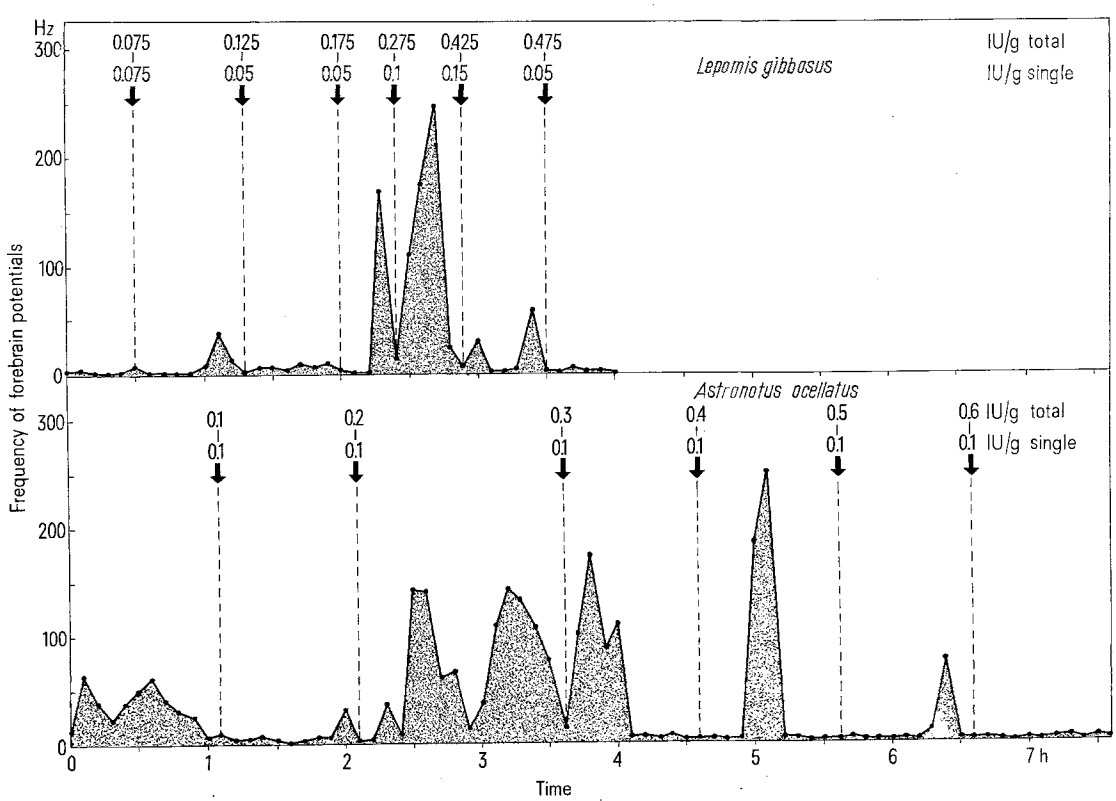
Prolactin-Sensitive Neurons in the Forebrain of Some Fishes

Material and methods. As experimental animals 45 individuals of the following species were used: *Lepomis gibbosus* (Centrarchidae), *Astronotus ocellatus* (Cichlidae), and *Carassius auratus gibelio* (Cyprinidae). They were anesthesized before trepanation with MS 222 (Sandoz), immobilized with Flaxedil (Boehringer), attached to a fish-holder and provided with running tap water. Platinum clad tungsten carbide electrodes (Transidyne type 504 and 514) with tip diameters of 8 and 5 µm, resp., positioned by micromanipulators were used for recording. Injections of prolactin (NIH-P-S8 and Ferring) were performed intramuscularly with micrometer syringes through flexible cannulae. Recordings were taken from 1 or 2 points per fish in the area dorsalis of the telencephalon. At the end of the experiments, lasting as long as 10 h, the position of the electrode tip was marked by HF and DC coagulation, respectively. Brains were fixed in 10% formaldehyde solution by immersion, serial sections (15 µm) cut after embedding in Paraplast (Shandon) and stained according to KLÜVER-BARRERA and BODIAN.

Results. After implantation of the electrode into the forebrain there were picked up prepotentials, sum potentials, and spikes, the frequeny of which decreased within 30 to 50 min. When the spontaneous activity fell to a constant low level prolactin was injected in single doses of 0.05 to 0.2 IU per g body weight. At positive points the evoked activation mostly began with positive prepotentials, typically followed by trains of spikes with high frequency (up to 300 Hz) and also high amplitudes. Such activation may last up to 15 min. The mean latency period between injection and the appearance of evoked potentials differed, in *Lepomis* it was 10 to 30 min, in *Astronotus* 30 to 60 min. In *Astronotus* the mean 'onset dose' was 0.2 to 0.3 IU per g, inhibition appeared between 0.5 and 0.8 IU/g, in *Lepomis* the effective as well as the inhibiting dosage was lower (Figure). *Tilapia leucosticta* and *Carassius a. gibelio*, on the other hand, only showed a slight continuous increase of frequency (arousal) without an 'off-effect' even after very high amounts of prolactin (1.4 IU/g).

