5

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Autoantibodies to vasopressin secreting cells (AVP-ɕ) in children with idiopathic diabetes insipidus of central origin.

To investigate the role of autoimmunity in the pathogenesis of idiopathic DI, antibodies (Ab) to AVP-ɕ have been evaluated in the serum of 57 patients. After clinical and neuroradiological investigation patients were classified into : idiopathic (n=23), DI with central lesion (n=19) and familial or DIDMOAD syndrome (n=13). Sera were tested for the presence of AVP-ɕ-Ab by indirect immunofluorescence using fresh human fetal hypothalamus as substrate. Absence of extinction of the reaction by AVP indicate that Ab are not directed to the hormone itself but to some component of the AVP-ɕ. AVP-ɕ-Ab were present in 10 (43.5%) idiopathic cases (3 of them had associated endocrine autoimmune disease : hypothyroidism, Type I diabetes and thyroiditis). Among the symptomatic cases 3 had AVP-ɕ-Ab, 2 of them having histiocytosis-X. None of the familial or DIDMOAD cases had AVP-ɕ-Ab.

In conclusion : Autoimmunity may play a role in the etiology of idiopathic DI as shown by the presence of AVP-ɕ-Ab and associated autoimmune disease. Presence of AVP-ɕ-Ab in histiocytosis-X is intriguing and may be due to an autoimmune reaction induced by histiocytosis-X cells bearing histocompatibility antigen and infiltrating the hypothalamus.

6

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Photoaffinity labelling of MSH receptors on pigment cells.

The pituitary peptide hormone α-MSH plays a role in pigmentation and fetal development and as a neuropeptide it influences behaviour and learning. In order to study α-MSH at the molecular level we have introduced a method of photoaffinity labelling of MSH receptors on intact pigment cells with which the biological response of the labelled cells could be continuously monitored. When melanophores of skin of Anolis carolinensis or Xenopus laevis where irradiated with UV-light in the presence of photoreactive α-MSH containing the photolabel in position 1, 9, or 13, a long-lasting signal was generated inducing irreversible pigment dispersion. A number of control experiments proved that the effect was specific. Calcium was shown to be indispensable for hormone-receptor binding and for the transduction of the signal from the receptor to the adenylate cyclase. Catecholamines acting through an alpha-2 receptor could reversibly inhibit the longlasting response of Anolis melanophores. The Xenopus model was also used for studying receptor turnover and degradation in the presence and absence of calcium. These and other results showed that irreversible stimulation by covalent labelling of hormone receptors represents a useful approach for studying stimulus-response coupling in intact cells, particularly when there are only few cells available.

7

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α-MSH induces changes in protein phosphorylation in Cloudman S-91 mouse melanoma cells.

α-MSH stimulates pigment synthesis in melanocytes and melanoma cells by interacting with a specific membrane receptor/adenylate cyclase system which activates tyrosinase, the key enzyme for pigment formation. Since most of the steps leading to this enzyme activation are unknown, we have investigated a possible role of protein phosphorylation in the action of α-MSH on melanoma cells. Incubation of Cloudman S-91 mouse melanoma cells with ^{32}P-phosphate results in the incorporation of ^{32}P into a large number of phosphoproteins. In the presence of α-MSH a significant increase of ^{32}P incorporation was observed into two phosphoproteins with apparent molecular weights of 43,000 and 34,000 daltons, respectively. This increase was concentration dependent (significant at 10^{-8}M α-MSH) and reversible. The effect could be induced by melanotropic but not by non-melanotropic peptides. [Norleucine[4], D-phenylalanine[7]]-α-MSH which is 100 times more active than α-MSH in stimulating tyrosinase activity, was also superactive in increasing phosphorylation of the 43,000 and 34,000 dalton proteins. These results suppose that protein phosphorylation is involved in the stimulation of melanoma cells by α-MSH.

8

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Effect of opioid(pentazocine) and opioid-antagonist (naloxone) administration on plasma ß-LH, FSH and Prolactin(PRL) levels in the perinatal period.

