test, control animals had emitted 63 percent of their total activity for the 4-minute period, while animals with septal lesions had emitted only 31 percent. When retested the next day, control animals showed almost complete suppression of activity (median decrease, 95 percent), while the activity of animals with lesions was virtually identical to that of the first 2 minutes of the test on the first day (median decrease, 3 percent).

Lesions of 13 of the 19 test animals in the first experiment and 5 of the 7 animals in the second experiment have been verified, either histologically or by inspection of free hand-cut sections. All lesions were placed within the septal area. Sizes of lesions varied from large and complete destruction of the septal area to small medially placed lesions that spared the lateral portion of the septum. All animals with lesions showed the syndrome of hyperexcitability previously described (*9*) although hyperexcitability was more pronounced in animals with the larger lesions. No obvious relation was seen between size of lesion and passive avoidance deficit. Several animals with virtually complete destruction of the septal area had scores overlapping those of controls, while other animals with destruction limited to the medial septal area showed little or no avoidance learning.

These results clearly demonstrate that lesions of the septal area in mice of strain CF-1 result in marked deficits of both passive avoidance and fear conditioning and that these deficits are not due simply to the motivation resulting from increased food or water intake in animals with septal lesions, as indicated by previous reports.

That the deficits in our study do not stem from hyperactivity in animals with septal lesions is demonstrated by test minute I in the first experiment in which these animals were found to be less active than controls. Nor is the septal deficit simply a result of a burst of responding following the first shocked responses. In the second experiment animals with septal lesions actually took fewer shocks than controls in the first minute of the test but continued to make punished responses over the 4-minute test period. In the last 15-second period of this test 71 percent of the animals with septal lesions, but only 29 percent of the controls, were still moving.

The fact that animals with septal lesions appear less able to inhibit activity-contingent shock and show little or no evidence of activity suppression when replaced in the experimental chamber the following day strongly suggests that the lesions interfere with some central inhibitory mechanism. While our results also concur with the hypothesis that septal lesions reduce the punishing effect of shock (*10*) or reduce fear (*9*), recent studies in this laboratory have shown that mice with septal lesions, as well as controls, acquire a fear response in a test situation that does not require activity suppression (*11*).

The behavioral response underlying activity suppression in the present experiment is probably "freezing," a response that is dominant in cats, rats, and mice in a fear-arousing situation. Interference with this mode of responding would appear to account for the results of this experiment.

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Sensitivity of Cardiac Actomyosin to Calcium

Katz and Repke (*1*) have recently reported that reconstituted actomyosin from dog heart muscle has a calcium sensitivity similar to that from skeletal muscle and that half maximum activities of adenosine triphosphate hydrolysis for heart and skeletal muscle actomyosin occur at a *p*Ca of 6.20 and 6.25, respectively.

It should be pointed out that the *p*Ca at half maximum activity calculated in this case from the EGTA/CaEGTA ratio is of the same order of magnitude as that calculated with the use of the ATP/CaATP ratio from the previously reported data on the effect of Ca on cardiac natural actomyosin (*2*). Half maximum adenosine triphosphatase activity for natural heart actomyosin was obtained at a total calcium concentration of about $10^{-5}M$. If we take the association constants for the reactions, $H^+ + ATP^{-4} \leftrightharpoons ATP^{-3}$, $Mg + ATP^{-4} \leftrightharpoons MgATP^{-2}$, and $Ca + ATP^{-4} \leftrightharpoons CaATP^{-2}$, as 10^7, 8×10^4, and 3×10^4, respectively (*3*), the calculated *p*Ca is 5.87. There is some uncertainty in the values of the association constants. If, for instance, the association constant for $CaATP^{-2}$ is taken to be the same as that for $MgATP^{-2}$, that is, 8×10^4, *p*Ca becomes 6.25. Undoubtedly the same uncertainty attaches to the calculation of *p*Ca from the EGTA-CaEGTA equilibrium which involves the four protonation equilibrium constants of EGTA and the corresponding association constants for the Ca complexes.

Syneresis of cardiac myofibrils has been reported (*4*) to be totally inhibited even with an added calcium concentration of $5 \times 10^{-6}M$, but there is no inhibition at a total calcium concentration of $3 \times 10^{-5}M$. This concentration is somewhat higher than that required for skeletal myofibrils under the same (*4*) or similar (*5*) experimental conditions but could probably be accounted for by other calcium-binding contaminants present with heart myofibrils (*6*).

These data support the general concept that only a very small concentration of free Ca^{++}, of the order of 10^{-6} to $10^{-7}M$, is necessary for Mg-activated adenosine triphosphatase activity of the cardiac as well as the skeletal muscle actomyosin system.

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