

A Hypothesis Concerning Schizophrenia

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Opinion

In 1965, Bell noted that amphetamine psychosis mimicked schizophrenia [1]. Later, van Ree and Otte [2] elucidated that amphetamine and alpha-endorphin had similar effects [2] in the Central Nervous System, while Wiegant et al. [3] found increased levels of gamma and alpha-endorphin in the hypothalamic tissue of schizophrenic human cadavers [3].

Theresa Hannon's suggestion is that this endogenous alpha-endorphin isn't degraded, and so tends to pile up in the CNS; an analysis of alpha-endorphin's role in the endorphin metabolic pathway is provided by Burbach et al. [4].

The aminopeptidase responsible for degrading alpha-endorphin in the CNS has been identified as Aminopeptidase N (also known as CD13 and Alanyl (Membrane) Aminopeptidase); Hannon suspects that this enzyme is miscoded in the case of schizophrenics, such that it fails to degrade alpha-endorphin. A human alpha-endorphin ELISA Assay which may reveal the resulting excess of alpha-endorphin is suggested [5].

The perceptive reader may be wondering why Hannon has selected the human gene 'ANPEP' for detailed study; the reason is that ANPEP codes for Alanyl (Membrane) Aminopeptidase in humans. Interestingly, ANPEP exists as more than one isoform: Hannon would argue that the first isoform is expressed in childhood and another isoform is expressed from adolescence onwards. Childhood Schizophrenia might be explained by a defect common to both isoforms (alternatively spliced over time), while Adolescence-Onset Schizophrenia might be explained by miscoding of the second (later) isoform. In humans, ANPEP is located on Chromosome 15; its NCBI Accession Number is NC_000015.10, and its range is 89784895..89814854.

CD13 isn't just expressed on CNS synaptosomes but is also present on the plasma membrane of skin fibroblasts [6]. This would indicate

that defects in ANPEP could be characterized by ordinary skin fibroblast biopsies (taken from children and adults). Human ANPEP mRNA has been sequenced; its NCBI Accession Number is NM_001150.2. This has been mentioned as Lorenz et al have noted in 2011 that cells can ingest mRNA and translate it (to some extent) into working protein [7].

An animal model of Schizophrenia exists: namely, mad dogs. Intravenous injection of this mRNA into these animals should correct their (canine) psychosis- although (as NM_001150.2 codes for a human protein) there would be a risk of an immune response. Correction of canine psychosis should provide evidence that NM_001150.2 ought to correct Human Schizophrenia.

References

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