The effects of Cd^{2+} on the responsiveness of the rat anococcygeus muscle and vas deferens to electrical stimulation, noradrenaline, tyramine and K^+

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Toda (1973) found that Cd^{2+} inhibited the responses of rabbit isolated aortas to K^+, Ba^{2+} and noradrenaline (NA); NA was found to be the most resistant (Toda, 1973). The Ca^{2+}-induced contractions of cerebral, coronary and mesenteric artery preparations were antagonized by Cd^{2+} (Hayashi & Toda, 1977). The effects of Cd^{2+} on the rat vas deferens and anococcygeus muscle preparations have been investigated because of their possession of a rich sympathetic innervation.

Specially constructed tissue holders were used which allow adequate superfusion and perimural stimulation (Fadloun & Leach, 1978). The tissues were superfused at a rate of 3 ml/min using Krebs solution at 37°C aerated with 95% O_2/5% CO_2. The stimulation parameters used were: pulse width 0.1 ms, 40–20 V, 1–25 Hz, stimulation period 15–30 seconds. The effects of NA, tyramine and K^+ were also tested. Tyramine added at intervals greater than 10 min for vas deferens and 15 min for anococcygeus muscle did not produce evidence of tachyphylaxis. The preparations could be used for periods for up to 5 h or longer.

Cd^{2+} (0.8–4 μM) were found to inhibit the responses of anococcygeus muscle preparation to perimural stimulation at low frequencies (1–12 Hz). The responses of the vas deferens preparation to perimural stimulation were inhibited at all frequencies (1–25 Hz) by Cd^{2+} (8–40 μM). K^+, NA and tyramine responses were inhibited by Cd^{2+} (0.8–4 μM) on the anococcygeus muscle preparation and for the vas deferens preparation using Cd^{2+} (8–40 μM). The effect of Cd^{2+} inhibition was most marked on the K^+-induced responses, whilst NA was the least affected in both preparations. The lowest concentration of Cd^{2+} 0.8 μM and 8 μM for anococcygeus and vas deferens tissues respectively, affected the responses to perimural stimulation without significantly affecting those to NA. The Cd^{2+}-induced inhibition was irreversible in as much as washing with Krebs failed to restore the responses in both preparations.

To investigate the effect of modified Ca^{2+} concentrations on the Cd^{2+}-induced inhibition, Ca^{2+}, 4.08, 1.27 and 0.63 mM Krebs solutions were tested. In both preparations, perimural stimulation and K^+-induced responses were inhibited using Ca^{2+} (1.27 mM), whilst NA and tyramine responses remained unaffected. Ca^{2+} (0.63 mM) Krebs reduced all four test responses in both tissues. Ca^{2+} (4.08 mM) Krebs potentiated the responses of the four test responses, stimulation and K^+ responses were the most affected.

Cd^{2+} (0.8 μM) added to anococcygeus muscle and (8 μM) to the vas deferens in the presence of Ca^{2+} (1.27 mM) enhanced the inhibition to the four test responses in both preparations. The response of anococcygeus muscle to perimural stimulation at (25 Hz) which was unaffected by Cd^{2+} (0.8 μM) in normal Krebs was inhibited by Cd^{2+} (0.8 μM) and Ca^{2+} (1.27 mM). Doubling Ca^{2+} concentration to 4.08 mM reduced the inhibition seen with the four test procedures caused by Cd^{2+} (4 μM) on the anococcygeus muscle and Cd^{2+} (40 μM) on the vas deferens.

Cysteine (0.5 mM) partially restored the Cd^{2+}-inhibited responses of both tissues to perimural stimulation, K^+, NA and tyramine. The degree of restoration was dependent on Cd^{2+} doses used.

Yohimbine (10 ng/ml) on anococcygeus muscle and (50 ng/ml) on vas deferens was found to potentiate the responses of both tissues to perimural stimulation after Cd^{2+}-induced inhibition had been established. Yohimbine at the same concentrations did not affect the responses to NA in either tissue.

It is concluded, therefore, that Cd^{2+} possess a higher affinity towards presynaptic sites. The Cd^{2+}-induced inhibition could be explained by inhibition of sulphhydryl groups or by antagonism of Ca^{2+} or by both.

References

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