Neurochemical and neuroendocrine reactions during non-neurological surgery

Akademisk avhandling

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av
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Avhandlingen baseras på följande delarbeten:

I. Anckarsäter R, Vasic N, Jidéus L, Kristiansson M, Zetterberg H, Blennow K, Anckarsäter H. **Cerebrospinal fluid protein reactions during non-neurological surgery.** *Acta Neurol Scand. 2007 Apr;115(4):254-9.*

II. Anckarsäter R, Zetterberg H, Månsson JE, Blennow K, Anckarsäter H. **Non-neurological surgery results in a neurochemical stress response.** *J Neural Transm. 2008 Mar;115(3):397-9.*

III. Anckarsäter R, Zetterberg H, Blennow K, Anckarsäter H. **Association between thyroid hormone levels and monoaminergic neurotransmission during surgery.** *Psychoneuroendocrinology. 2007 Sep-Nov;32(8-10):1138-43.*

IV. Bromander S, Anckarsäter R, Ahrén B, Kristiansson M, Blennow K, Holmäng A, Zetterberg H, Anckarsäter H, Wass C. **Cerebrospinal fluid insulin during non-neurological surgery.** *Manuscript submitted for publication.*

GÖTEBORGS UNIVERSITET
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Neurochemical and neuroendocrine reactions during non-neurological surgery

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Abstract

Objective: To study changes in serum and cerebrospinal fluid (CSF) proteins, monoamine metabolites and hormones during non-neurological surgery. *Subjects and methods:* Thirty-five patients without neurological or psychiatric disorders undergoing knee replacements had CSF and serum samples drawn from spinal and arterial catheters before, three hours after and on the morning after surgery. *Results:* The CSF/serum albumin ratios decreased significantly during the study period, especially after the interventions. In contrast, CSF concentrations of beta-2-microglobulin (β2M) increased significantly during surgery and remained high. The CSF concentrations of beta-trace protein (βTP) remained unchanged. The dopamine metabolite homovanillic acid (HVA) and the serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA) increased sharply in the CSF during surgery and reached 188% and 166% of their initial concentrations on the morning after the intervention. The CSF concentrations of the norepinephrine metabolite 3-methoxy-4-hydroxyphenylglucol (MHPG) increased modestly (non-significantly) during and after surgery. The HVA/5-HIAA ratios initially increased but returned almost to their initial level during the night after surgery. During and after surgery, serum thyroid hormones and the T3/T4 ratio decreased, while the CSF T3/T4 ratio instead increased. At baseline, the CSF MHPG concentrations were significantly correlated to the serum T3/T4 ratios. The base-line CSF thyroid hormones were strongly correlated with the subsequent changes in monoamine metabolite concentrations during and after surgery. Serum insulin concentrations first decreased modestly but then increased sharply after surgery with a wide interpersonal variation, while the CSF insulin concentrations changed in the same directions, albeit with smaller amplitudes. Due to the increase in serum insulin, the CSF/serum insulin ratios decreased. *Conclusions:* Central nervous system protein reactions to a non-neurological surgical intervention include sharply decreased permeability of albumin into the CSF and signs of intrathecal inflammatory activity. There was a strong increase in serotonergic and dopaminergic neurotransmission during surgery, with a comparatively stable relationship between the metabolites from these systems. Changes in thyroid hormone and insulin metabolism during surgery are not similar peripherally and in the central nervous system. Thyroid hormone activity may influence brain monoaminergic neurotransmission. No correlations between the CSF/serum ratios of albumin, βTP, insulin and T4 were found, consistent with separate transport mechanisms from the blood into the CSF for these substances in humans in vivo.

Key-words: *albumin, beta-2-microglobuline, blood brain barrier, cerebrospinal fluid, inflammation, spinal anesthesia, stress*

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