Summary

Quantitative analysis of D2 dopamine receptors in clinically non-functioning pituitary adenomas

Introduction
Clinically non-functioning pituitary adenomas account for about one-third of pituitary tumors. The majority of them are pathologically classified as gonadotropinomas or null-cell adenomas without hormonal expression. The rest represent silent corticotroph adenomas and plurihormonal tumors. Conservative therapy with dopamine agonists is effective in some cases only depending on the expression of dopamine 2 receptors (D2R).

Objective
The aim of this study was to quantitatively estimate D2R expression in clinically nonfunctioning
pituitary adenomas and correlate the results with adenoma type according to pathological classification.

Methods and results
Out of the 87 adenomas investigated, 63 expressed gonadotropins, 7 were silent corticotroph adenomas, 7 were plurihormonal tumors, and only 6 did not express any pituitary hormone on immunohistochemical investigation. With the use of the reverse transcriptase real-time PCR technique, D2R mRNA was expressed in all adenomas with very heterogeneous quantity. The expression was very low in corticotroph adenomas (relative median quantity after normalization to housekeeping gene 0.01) and lower in plurihormonal tumors (median 0.4) than in gonadotroph (median 1.3) and null-cell adenomas (median 1.9). The difference between corticotroph
adenomas and plurihormonal tumors in comparison with other pathological types was statistically significant. The expression of D2R did not depend on the presence or absence of gonadotropins.
Expression of SSTR2, 3 and 5 mRNA was also very heterogeneous. SSTR5 was present only in 40 % of adenomas, SSTR 2 a 3 were present in all of them. D2R expression was statistically higher than SSTR2, 3 a 5 expression in gonadotrophs. However in D2R expression was significantly lower than SSTR2 expression in silent corticotrophs. There was no correlation between D2R and somatostatin receptors.

Conclusions
We conclude that D2R expression is very low in corticotroph adenomas and significantly lower in plurihormonal tumors. The positivity of gonadotropins does not predict the D2R quantity. Expression of SSTR2 and 3 is same in all histopathological types, expression of SSTR5 is higher in silent corticotroph adenomas. There is no correlation between D2R and somatostatin receptors, only expression of SSTR2 and 3 correlated. Very heterogeneous expression of dopamine and somatostatin receptors may be the reason why experimental use of dopamine and somatostatin analogs and „dopastatins“ is not clinically effective in the majority of CNFAs.

Key words: clinically non-functioning pituitary adenoma, dopamine receptor, somatostatin receptor