

SCIENTISTS CONFIRM THAT ALZHEIMER'S IS A PRION DISEASE

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As of 2009, there are 5.3 million victims of Alzheimer's Disease in the US. And the epidemic is soaring as there are almost one-half million new cases each year – one every 70 seconds . . .

APRIL 2009 – UCSC – ALZHEIMER'S IS A PRION DISEASE

“Human prion diseases include classic and variant types of Creutzfeldt-Jakob disease, mad cow disease, Alzheimer's and Parkinson's.”

http://www.santacruzsentinel.com:80/localnews/ci_12180851

UCSC researchers find key to prion diseases

By Alia Wilson

Posted: 04/20/2009 01:30:05 AM PDT

SANTA CRUZ-- Researchers at UC Santa Cruz have discovered that in an inherited form of Creutzfeldt-Jakob disease, disrupted regulation of copper ions in the brain may be a key factor in the disease.

Prion diseases are fatal neurodegenerative brain disorders caused by a misfolded form of the normal cellular prion protein. **Human prion diseases include classic and variant types of Creutzfeldt-Jakob disease, mad cow disease, Alzheimer's and Parkinson's.**

Researchers at UCSC, discovered a relationship between changes in the copper-binding properties of abnormal prion proteins and the clinical features of prion disease in patients with certain rare, genetic mutations. They described their findings in a paper published by PLoS Pathogens on Thursday.

"The loss of copper regulation may play a very important role in prion disease progression," said Glenn Millhauser, professor of chemistry and biochemistry at UCSC and corresponding author of the paper.

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<http://news.ucsc.edu/2010/10/prusiner-lecture.html>

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Nobel laureate Stanley Prusiner to speak at UCSC on Friday, October 15, 2010

Nobel laureate Stanley Prusiner, M.D.--who discovered the infectious proteins that cause "mad cow disease" in cattle, Creutzfeldt-Jakob disease in humans, and other neurodegenerative diseases--will discuss the latest developments in this field in a lecture at UC Santa Cruz on Friday, October 15, at 5 p.m. in the Baskin Auditorium. The event is free and open to the public.

"Prusiner will discuss "Increasing evidence that prions cause most neurodegenerative diseases."

In all prion diseases, a normal, benign cellular protein acquires an altered shape that results in pathological changes in the brain. The most common prion disease in humans is Creutzfeldt-Jakob disease (CJD). Other, more common neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, and frontotemporal dementia have also been found to involve abnormal protein conformations.

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The human prion is resistant to both heat and chemicals and is reported to be up to a hundred thousand times more difficult to deactivate than the animal form of infective agent which causes well known diseases in cattle, such as mad cow disease, and scrapie in sheep. "

<http://www.sciencealert.com.au/news/20091310-19987.html>

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<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2807690/?log%24=activity>

Prion protein and Alzheimer disease

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Received July 2, 2009; Accepted September 2, 2009.

“Alzheimer and prion diseases are neurodegenerative disorders characterised by the abnormal processing of amyloid- β ($A\beta$) peptide and prion protein (PrP^C), respectively. Recent evidence indicates that PrP^C may play a critical role in the pathogenesis of Alzheimer disease.

There are a number of neuropathological similarities and genetic links between AD and prion diseases. The coexistence of AD pathology in CJD has been reported⁶ and PrP^C has been shown to co-localise with $A\beta$ in plaques.⁷ These compound PrP^C - $A\beta$ plaques were shown to be present in most CJD patients with associated AD-type pathology⁸ and it has been proposed that PrP^C may promote $A\beta$ plaque formation.⁹ A genetic correlation between PrP^C and AD has also been reported. A systematic meta-analysis of AD genetic association studies revealed that the gene encoding PrP^C (*PRNP*) is a potential AD susceptibility gene¹⁰ and the Met/Val 129 polymorphism in *PRNP* has been reported to be a risk factor for early-onset AD.^{8,11,12} However, in 2007 we reported an interaction between PrP^C and the rate-limiting enzyme in the production of $A\beta$, the β -secretase BACE1,¹³ and more recently, two further studies have also found direct links; PrP^C has been reported to be a receptor for $A\beta$ oligomers¹⁴ and the expression of PrP^C is controlled by the amyloid intracellular domain (AICD).¹⁵ **In this review, we discuss these molecular and cellular links between AD and PrP^C**

WED. OCTOBER `13, 2010

<http://www.alzheimers-research.org.uk/news/article.php?type=News&id=705>

"Professor Hooper said: "Our team has already been able to see an interaction between amyloid and prion, and we now want to monitor exactly what is happening and what the consequence of that interaction is. "

also

" "We already know that in Alzheimer's, amyloid builds up in the brain, harming the brain cells and causing them to die, **but recent research has**

shown the protein attaches to prion before it inflicts its damage.

