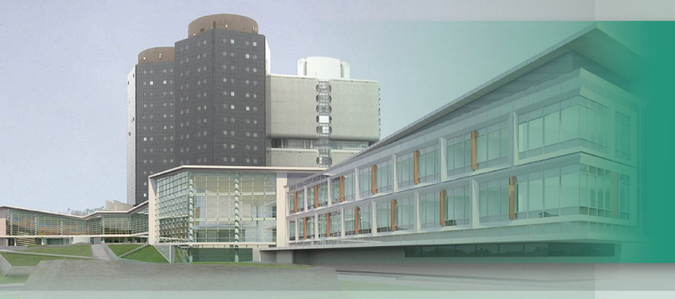

Current Role of Melanocortin in Erectile Dysfunction

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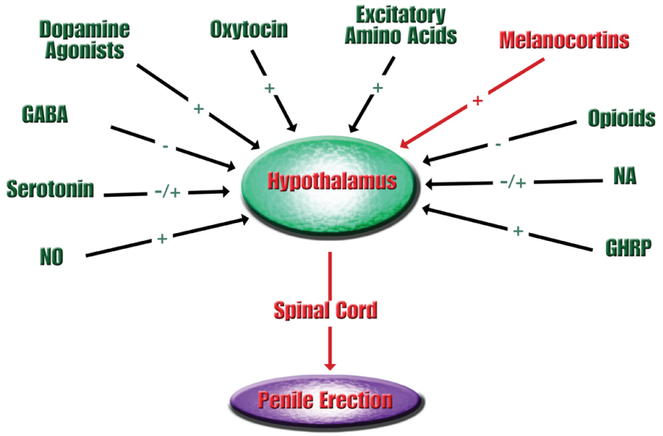
Introduction

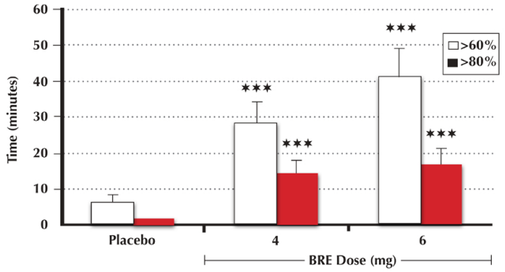
The 5 phases of male sexual function includes, libido, penile erection, ejaculation, orgasm and detumescence. In patients with erectile dysfunction peripherally acting phosphodiesterase 5 (pde-5) inhibitors are useful to improve erectile dysfunction. A new pharmacologic agent, Melanocortin is a centrally acting agent that improves penile erection. Melanocortin primarily acts on MC3 and MC4 receptors in the hypothalamus. MC4 receptors are emerging as the main mediators of penile erection. Currently there are several directly acting melanocortinergic agents that include HP-228, THIQ, and bremelanotide (PT-141). This poster will review the current pharmacological role of melanocortin in penile erection.

Methods

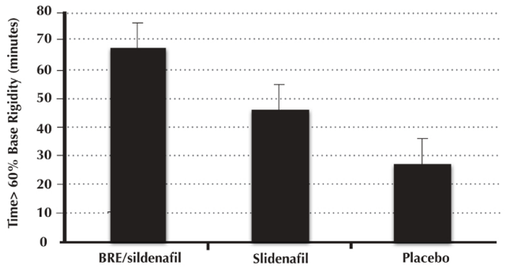
A review of recent literature data from various medical search engines was analyzed to determine the current pharmacology of melanocortin in human and animal research subjects. Role of melanocortin related to penile erection is discussed. Search terms used were melanocortin, erectile dysfunction and male sexual dysfunction. Gene manipulation in animal models to remove MC3 receptors was also studied.



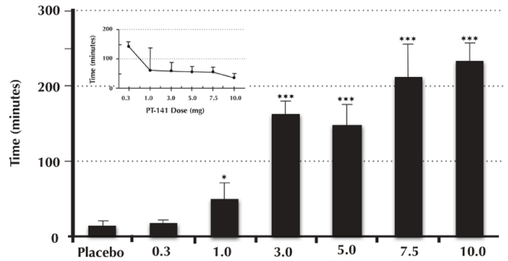
Hypothalamic control of penile erection and sexual behavior is modulated by a variety of biochemical pathways. Dopamine appears to be the primary erectogenic neurotransmitter, and serotonin acts as an inhibitor. The research involving manipulation of the melanocortin system has been the topic as the new treatment for Penile erectile dysfunction. Reprinted with permission from Macmillan Publishers Ltd: *International Journal of Impotence Research (Rosen et al. [45])*, copyright (2008).



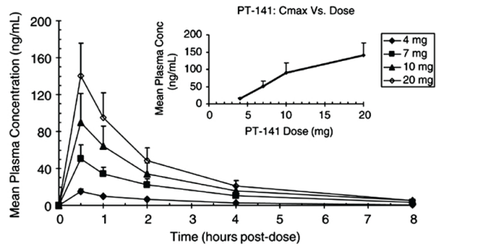
Duration of base rigidity 60 or 80% by Rigiscan after subcutaneous administration of bremelanotide among men with ED and an inadequate response to sildenafil (N=25). *** P<0.001, compared with placebo.45 ED, erectile dysfunction. Reprinted with permission from Macmillan Publishers Ltd: *International Journal of Impotence Research (Rosen et al. [45])*, copyright (2004).



RigiScan monitoring results for bremelanotide+sildenafil versus sildenafil alone and placebo. Time of base rigidity 60% during a 2.5-h RigiScan monitoring session (30 min to 3 h postdose).47 Reprinted with permission from Macmillan Publishers Ltd: *International Journal of Impotence Research (Rosen et al. [45])*, copyright (2004).



Base rigidity 60% in normal volunteers after s.c. administration of PT-141. Duration of base rigidity 60% in normal healthy males treated with 0.3–10 mg PT-141 during a 6.5 h RigiScan™ monitoring session. Inset: Time to detection of the first erectile event that was measured at 60% base rigidity and persisted for at least 3 consecutive minutes. * P< 0.05; ** P< 0.01; *** P<0.001, compared to placebo. Reprinted with permission from Macmillan Publishers Ltd: *International Journal of Impotence Research (Rosen et al. [45])*, copyright (2004).



Intranasal PT-141 pharmacokinetics. Mean (s.e.) plasma PT-141 concentration–time profile following single-dose PT-141 administration in healthy males (Phase 1 Study). Inset: Mean C max of PT-141 plasma concentrations at doses of 4–20 mg. Reprinted with permission from Macmillan Publishers Ltd: *International Journal of Impotence Research (Rosen et al. [45])*, copyright (2004).

Results

Data from the search engines reveals that Melanocortin may be a useful agent in patients with erectile dysfunction secondary to underlying co morbidities. Data from phase II clinical trials of bremelanotide supports the use of melanocortin-based therapy in patients with erectile dysfunction. Melanocortin may also improve sexual desire and arousal in women.

Conclusion

Currently the first line oral treatment options for erectile dysfunction are the peripherally acting pde-5 inhibitors. Patients who have failed pde-5 medications or have contraindications may soon have another option. In patients who use pde-5 inhibitors to improve erectile dysfunction and develop hypotension, melanocortin may be an alternative to overcome this serious side effect especially in patients who are contraindicated because of concurrent use of nitrates or nitric oxide donors. Stimulation of the melanocortin system has shown to be effective to treat erectile dysfunction. Further studies are needed to study the pharmacodynamics of melanocortin in human subjects.

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