Discussion. The evoked potentials picked up mostly from the area dorsalis pars dorsalis of the forebrain in *Lepomis* and *Astronotus* seemed to be prolactin-specific. Injections of distilled water, saline, bovine albumin, and luteinizing hormone (LH) failed to induce an activation at comparable positions. Injection of cavian antibody against mammalian prolactin decreased the prolactin induced activity in *Lepomis* within 15 min. Because of the appearence of increasing synaptic activity long before trains of spikes are generated, it seems improbable that primary receptor neurons are involved for prolactin within the dorsal forebrain. Moreover the latency of 0.5 to 3 min until continuous spike bombardment began suggests that the hormone receptor neurons lay within the hypothalamus, which is highly reciprocally connected with the telencephalon through the median and lateral forebrain bundle. It should be mentioned here that microinjections of prolactin in minute doses into the dorsal forebrain through 100 µm-cannula-electrodes failed to bring up changes of the electrical activity.

There is some evidence that the forebrain of fishes has generally modulating functions similar to the limbic system in mammals[1–3] but it may also activate behaviour patterns specifically[4,5]. Our results suggest that such



Dose-response curves of *Lepomis gibbosus* (L) and *Astronotus ocellatus* (A). Arrows indicate time of prolactin injection, numbers single and total doses, resp.

regulation processes on the niveau of the forebrain may be influenced by hormones[3,6].

Zusammenfassung. Intramuskuläre Injektionen von Schafprolaktin in immobilisierte *Lepomis gibosus* und *Astronotus ocellatus* verändern die elektrische Aktivität von Vorderhirnneuronen; niedrige Dosen steigern, hohe hemmen sie. *Tilapia leucosticta und Carassius auratus gibelio* reagieren nur mit geringer kontinuierlicher Aktivierung.

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COGITATIONES

Hormones, Thymus and Lymphocyte Functions

The function of the thymus for the development of the immunological system is now well established. Recent work has proved that the thymus is under hormonal control[1-6] and evidence has been provided that the thymus may act as an endocrine gland and thereby influence other endocrine glands[7,8]. With but few exceptions the thymus-derived lymphocytes (T-lymphocytes) have thus far been investigated almost entirely with respect to their immunological functions. A major theme of this communication is that T-lymphocytes are the cellular end-product of hormones-thymus interrelation and have important functions quite apart from those familiar to the immunologist. This view is supported by numerous findings on the various wasting syndromes whose aetiopathogenesis and symptomatology serve as models for this thesis. In essence it is proposed that wasting syndromes express the intimate interrelation between the development of lymphatic tissue function and the endocrinological system and that the lymphocytes deriving from this interaction are *multifunctional*, since they can prevent the complex symptomatology of certain wasting syndromes (see Table I and II).

The term 'multifunctional lymphocyte' is used to refer to both classical immunological functions of T-lymphocytes and their participation in other less well defined homeostatic control mechanisms. It is entirely possible that these functions measurable by other than immunological parameters involve the same underlying mechanisms as the immunologic ones and may even be performed by the same lymphocytes[15]. In what way such 'nonimmunological' functions of lymphocytes should be exerted is not presently clear. One possibility is that lymphocytes have a 'trephocytic' function[10]. The existence of tissue specific factors produced by lymphoid cells and their significance in morphostasis has been proposed by Burwell[11]. Another consideration is that lymphokines may be set free upon stimulation of T-lymphocytes by certain tissue cells and in turn influence cells of various organs. It seems to us that a strictly immunological approach to the T-lymphocyte-derived mediators might prove to be a too limiting view of lymphocyte function.

Wasting syndromes as models for abnormal thymus-endocrine glands interrelation. In establishing the importance of the thymus much information has been obtained through study of the deficits produced by neonatal thymectomy in rodents, including the wasting syndrome, impaired cell-mediated immunity and to a lesser extent reduced humoral immune responses. The 'wasting' or 'runting' syndrome occurring in some strains of mice and in other species after neonatal thymectomy has been reviewed at length[16-31]. The prevailing view is that in neonatally thymectomized mice this syndrome is the result of immunological impairment. Studies performed in neonatally thymectomized mice born and bred in germ-

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