Led by Professors Nigel Hooper and Chris Peers, the team at Leeds will seek to understand how this happens, and what role the prion protein plays in Alzheimer's. "

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<http://www.amsvans.com/blog/2935-is-alzheimers-disease-ad-contagious-surprising-results/>

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Is Alzheimer's Disease (AD) Contagious? Surprising Results

posted on Oct 26, 2010 by Sherri in the Disability News, Fun, Health, Healthcare, Interesting Links, Technology category

Researchers in Tübingen, Germany have discovered that certain protein plaque deposits that cause Alzheimer's disease can be infectious not only when they are injected directly into the brain, but also when they are injected

anywhere else in the body. By injecting healthy mice with the diseased gray matter, those mice develop Alzheimer's-like symptoms within just four months time.

“In 2006, a team of German scientists reported that injection of dilute extracts from human Alzheimer’s brain tissue, or from Abeta-laden mouse brain tissue, into the brains of transgenic mice (genetically modified to produce the human form of Abeta) stimulated Abeta build-up within the mouse’s brain. In this month’s issue of Science, the same team of scientists have discovered that the healthy mice can be injected into their stomachs, legs, or anywhere on the body and have the same affect on the brain.”

“At this time, the cause and the cure for the disease are both unknown, but discovering that these proteins can act as prion-like pathogens offers so much more possibility for research”

The development of Alzheimer’s disease in otherwise healthy mice indicate that there is a previously unknown mechanism that allows infectious tissue to move around the body and pass through the barriers that protect the brain. Although they do not know how this occurs, they do know that the disease does not have to be injected directly into the brain for the disease to occur. It does, however, occur more rapidly when directly introduced into the brain than in any other part of the body.

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<http://healthyseason.blogspot.com/2010/08/brain-disease-could-affect-more-people.html>

Sunday, August 15, 2010

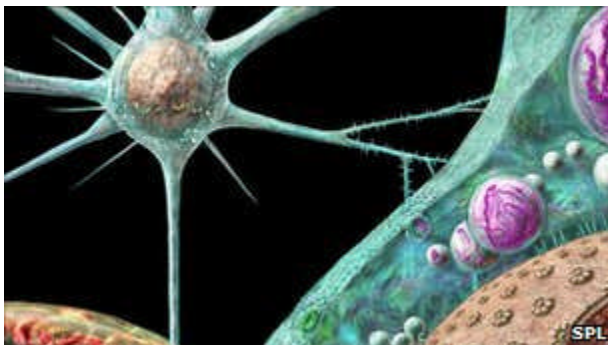
Brain disease could affect more people, research finds

By Caroline Parkinson
Health reporter, [BBC News](#)

A new form of brain disease, similar to Creutzfeld-Jakob Disease, could affect more people than previously thought, researchers in the US say.

It had been thought that only people with one genetic profile were

*vulnerable to the prion disease **VPSPr**.*



Healthy prions sporadically change in patients with the disease

But in an Annals of Neurology study, Case Western Reserve University experts found people with all three possible gene patterns are affected by VPSPr.

They say the findings could help with the treatment of prion diseases. Although it is a prion disease like vCJD, VPSPr is not linked to eating infected meat.

“Since this new disease shows several differences to other prion diseases, it is most likely that VPSPr is caused by a mechanism that is different from other prion diseases ”

End Quote Professor Pierluigi Gambetti Ohio State University

However, like CJD, the new condition happens sporadically.

It was first identified because of the fast-advancing form of dementia seen in those affected. They were also unable to speak or move.

But tests for CJD proved negative.

Further molecular examination showed VPSPr was a prion disease, but one which looked very different to those already known.