Opioid and naloxone administration induces sex-dependent changes of gonadotropins in newborn rats which has not yet been studied in human newborns. We measured plasma ß-LH, FSH and PRL with specific RIAs in mothers(n=23) during labour before and 60' after pentazocine and in their newborns just after birth and 20' after naloxone administration. Pentazocine(30mg i.m.) was given as an analgesic to the mother. Naloxone(0.01mg/kg i.m.) was administered as a routine treatment in our hospital to the baby immediately after delivery to prevent opioid induced apnoea. In mothers there were no significant differences of ß-LH, FSH and PRL before and after pentazocine. In cord blood of female newborns ß-LH was significantly lower(5.23mU/ml) following maternal pentazocine as compared with controls(9.06mU/ml, $p<0.05$). After naloxone there was no change of ß-LH, but the levels remained lower(3.96mU/ml) as compared with controls(9.75mU/ml, $p<0.001$). FSH in the female newborns showed a similiar pattern as ß-LH being suppressed in cord blood after maternal pentazocine(0.32mU/ml, $p<0.001$) and showing no change after naloxone(0.27mU/ml). In male newborns, however, there were no significant differences of ß-LH and FSH following pentazocine and naloxone administration. We speculate that there is a sex specific difference at the receptor site controlling gonadotropin secretion in human newborns.

9

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The metabolic and endocrine responses of neonates to surgical stress.

Little is known of the ability of preterm and term neonates to respond to surgical stress. We have measured circulating levels of metabolic fuels and hormones pre-operatively; at the end of surgery and post-operatively in 27 neonates (20 term, 7 preterm) subjected to surgery. The overall results (table) show significant perioperative changes in fuel and hormone levels confirming that neonates can mount a stress response. Further analysis shows that the pattern of response is different to adults, and is influenced by severity of surgery and gestational age. Definition of the stress response to surgery in different groups of neonates may improve clinical management and prevent metabolic complications

M±SEM	Pre-op	End-op	8 hr	12 hr	24 hr
Glucose mmol/l	4.6±0.3	10.0±0.7**	5.9±0.6*	8.2±0.6*	5.2±0.3
Lactate "	1.5±0.1	2.7±0.3**	1.9±0.2	1.8±0.1*	1.8±0.2
Pyruvate "	.10±.01	.14±.01**	.12±.01	.11±.01	.10±.01
Alanine "	.22±.02	.24±.02	.23±.02	.23±.02	.23±.01
FFA "	.38±.10	.63±.07*	.51±.17	.35±.08	.27±.04
Ketones "	.19±.03	.32±.07*	.17±.03	.15±.03	.16±.03
Glycerol "	.16±.02	.21±.02**	.15±.01	.16±.01	.14±.01
Insulin mU/l	12±2	15±3	21±4	17±4**	22±4**
Glucagon pmol/l	29±6	31±7	23±5	16±5*	16±5**
Adrenaline ng/ml	.06±.02	.20±.06***	.05±.01	.01±.01	.01±.01
Noradrenaline ng/ml	.54±.09	.92±.14***	.70±.14	.56±.10	.62±.09

***p<0.001, **p<0.01, *p<0.05

10

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Cross-sectional and longitudinal studies of sleep in children with abnormal stature.

Growth hormone secretion is associated with slow wave sleep. We report an analysis of the slow wave sleep patterns of normal children (n = 34), children with short stature of differing aetiology. (Psychosocial 6, Poor appetite 6, small/delayed puberty 11, genetic short stature 8) and 11 children with tall stature.

All except the group with tall stature were studied at home for 2 consecutive nights using an Oxford Medilog Recorder of EEG, EOG and EMG. The 2 nights were combined to give the following results.

	I%	II%	III%	IV%	REM%	Wake%
Normal	0.4	39.4	7.6	23.4	28.4	0.9
Genetic small	0.4	36.5	8.8	21.2	32.6	0.5
Psychosocial	0.4	42.2	4.9	17.6	31.5	3.3
Poor appetite	0.5	37.2	7.5	21.9	32.2	0.5
Small/delay	0.4	41.5	7.5	23.3	25.8	1.5
Tall	0.5	49.1	6.4	20.3	18.9	4.9

Longitudinal studies in children with severe psychosocial dwarfism during environmental change show reversal of the Stage IV sleep deficit and normal GH secretion with an increased growth velocity.