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Hypothesis: Why PDE Inhibitors should be Examined in Treatment of Creutzfeldt-Jakob and Prion Diseases

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ABSTRACT

cGMP and cAMP are both cyclic nucleotides that act as second messengers in intracellular signaling pathways. Both cGMP and cAMP have been found to be significantly depleted in Creutzfeldt-Jakob disease (CJD). The way to recover cGMP and cAMP levels is through Phosphodiesterase (PDE) inhibitors that some of them, like Viagra, are currently in treatment for Erectile Dysfunction. Therefore, it's possible to hypothesize that PDE inhibitors may have a role in CJD treatment, which should be examined further.

cAMP (cyclic adenosine monophosphate) and cGMP (cyclic guanosine monophosphate) are both intracellular second messengers that play crucial roles in cellular signaling and regulation. They are involved in a wide range of processes, including gene expression, metabolism, memory, and immune function. cAMP and cGMP often work in conjunction, with cGMP influencing cAMP levels via phosphodiesterases.

Creutzfeldt-Jakob disease (CJD) patients (n=15) had lower cAMP (−70%) and cGMP (−55%) concentrations in CSF compared with controls (n=11) [1]

Phosphodiesterase (PDE) inhibitors are a class of drugs that target specific PDE enzymes to prevent the breakdown of cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP). By inhibiting these enzymes, PDE inhibitors increase the concentration of these cyclic nucleotides, which are important signaling molecules in various cellular processes.

Phosphodiesterase inhibitors exert their effects on their targeted phosphodiesterase enzymes (PDE-3, PDE-4, PDE-5), preventing cGMP or cAMP degradation, further increasing their levels in smooth muscle cells, causing relaxation and vasodilatory effect in target cells [2]

Phosphodiesterase-5 (PDE5) inhibitors such as sildenafil (Viagra), tadalafil (Cialis), vardenafil (Levitra), and avanafil (Stendra) are clinically indicated for the treatment of erectile dysfunction. Being PDE inhibitors they could perhaps be studied in CJD as well.

CJD is one of the prion diseases, it has sister diseases in animals: mad cow disease and Chronic (muscle) wasting disease (CWD) in deer, elk, and moose. There are also rare other prion diseases in humans.

When considering the significantly lower cGMP and CAMP levels found in CJD. And because PDE inhibitors are known to recover cGMP and cAMP levels, I would suggest it as a possible

therapeutic that needs to be learned in this regard. This is of course only a hypothesis that needs to be examined.

References

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