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IMMUNOHISTOCHEMICAL EVIDENCE FOR ENDOCANNABINOID PRODUCTION IN THE HUMAN DETRUSOR

Hypothesis / aims of study

Systemic administration of cannabinoids has been attributed a beneficial effect in detrusor overactivity, both in human clinical trials and in animal models. (1) Cannabinoids exert their function through the cannabinoid receptors CB 1 and CB 2. While CB 2 receptors are present on cells of immunological origin, the CB 1 receptors are expressed in the central and peripheral nervous system. CB 1 receptors have also been described in the detrusor muscle in a patchy structure surrounding the interstitial cells of the bladder. Endocannabinoid signalling in the detrusor has never been reported, although administration of a CB 1 agonist in an isolated mouse bladder inhibits electrically-evoked contractions, whereas CB 1 antagonists potentiate electrically-evoked contractions in this tissue by an undetermined mechanism. (2)
Fatty acid amide hydrolase (FAAH) is an enzyme involved in the hydrolysis of bioactive lipids such as the endocannabinoids anadamide and 2-arachidonoylglycerol (2-AG). (3)
We performed immunohistochemistry on the normal human bladder to demonstrate the presence of FAAH and compared it to the immunohistochemical localisation of the CB 1 receptor.

Study design, materials and methods

Full thickness human bladder samples were obtained from patients undergoing cystectomy for oncological problems. The patients had no anamnestical evidence of overactive bladder disease. Macroscopically normal bladder pieces were taken, this was confirmed by a standard HE staining.
The tissue was immediately frozen in nitrogen cooled isopentane and processed into 5 µm slides. Two different commercial polyclonal antibodies to FAAH were used (Alpha Diagnostics FAAH11-A and Chemicon AB5644P). A poly-envision technique was employed to enhance the quality of immunohistochemical staining.
Adjacant slides were stained for the cannabinoid receptor CB1 and for the kit receptor.
Controls consisted of omission of the primary antibodies.

Results

Both FAAH antibodies show specific staining and have comparable results.
There is no immunoreactivity for FAAH in the urothelium or in the suburothelium, but patches of FAAH-IR are located in the fibromuscular axes of the detrusor and on the smooth muscle cells surrounding them.
In adjacent slides, CB1 immunoreactivity is absent in the urothelium or suburothelium, but is present in patches on the detrusor smooth muscle cells adjacent to the fibromuscular axis. Double staining with the kit receptor reveals the presence of a kit-positive interstitial cell in the middle of this CB 1 patch. Kit positive cells are also observed in the suburothelium but at this level no CB 1 immunoreactivity is noted.

Interpretation of results

In accordance with previous observations, kit-positive interstitial cells are present in two distinct networks, the first in the suburothelium and the second in the fibromuscular axis of the detrusor. CB 1 is present on the border of the smooth muscle cells in a patch-like structure surrounding the kit positive interstitial cells of the detrusor.
The immunohistochemical presence of FAAH in the interstitial cells of the detrusor and in the surrounding smooth muscle cells suggests that the enzyme is active at this level to degrade endogenously released cannabinoids. It gives indirect evidence for endocannabinoid signalling in the bladder.

Concluding message

These data suggest that there is a role for endocannabinoid signalling in the normal human bladder. Pharmacological interaction with this process could be a future target for treating overactive bladder disease.

References

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