Effects of manipulating pallidal and nigral GABA on striatally-mediated head-turning in the rat

A.R. CROSSMAN, L.A. LEE & P. SLATER

Departments of Anatomy and Physiology, University of Manchester, Manchester M13 9PT

The neostriatum projects to the globus pallidus (GP) and substantia nigra (SN), these pathways being important in mediating motor influences of the neostriatum. There is much interest in GABA as a neurotransmitter within the GP and SN (Yoshida, 1974). We have examined the influence of transmitter agonists and antagonists injected into GP and SN on a motor response obtained by stimulation of the striatum. Bipolar stimulating electrodes were implanted unilaterally in the neostriatum of 21 female Sprague-Dawley rats (170-220 g). Stimulation with biphasic pulses (0.1–0.3 mA; 25 Hz) caused contralateral head-turning. The duration of threshold stimulation needed for a 90° head-turn was recorded 10 times at 2 min intervals. Drugs were dissolved in 1 μl of saline and injected into the ipsilateral GP or SN through an implanted cannula. The animals were retested using the same stimulus parameters. The initial head-turn latency of every animal was 2–8 s and was unaffected by saline injection into GP or SN.

Endogenous GABA levels were elevated using the GABA-transaminase inhibitor γ-acetylenic GABA (GAG; Jung, Lippert, Metcalf, Schechter, Böhlen & Sjoerdsma, 1977). Injection of GAG (20 μg) into GP produced slow ipsilateral circling. Head-turn latency was significantly increased 4 h after GAG ($n=5$; $P<0.01$) and in some cases head-turning was abolished. Head-turn latency was also increased 4 h after injection of 20 μg GAG into SN (5 of 6 tested; $P<0.01$). The putative GABA agonist baclofen was less effective. In the GP (20 ng) the response time of only 2 of 4 animals tested was significantly increased whereas in the SN baclofen (5–20 ng) had no effect ($n=8$). Picrotoxin produced an immediate facilitation of the head-turn when injected into GP (1–2 μg; 12 of 15 tested; $P<0.05$) and SN (100 ng; 5 of 6 tested; $P<0.05$). Larger doses in both sites induced immediate contralateral circling consistent with the findings of Tarsy, Pycock, Meldrum & Marsden (1975) and Pycock, Horton & Marsden (1976). In contrast, strychnine (1–2 μg) injected into GP significantly slowed the response of 4 rats from 11 tested and in SN significantly shortened the response latency of 4 rats from 10 tested.

Several substances unrelated to GABA were examined. In both GP and SN substance P (1 ng–1 μg) transiently and weakly facilitated the head-turn whereas the 5-HT agonist 5-methoxy-*N,N*-dimethyltryptamine had no effect. Atropine injected into SN (1–2 μg) significantly increased the response latency of only 4 of 14 animals and had no effect in GP.

The most clear and consistent modulation of head-turning resulted from manipulation of GABA in GP and SN. Both regions influence striatally-mediated movement and these findings are consistent with an important role for GABA in striato-pallidal and striato-nigral function.

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