Apomorphine and Haloperidol Influence Electric Behaviour of a Mormyrid Fish

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The electric behaviour of the mormyrid *Gnathonemus petersii* is changed by dopaminergic drugs applied to the aquarium water. The upper limit of the interpuls interval distributions is significantly shifted to shorter intervals by apomorphine-HCl (.082–.328 mg/ml), and to longer intervals by haloperidol (.041–.164 mg/ml). The effect of apomorphine is antagonized by haloperidol. Probably, a dopamin system is involved in the neural control of the electric organ.

Introduction

The electric organ discharges (EOD) of the weakly electric fish *Gnathonemus petersii* form a time series with a continuous range of interpuls intervals from about 14 to 400 ms. EOD patterns have some individual characteristics, they show diurnal changes, and vary in context with interspecies communication and with spatial orientation [1]. They may be presented as nonsequential interpuls interval histograms [2] sampled over a set period of time (Fig. 1). In this paper an investigation is presented aiming at the involvement of neurotransmitter systems in the control of the mormyrid electric organ. Since the electric organ of mormyrids is a muscular organ by ontogeny, it seems natural to test for the dopamin system which in other vertebrates, especially mammals, is known to play a central role for the control of motor activity [3]. The test is performed by application of a dopamin agonist, apomorphine, and a dopamin antagonist, haloperidol.

Methods

Seven fishes of undetermined sex, ranging in length from 12 to 18 cm, were used. They were individually kept in glass tanks (bottom area 59 cm × 36 cm) filled with 25 l of water (for the biggest fish 100 cm × 40 cm and 60 l). The water was aerated and kept at 25 ± 1 °C. A 12/12 h light/dark schedule (light from 8 a.m. to 8 p.m.) was maintained. EODs were measured with four stainless steel electrodes in the tank corners which in diagonally opposed pairs were connected to differential amplifiers. The amplified EOD was used to trigger a standard square pulse which was fed to the user port of a personal computer. The computer was programmed to measure the elapsed time between the onset of successive pulses (interpuls interval, II). Time resolution was .25 ms for IIs up to 32 ms, and II/128 for IIs longer than 32 ms. IIs of equal length were accumulated during a measuring period of 15 min and thus an interpuls interval histogram (IIH) constructed.

An experiment was started with at least four control measurements prior to substance application. The substances apomorphine-HCl (Sigma) and haloperidol (Sigma), were dissolved in 1 ml of 10% ascorbic acid, added to 400 ml water, and thoroughly mixed. This solution, on application, was evenly spread over the water surface of the fish tank. The experiment was stopped by transferring each fish to a tank with fresh water and keeping it there for one to two hours. The experimental tank was emptied, cleaned, and refilled with aerated warm water. Then the fish was replaced to the familiar tank and given food. Experiments on the same fish were performed at the most each second day keeping it in the experimental schedule up to four weeks.

Experiments and Discussion

A quantitative description of the form of the interpuls interval histograms (IIH) and their variations is not easily performed due to considerable inter-individual differences. However, it turned out that in all animals the upper limit of the IIH was quite sensi-

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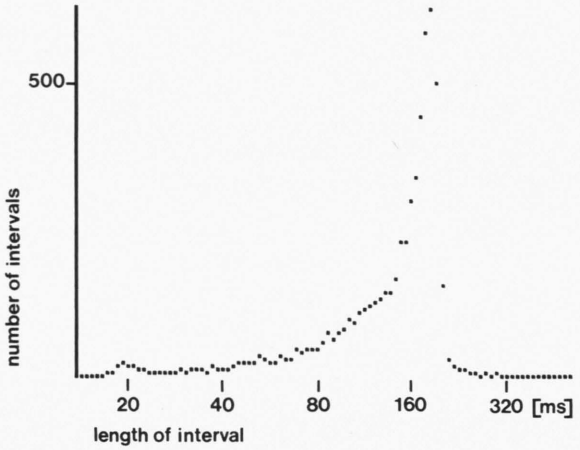

Fig. 1. Interpuls interval histogram (IIH) of a *G. petersii* accumulated over a period of 15 min.

tively affected by the applied drugs apomorphine and haloperidol. Thus, a threshold interval – upper limit interval (UTI) – was defined for the long end of the IIH as the interval beyond which 200 intervals occurred during the 15 min measuring period.

Fig. 2 shows the time course of the experiments with apomorphine-HCl .164 mg/l, haloperidol .082 mg/l, and the combination of both. The upper threshold interval (UTI) is presented as the difference to the mean UTI of the four controls (measurements from 9–10 a.m.). On application of apomorphine, UTI is immediately reduced, the reduction being at least 40 ms during the course of the experiment. Application of haloperidol leads to a continuous increase of UTI up to 168 ms at the end of the experiment. When both substances are applied simultaneously, UTI shows the apomorphine effect during the first measurement after adding the substance, is almost zero in the second, and increases continuously during all following measurements running almost parallel to the haloperidol curve at a distance of −50 ms to −70 ms.

The described effects are in principle the same for the other substance concentrations used, too. They are selectively presented in Fig. 3a. As a control measurement, the third measurement before application was chosen for all experiments. The effect of apomorphine is shown for the second, of haloperidol for the fourth and of both substances combined for the third measurement after application. The apomorphine effect is for all concentrations a reduction of UTI, whereas the haloperidol effect is an increase.

