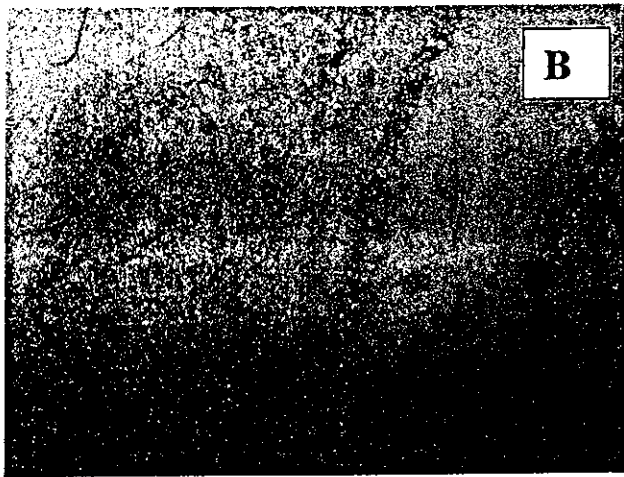
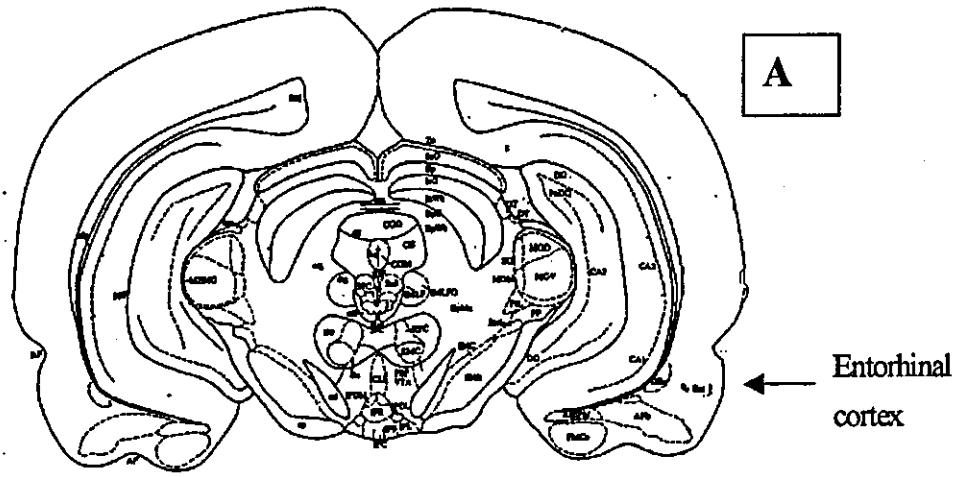
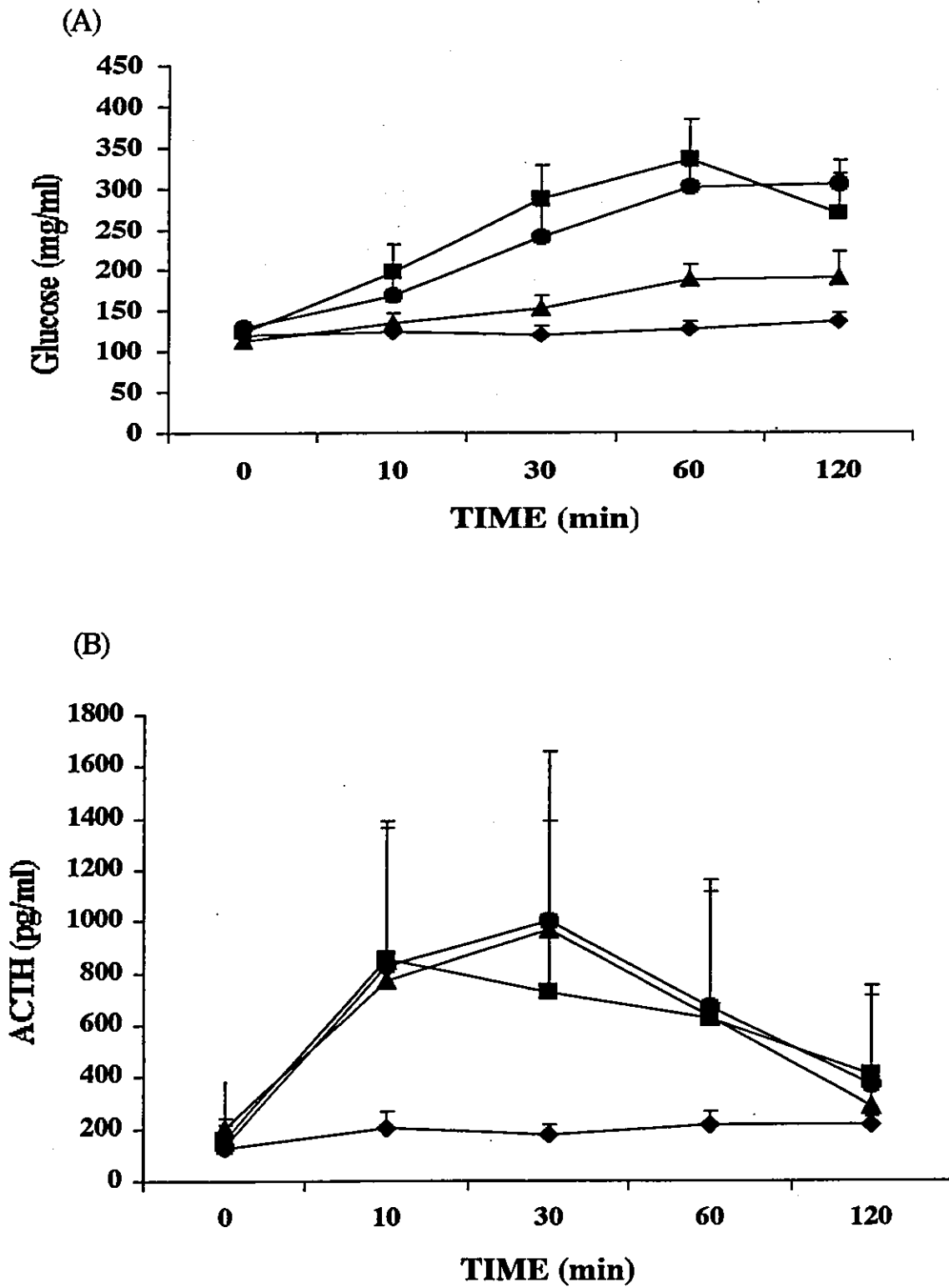


FIGURE 2



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