EFFECTS OF GAMMA AMINOBUTYRIC ACID ON SPONTANEOUS Ca^{2+} OSCILLATIONS IN ISOLATED PREPARATIONS OF RAT CHROMAFFIN CELLS

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1. Spontaneous $[Ca^{2+}]_c$ oscillations have been reported in the majority of chromaffin cells and were reconfirmed in the present study by a microfluorometric method with the Ca^{2+}-sensitive dye, fura-2, in about 60% of the rat adrenal chromaffin cells. The oscillations were promptly and reversibly arrested by application of gamma aminobutyric acid (GABA ; 50 μM-1mM) and, in the majority of the preparations used, the arrest was preceded by a transient and rapid rise in $[Ca^{2+}]_c$.

2. The oscillations were also arrested rapidly and reversibly by the $GABA_A$ agonist muscimol, but not affected by the $GABA_B$ agonist baclofen. These results indicate that the inhibitory effect of GABA may be mediated by $GABA_A$ receptors. The inhibitory effect of GABA could be due to a depolarization-induced activation and potential-dependent-inactivation of Ca^{2+} channels, as shown by the follwing results.

3. Oscillations were not observed in about 40% of the cells examined. In these quiescent cells, $[Ca^{2+}]_c$ remained stable at around 100nM, and a large spike-like rise in $[Ca^{2+}]_c$ was evoked by application of GABA (100 μM). The GABA-induced $[Ca^{2+}]_c$ rise was enhanced when $[Cl^-]_0$ was lowered, suggesting that GABA caused depolarization as a consequence of an increase in Cl^- efflux.

4. The oscillations were rapidly arrested when extracellular Ca^{2+} was chelated by EDTA or EGTA, and when Ni^{2+}, a non-selective Ca^{2+} channel blocker, was applied, indicating that extracellular Ca^{2+} entry is importantly involved in the oscillatory $[Ca^{2+}]_c$ rises.

5. Taking the present results and reported results into consideration, we now propose the following mechanism regulating the spontaneous $[Ca^{2+}]_c$ oscillations in rat chromaffin cells ; 1) the oscillations may correlate with spontaneous fluctuations in membrane potential, and depolarizing phases of the fluctuations may coincide with oscillatory Ca^{2+} entry through voltage-dependent Ca^{2+} channels, although the possible involvement of an intracellular mechanism of Ca^{2+} release cannot be excluded, and 2) GABA may open the Cl^- channels to cause depolarization followed by a plateau phase, which may be responsible for a transient and rapid rise follwed by gradual decay in $[Ca^{2+}]_c$.