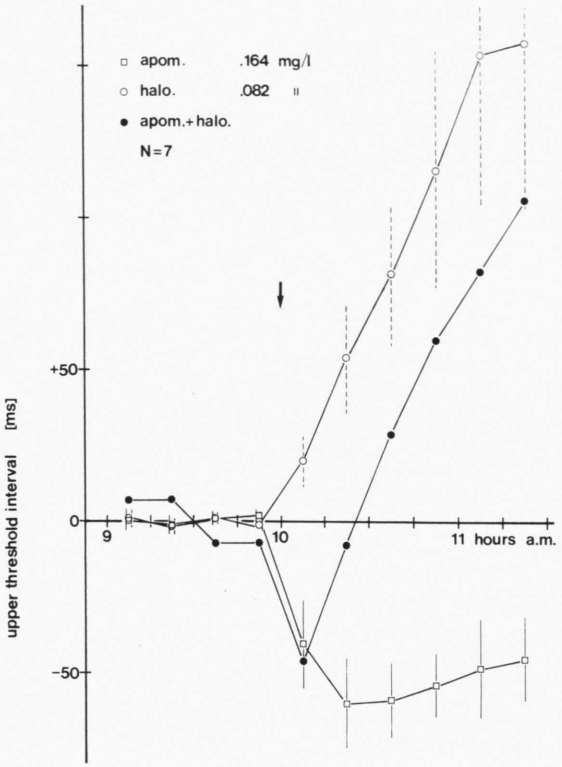

Fig. 2. Time course of upper threshold interval (UTI). First four measurements are the controls. Arrow indicates application of substances: apomorphine-HCl (squares), haloperidol (circles), both substances combined (dots). Means ± s.e.m. of differences to controls. (For clarity s.e.m. not shown in the curve with both substances, maximum value is 30.5 ms.)

The effect of both substances combined is in each case smaller than the effect of each single substance.

In a set period of observation, frequency changes in a particular II range are necessarily accompanied by reciprocal frequency changes in other ranges. Assumed that such ranges are not coupled in a predetermined way, any frequency change of IIs will be compensated for by changes of the number of IIs of longer duration. Thus, UTI might be a sensitive indicator for EOD activity change in any II range.

We searched for changes in II frequency in different ranges of the IIH. Significant changes of II frequency were found for IIs > 70 ms. As shown in Fig. 3b the number of intervals in this range is increased by apomorphine (with exception of the lowest concentration), whereas this number is reduced by haloperidol. Combined application of both sub-

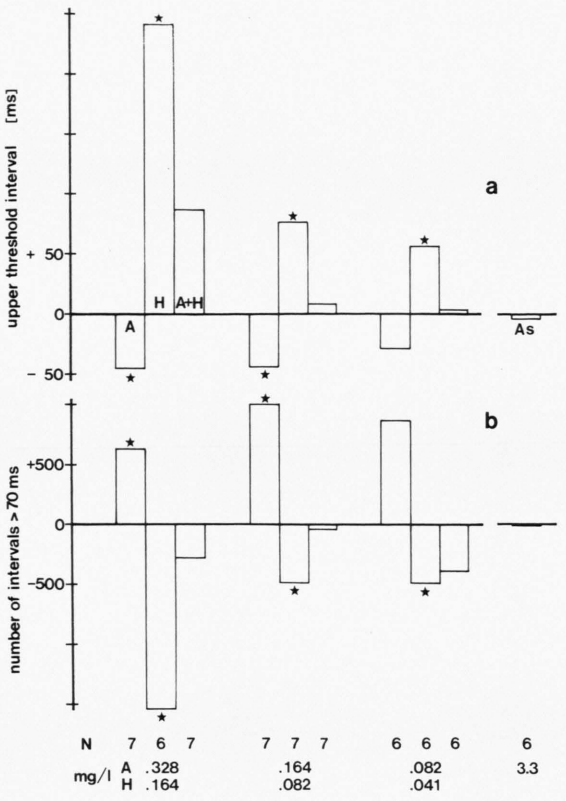

Fig. 3. Effect of different concentrations of apomorphine-HCl (A), haloperidol (H), both substances combined (A + H), and solvent (ascorbic acid, As). Differences of second (A), third (A + H), and fourth (H) measurement after substance application to second measurement (control) before substance application. Medians. Star: $p \leq .05$, WILCOXON matched pairs signed rank test, two sided. a) Effect on upper threshold interval, b) on number of interpuls intervals longer than 70 ms.

stances leads to an effect which is smaller than the effect of each substance alone and, for the third measurement after application, not significantly different from the control measurement.

Visual observation of motor behaviour indicates under both substances a slight increase of swimming activity. Whereas under control conditions the fish usually stayed in their hide, they left it after substance application for a round through the tank once or twice per minute. Combined application of both substances did not seem to antagonize this behaviour. About 90 min after application of the highest haloperidol concentration used (.164 mg/l), the fish very suddenly change to rapid and agitated forward swimming interrupted by short pauses. Also, maintenance of equilibrium is disturbed. This behaviour was not observed with the lower concentrations of haloperidol. Transferring the fish to water without substance restored normal behaviour within 30 min.

Both neuropharmaca used influence the electric organ discharge of *G. petersii* in concentrations which are comparable to doses effective in mammals [4], with haloperidol antagonizing the apomorphine effect. In conclusion, it seems probable that a dopamin system is involved in the neural control of the electric organ.

Acknowledgements

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[1] Electroreception (T. H. Bullock and W. Heiligenberg, eds.), John Wiley Sons, New York 1986.
[2] M.-J. Toerring and P. Moller, Beh. Brain Res. **12,** 291–306 (1984).
[3] T. W. Robbins and B. J. Everitt, Int. Rev. Neurobiol. **23,** 303–365 (1982).
[4] W. J. Schmidt, Physiol. Behav. **33** (5), 671–680 (1984).