Mechanism

The human prion protein gene comes in three variants, depending on which amino acid the prion proteins contain - valine (V) or methionine (M).

People can be VV, MM or MV.

The first clutch of cases identified all had the VV variant. However, these latest cases included people with the other variants too.

Despite extensive research, a relatively large group of neurodegenerative diseases associated with dementia remain undefined.

Pierluigi Gambetti, a professor of pathology at Case Western who led the research, told the BBC: "Since this new disease shows several differences to other prion diseases, it is most likely that VPSPr is caused by a mechanism that is different from other prion diseases currently known.

"This newly identified human prion disease provides us with an excellent opportunity to investigate new ways of causing the disease that abnormal prion proteins may follow.

"This in turn may facilitate our efforts to develop therapeutic strategies for these devastating neurodegenerative disorders."

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<http://creutzfeldt-jakob-disease.blogspot.com/2010/08/variably-protease-sensitive-prionopathy.html>

Interpretation: Because all 3 129 genotypes are involved, and are associated with distinguishable phenotypes, VPSPr becomes the second sporadic prion protein disease with this feature after Creutzfeldt-Jakob disease, originally reported in 1920. However, the characteristics of the abnormal prion protein suggest that VPSPr is different from typical prion diseases, and perhaps more akin to subtypes of Gerstmann-Sträussler-Scheinker disease. ANN NEUROL 2010;68:162-172

"The identification of these two additional PrPres fragments (PrPres #2 and 7kDa band) reminds features reported respectively in sporadic Creutzfeldt-Jakob disease and in Gerstmann-Sträussler-Scheinker (GSS) syndrome in humans."

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<http://neuropathologyblog.blogspot.com/2010/08/new-sporadic-prion-protein-disease.html>

In 2008, Pierluigi Gambetti, MD (*pictured*), and Wen-Quan Zou, MD, PhD, with collaborators, reported the discovery of this novel disease, which affected patients who exhibit only one of the three types of the prion protein gene. In this follow-up study, they discovered that all three genetic groups can be affected also by this novel disease which now joins sCJD in displaying this feature. However, VPSPr is associated with an abnormal prion protein that exhibits characteristics very different from those of sCJD, as well as other prion diseases, suggesting that it may be caused by a different mechanism, perhaps more akin to other neurodegenerative diseases, such as Alzheimer's disease. This finding may exemplify, for the first time, the possibility that the prion protein affects the brain with different mechanisms.

A-BETA = ALZHEIMER' S DISEASE

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- [Plaques and Tangles](#)

Amyloid Plaques. One of the hallmarks of Alzheimer's disease is the ... **Beta amyloid** is a protein fragment snipped from an **amyloid** precursor protein (APP). ...

www.ahaf.org/alzheimers/about/.../plaques-and-tangles.html - [Cached](#) - [Similar](#)

- [Beta amyloid - Wikipedia, the free encyclopedia](#)

- 4 visits - Jun 18

Amyloid beta (A β or Abeta) is a peptide of 39–43 amino acids that appears to be the main constituent of amyloid plaques in the brains of Alzheimer's disease ...

en.wikipedia.org/wiki/Beta_amyloid - [Cached](#) - [Similar](#)

The codistribution of plaques and CJD-associated changes suggests that PrP plays a central role in Abeta formation and that Abeta pathology and prion disease likely in fluence each other. The kindred described herein provides support that PrP(E200K) may result in increased Abeta deposition

<http://www.ncbi.nlm.nih.gov/pubmed/19822779>

[Arch Neurol.](#) 2009 Oct;66(10):1240-6.

Codistribution of amyloid beta plaques and spongiform degeneration in familial Creutzfeldt-Jakob disease with the E200K-129M haplotype.

[Ghoshal N](#), [Cali I](#), [Perrin RJ](#), [Josephson SA](#), [Sun N](#),
[Gambetti P](#), [Morris JC](#).

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Abstract

BACKGROUND: Dominantly inherited Creutzfeldt-Jakob disease (CJD) represents 5% to 15% of all CJD cases. The E200K mutation in the prion protein (PrP) gene (PRNP) is the most frequent cause of familial CJD. Coexistent amyloid beta (Abeta) plaques have been reported in some transmissible spongiform encephalopathies but to date have not been reported in familial CJD with the E200K mutation.

