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December 16, 2005

Judith Kidwell, HFS-265
5100 Paint Branch Parkway
College Park, MD 20740

Re: Enclosed study by Perry et al.

Docket No: 2005-0377/CP 1

Dear Ms. Kidwell,

Here is the final study you wanted. In my estimation, George Perry's study makes a lot of sense. The question everyone asks is why does Alzheimer's wait to age 60 or 65 before it manifests itself? Why not earlier? Down's syndrome dementia, of course, takes place earlier.

One of Perry's findings that lifetime caloric intake, particularly in the 60 year and older group, averages higher in the persons who will develop AD than in the control groups. This squares with findings of epidemiology literature, particularly for those individuals carrying the APOEε4 allele. Obesity itself is a risk factor for AD, as is metabolic syndrome.

□ Role of Hypothalamus in Weight Control Overlaps Brain Aluminum Control

As noted in the petition, the hypothalamus of the brain secretes the powerful aluminum chelation chemical: i.e. PRP-1 (1) which has a role in control of brain glucose among other functions, and also has receptors for another powerful aluminum chelation chemical: i.e. PYY (2). The later chemical secreted by the gut is a competent appetite suppression agent.

Hence, we are seeing an overlap of obesity and control of brain aluminum in brain chemistry. It is likely that there are other brain chemicals that chelate aluminum, but this research is just beginning. The hypothalamus will degenerate with aging which may offer one explanation as to why AD takes hold in the 65 and over age group and not earlier.

□ New Findings About the Hypothalamus Degeneration in Aging Process

A series of new studies look at the effect of hypothalamic neurodegeneration on energy balance in the aging process. As Xu point out,

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"Normal aging in humans and rodents is accompanied by a progressive increase in adiposity". (3) That team found that the degeneration of the hypothalamic neurons producing proopiomelanocortin (Pomc) neuropeptides is responsible.

Similar results of selective death of appetite stimulating or inhibiting neurons were reported in Science in October by Luquet (4) and by Kokoeva (5) leading to the attached editorial, "Does brain cell growth drive weight loss?"

Of additional interest is Stewart's January article in Archives of Neurology (6) that persons who are just about to manifest overt dementia show a warning weight loss. It is likely that hypothalamus degeneration in these persons is much more complete. (Control of brain aluminum via hypothalamus secretions may also be severely depressed as the neurons have died.)

The extent to which aluminum will kill hypothalamus neurons as it does other neurons is not known, but that section of the brain clearly interacts with the metal in a strong protective role as noted. (The brain does not believe that aluminum is safe.)

With best regards,



Erik Jansson, Exec. Dir.

- (1) A.A. Gaoloyan et al, Hypothalamic proline-rich polypeptide protects brain neurons in aluminum neurotoxicosis, *Neurochem Res* 29 (2004) 1349-57
- (2) B.M. Bert et al, Peptide YY administration decreases brain aluminum in the Ts65Dn Down Syndrome mouse model, *Growth, Development & Aging* 64 (2000) 3-19
- (3) A.W. Xu et al, Effects of hypothalamic neurodegeneration on energy balance, *PLOS Biology* (open access) 3/12 (Dec. 2005) e415, 9 pages
- (4) S. Luquet et al, NPY/AgRP neurons are essential for feeding in adult mice but can be ablated in neonates, *Science* 310 (Oct. 28, 2005) 683-5
- (5) M.V. Kokoeva et al, Neurogenesis in the hypothalamus of adult mice: potential role in energy balance, *Science* 370 (Oct. 28, 2005) 679-82
- (6) R. Stewart et al, A 32-year prospective study of change in body weight and incident dementia, *Arch Neurol* 62 (Jan 2005) 55-60