2014

Pilot Data on Brain-to-Blood Efflux of B-Amyloid Peptides in Man

Steve Meaney
*Technological University Dublin*, steve.meaney@tudublin.ie

Maura Heverin
*Karolinska Institute*

Ingemar Bjorkhem,
*Karolinska Institute*

Dorotea Religa
*Karolinska Institute*

John Wahren
*Karolinska Institute*

Follow this and additional works at: [https://arrow.tudublin.ie/scschbioart](https://arrow.tudublin.ie/scschbioart)

See next page for additional authors

Part of the Nervous System Diseases Commons

**Recommended Citation**


This Article is brought to you for free and open access by the School of Biological Sciences at ARROW@TU Dublin. It has been accepted for inclusion in Articles by an authorized administrator of ARROW@TU Dublin. For more information, please contact yvonne.desmond@tudublin.ie, arrow.admin@tudublin.ie, brian.widdis@tudublin.ie.

This work is licensed under a [Creative Commons Attribution-Noncommercial-Share Alike 3.0 License](https://creativecommons.org/licenses/by-nc-sa/3.0/)
Authors
Steve Meaney; Maura Heverin; Ingemar Bjorkhem; Dorotea Religa; John Wahren; and Ulf Diczfalusy

This article is available at ARROW@TU Dublin: https://arrow.tudublin.ie/scschbioart/112
2014

Pilot data on brain-to-blood efflux of b-amyloid peptides in man

Steve Meaney
Maura Heverin
Ingemar Bjorkhem
Dorotea Religa
John Wahren

See next page for additional authors

Follow this and additional works at: http://arrow.dit.ie/despart

Part of the Art and Design Commons, and the Nervous System Diseases Commons

This Other is brought to you for free and open access by ARROW@DIT. It has been accepted for inclusion in Articles by an authorized administrator of ARROW@DIT. For more information, please contact yvonne.desmond@dit.ie, arrow.admin@dit.ie.
Authors
Steve Meaney, Maura Heverin, Ingemar Bjorkhem, Dorotea Religa, John Wahren, and Ulf Diczfalusy
Results

- Alzheimer's disease (AD) is the most common cause of dementia and affects nearly 40,000 individuals in Ireland.
- The β-amyloid peptide (Aβ) plays a key role in the pathogenesis of the AD and the presence of Aβ plaques in the brain is diagnostic.
- The hypothesis posits that Aβ deposition is a critical factor in the disease process and that production and clearance of Aβ are key drivers of the disease.

Hepatic uptake:

- Aβ produced in the brain passes into the blood, either directly across the blood-brain barrier or via the cerebrospinal fluid (CSF). It is carried in a complex with different proteins. The liver, kidney, and spleen can take up and metabolize Aβ via various proteases. LRP1-low density lipoprotein receptor related protein 1; Aβ=albumin; TTR=transthreonytin; AAT=α1-antitrypsin; NEP=nephelisin; IDE=insulin degrading enzyme; PLG=plasmin; ACE=angiotensin converting enzyme

Peripheral clearance

- The aim of this work was to investigate if the concentration Aβ peptides is different in jugular venous plasma and arterial plasma and so estimate direct values for both brain-to-blood Aβ efflux and hepatic clearance in man.

Experimental Methods

- Pilot data on brain-to-blood efflux of β-amyloid peptides in man

4.

The aim of this work was to assess the organ uptake and efflux of Aβ peptides in human volunteers following an overnight fast. Plasma was frozen at -80°C until required for analysis.

• Ethics: All experiments involving human volunteers were reviewed and approved by the ethics committees at the Huddinge Hospital and the Karolinska Hospital. Participants gave informed consent to participate in the study.

• ELISA for Aβ: Specific antibodies against Aβ40 and Aβ42 were used as primary antibodies. The reporter antibody was horseradish peroxidase-linked anti-rabbit IgG and color was developed with 0-phenylenediamine. The detection limit for synthetic Aβ40 and Aβ42 was 1 pM. All samples were analyzed in the linear range of the ELISA.

Data Analysis: The concentration of Aβ40 and Aβ42 in the arterial and venous plasma was compared using a non-parametric approach. The significance level was set at 0.05. The molar concentrations of Aβ40 and Aβ42 were calculated. The percent extraction of individual Aβ species was calculated according to:

Percent extraction = (C1-C0)/C1 x 100

Negative values were considered to represent a net output. Daily fluxes were estimated according to:

Daily extraction = (C1-C0) x organ plasma flow

For the purposes of this calculation the cerebral and hepatic plasma flow were set at 650 L/d and 1000 L/d respectively.

Discussion

• This is the first attempt to directly quantify the brain-to-blood passage of Aβ in man. The daily cerebral output of Aβ40 was estimated to be 1 ng.d-1 and that of Aβ42 was estimated to be 3 ng.d-1.

Although the data was not statistically significant the values are in reasonable agreement with data from a transgenic rat model of 1.6 ng.d-1 for Aβ40.

There are two main limitations to this work:

i) The main limitation in the current study is the small number of samples available which has affected the power of the study.

ii) A further limitation is that the material analysed was collected in connection with a previous study on brain-striker homeostasis. Given the paucity of the data available we considered it prudent to commence these investigations on a pilot basis and use the data to design larger studies.

• Based on the data available in connection with this study we estimate that a sample size of 40 would be required to have an 80% power to detect a difference in percent extraction of 13.5%.

While this is an ambitious number of participants for a relatively invasive procedure we believe that the data generated would be very valuable for the field

References