OBJECTIVE: To characterize a family with CJD in which Abeta plaques codistribute with spongiform degeneration.

DESIGN: Clinicopathologic and molecular study of a family with CJD with the E200K-129M haplotype.

SETTING: Alzheimer disease research center.

PARTICIPANTS: Two generations of a family.

MAIN OUTCOME MEASURES: Clinical, biochemical, and neuropathologic observations in 2 generations of a family.

RESULTS: In this kindred, 3 autopsied cases showed pathologic changes typical for the E200K-129M haplotype, including spongiform degeneration, gliosis, neuronal loss, and PrP deposition. Moreover, 2 of these cases (ages 57 and 63 years) showed numerous Abeta plaques codistributed with spongiform degeneration. APOE genotyping in 2 cases revealed that Abeta plaques were present in the APOE epsilon4 carrier but not in the APOE epsilon4 noncarrier. Two additional cases exhibited incomplete penetrance, as they had no clinical evidence of CJD at death after age 80 years but had affected siblings and children.

CONCLUSIONS: To our knowledge, this is the first description of Abeta plaques in familial CJD with the E200K mutation. The codistribution of plaques and CJD-associated changes suggests that PrP plays a central role in Abeta formation and that Abeta pathology and prion disease likely influence each other. The kindred described herein provides support that PrP(E200K) may result in increased Abeta deposition.

PMID: 19822779 [PubMed - indexed for MEDLINE] **PMCID:** PMC2796207 [Available on 2010/10/1]

A neuropathological subset of Alzheimer's disease with concomitant Lewy body disease and spongiform change

Abstract

The neuropathological heterogeneity of Alzheimer's disease (AD) is increasingly recognized. Diffuse Lewy body disease, for example, most frequently occurs in cases fulfilling histopathological criteria for AD, and these patients usually present with dementia rather than parkinsonism. **We report five cases of concomitant AD and diffuse Lewy body disease with still another coexistent neuropathological feature: localized and stereotyped spongiform change in the neuropil. This spongiform change was most striking in the superior and inferior temporal, entorhinal, and insular cortex and the amygdala and was virtually indistinguishable from that seen in Creutzfeldt-Jakob disease.** Electron microscopic study on one case revealed membrane-containing vacuoles in close association with neuritic plaques and paired helical filament-filled processes. Immunocytochemistry using antibodies to prion proteins (PrP_{sc} or PrP₂₇₋₃₀) failed to label plaque or vascular amyloid in the five cases. Four primates inoculated with brain tissue from one case have not evidenced neurological disease in the 3 years since the transmission experiment. **We conclude that these cases represent a neuropathological subset of AD with relatively widespread Lewy bodies and a localized spongiform change, predominantly involving the medial temporal region. Despite the light and electron microscopic commonality with Creutzfeldt-Jakob disease,** there is no clear evidence that these cases represent a form of transmissible spongiform encephalopathy.

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[abeta = AD]

Involvement of Dab1 in APP processing and β -amyloid deposition in sporadic Creutzfeldt–Jakob patients

Abstract

Alzheimer's disease and prion pathologies (e.g., Creutzfeldt–Jakob disease (CJD)) display profound neural lesions associated with aberrant protein processing and extracellular amyloid deposits. Dab1 has been implicated in the regulation of amyloid precursor protein (APP), but a direct link between human prion diseases and Dab1/APP interactions has not been published. Here we examined this putative relationship in 17 cases of sporadic CJD (sCJD) post-mortem. Biochemical analyses of brain tissue revealed two groups, which also correlated with PrP^{sc} types 1 and 2. One group with PrP^{sc} type 1 showed increased Dab1 phosphorylation and lower β CTF production with an absence of A β deposition. The second sCJD group, which carried PrP^{sc} type 2, showed lower levels of Dab1 phosphorylation and β CTF production, and A β deposition. **Thus, the present observations suggest a correlation between Dab1 phosphorylation, A β deposition and PrP^{sc} type in sCJD.**

<http://dementianews.wordpress.com/2010/11/17/brain-disease-vpspr-could-affect-more-people/>

Brain Disease VSPPr Could Affect More People

Abstract

US researchers think a new form of brain disease, similar to Creutzfeldt-Jakob Disease, could affect more people than expected previously. It involves a fast-advancing form of dementia. Tests for CJD were negative. Molecular examination showed VSPPr was a new prion disease. Healthy prions sporadically change in some patients. Unlike vCJD, VSPPr is not linked to eating infected meat. Like CJD, this new condition happens sporadically.

