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Lectures

MAPPING THE CEREBRAL CORTEX OF MAN WITH PET AND FMRI: THE PHYSIOLOGICAL FOUNDATIONS. L 1

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Whereas positron emission tomography (PET) in general is a method for localising and measuring neurochemical markers in living brains of animals and men, in practice functional mapping of the cerebral cortex relies on measurements of regional cerebral metabolism, regional cerebral blood flow (rCBF) or physical effects related to these two physiological variables. This is because the regional cerebral metabolism and regional cerebral blood flow mainly reflect the local synaptic activity of the brain. Whereas the regional cerebral metabolic rate for oxygen, glucose and the phosphorylation rate of glucose mainly reflect the activity and energy consumption of the Na^+/K^+ pump, the chemical mechanisms by which the regional cerebral blood flow is regulated in the brain are not understood in detail. The rCBF though is accurately regulated at the capillary level with an accuracy corresponding to active columns or less (100 μm). The rCBF at this local level is under influence of the local synaptic activity reflecting local synaptic traffic related to specific information processing, but also to attentional mechanisms raising the synaptic activity more globally, or even restricted to more regional influences by other attentional mechanisms. When the synaptic activity in a region increases, the rCBF often increases more than the regional cerebral oxidative metabolism. This results in an increased oxygen availability and an increased concentration of oxyhemoglobin locally in the cortex. This is the basis for functional mapping with magnetic resonance tomography based on the so-called BOLD effect. The evidence from PET and fMRI measurements as well as animal experiments is that the synaptic activity does not increase in single columns, but in larger patches and fields, which may constitute the functional unit of the cerebral cortex. Some common strategies for revealing the functional contribution of these cortical fields will be presented.

L 2 VARIED REGULATION OF SALT REABSORPTION BY THE COLLECTING DUCT. J. A. Schafer. Dept of Physiology & Biophysics, Univ. of Alabama at Birmingham, Birmingham, AL. (USA). J. Physiol. Biochem. (Rev. esp. Fisiol.), 53 (1), 8, 1997.

The recent finding that a single mutation in one subunit of the amiloride-sensitive Na^+ channel is responsible for Liddle's syndrome (SHIMKETS *et al.*, *Cell* 79, 407, 1994) underscores the importance of Na^+ transport regulation in the cortical collecting duct (CCD). Uncontrolled reabsorption of Na^+ by the CCD in Liddle's syndrome produces the equivalent of hyperaldosteronism, and is sufficient to cause severe hypertension. Such regulatory abnormalities may occur not only in the Na^+ channel itself but also in the hormone receptors and intracellular second messenger systems that regulate it. Aldosterone has long been recognized as a major regulator of Na^+ reabsorption, but arginine vasopressin (AVP), which increases the water permeability (P_f) of the luminal membrane of the CCD has more recently also been implicated in enhancing Na^+ reabsorption. In the rat CCD AVP produces a stable stimulation of Na^+-reabsorption, and its actions are markedly synergistic with the effects of aldosterone and deoxycorticosterone (DOC). In the isolated perfused rat CCD the high rates of Na^+ reabsorption produced by AVP in combination with aldosterone or DOC are reversibly inhibited by low doses (1 to 100 nM) of epinephrine, and higher doses (1 to 10 μM) of dopamine, a hormone whose endogenous production in the kidney is increased by salt-loading. The effect of epinephrine is reversed by yohimbine and that of dopamine by clozapine, suggesting involvement of an α_2-adrenoceptor and a D_4 dopamine receptor, respectively. Both hormones appear to act through G_i to inhibit adenylyl cyclase because they inhibit AVP-dependent cAMP generation. The effect of dopamine is also prevented when transport is stimulated by cyclic AMP analogs, although epinephrine still produces some inhibition. RT-PCR examination of RNA extracted from the microdissected rat CCD shows expression of both α_{2A} and α_{2B} adrenoceptor isoforms as well as all three α_1 adrenoceptors, and the D_4 dopamine receptor. These and other results indicate that the diuresis and natriuresis associated with salt loading may be promoted by the actions of catecholamines and dopamine even if AVP and aldosterone levels are elevated. For example, we have observed that isolated perfused CCD segments from rats which have been maintained on a 4% salt diet and given DOC exhibit very low rates of Na^+ transport and a very blunted P_f response to AVP. One explanation for this effect could be the persistence *in vitro* of the inhibitory effects of high *in vivo* levels of dopamine and epinephrine. On the other hand, defects in either the catecholamine or dopamine inhibitory pathway might result in the decreased natriuretic response to a salt load that is characteristic of salt-dependent essential hypertension.

PHYSIOLOGICAL BREAKTHROUGHS: PAST LIMITATIONS AND PRESENT POSSIBILITIES. L 3

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The remarkable developments in electronic techniques in recent years now permit the study of physiological variables under conditions that previously seemed beyond reach. New techniques not only simplify many procedures, they permit novel experimental approaches.

Miniaturization of equipment used for the telemetric transmission of data has reduced the bulk of equipment as well as its cost. Experimental methods have been improved and data can often be obtained from unrestrained animals and even from free-ranging wild animals under natural conditions. The reduced size and power consumption of modern devices permit a reduction of battery size and weight, extending their lifetime and increasing transmission distances. For example, miniaturized telemetry equipment has been used to record physiological variables from birds in free flight during extended periods.

The use of microprocessors constitute another major avenue for recording of data from unrestrained, free-living animals under natural conditions. Such use of microprocessors depends on the recovery of the recording equipment from free-ranging animals, but when this has been possible, the acquisition of new information has been highly successful. For example, continuous data logging from seals over periods of several months and migrations over thousands of kilometers has been used to record diving times and depth, swimming speeds, respiratory and circulatory parameters, and so on. This lecture will give an overview of these and other remarkable advances in our knowledge of animal physiology.