The human prion protein gene has three variants, depending on which amino acid – valine (V) or methionine (M) – occurs in the prion proteins. People can be VV, MM or MV. It had been thought only people with one genetic profile were vulnerable to the

prion disease VPSPr, but the latest cases examined include people with the other variants. All three possible gene patterns are affected by VPSPr.

<http://www.dana.org/news/features/detail.aspx?id=29246>

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Alzheimer's-Associated Protein Shows a Greater Prion-like 'Infectiousness' Than Expected

By [Jim Schnabel](#)

October 22, 2010 EXCERPTS

“This body-to-brain spread isn’t likely to be occurring in actual cases of Alzheimer’s. But it shows in a striking way that disease-linked forms of A-beta can spread like prions, if much less efficiently. Marc Diamond, a neurologist at the University of Washington at St. Louis who has done much-cited work in this area, calls the study “a proof of concept that an amyloid protein other than prion protein can get into the brain from the periphery.”

“ Amyloid fibrils are found in people with Alzheimer’s disease, Parkinson’s disease, Huntington’s disease, Creutzfeldt-Jakob disease, type 2 diabetes, and a host of other diseases, many of them involving the degeneration of neurons. The proteins that form amyloid fibrils in these diseases include A-beta, tau, alpha-synuclein, and prion protein.”

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“I think it should concern laboratory personnel who handle fresh brain material, and in particular people like us who try to isolate, concentrate and analyze A-beta from the brain,” says Jucker. “We have made a significant investment in increasing safety precautions in our lab.”

Further work will be required to determine precisely how A-beta clusters can cross from the body into the brain. Diamond suggests that the first stop, as for infectious prions, might be in amyloid-devouring cells of the immune system. Jucker hints that A-beta is carried by such cells across the

blood-brain barrier in cerebral vessels: “My guess,” he says, “is that it crosses via the blood and cellular blood components.”

JUST AS BSE (Mad cow Disease) is known to cause variant Creutzfeldt-Jakob Disease in humans – recent research indicates that Chronic Waste Disease (CWD) can jump species and cause prion disease in people who eat venison/ meat from cervids:

<http://www.michigan-sportsman.com/forum/showthread.php?t=347765>

CWD PRION 2010

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**International Prion Congress: From agent to disease
September 8–11, 2010 Salzburg, Austria**

PRION 2010 is the top Global Annual TSE Conference in prion research, following a sequence of PRION meetings that were originally organized by the EU Network of Excellence NeuroPrion.

Read more at Michigan-Sportsman.com: [Cwd prion 2010 - The Michigan Sportsman Forums](http://www.michigan-sportsman.com/forum/showthread.php?t=347765#ixzz14GJY5q3D)
<http://www.michigan-sportsman.com/forum/showthread.php?t=347765#ixzz14GJY5q3D>

Generation of a Novel form of Human PrPSc by Inter-species Transmission of Cervid Prions

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USA**

Prion diseases are infectious neurodegenerative disorders affecting humans and animals that result from the conversion of normal prion protein (PrPC) into the misfolded and infectious prion (PrPSc). Chronic wasting disease (CWD) of cervids is a prion disorder of increasing prevalence within the United States that affects a large population of wild and captive deer and elk. CWD is highly contagious and its origin, mechanism of transmission and exact prevalence are currently unclear. The risk of transmission of CWD to humans is unknown. Defining that risk is of utmost importance, considering that people have been infected by animal prions, resulting in new fatal diseases. To study the possibility that human PrPC can be converted into the infectious form by CWD PrPSc we performed experiments using the Protein Misfolding Cyclic Amplification (PMCA) technique, which mimic in vitro the process of prion replication.

Our results show that cervid PrPSc can induce the pathological conversion of human PrPC, but only after the CWD prion strain has been stabilized by successive passages in vitro or in vivo. Interestingly, this newly generated human PrPSc exhibits a distinct biochemical pattern that differs from any of the currently known forms of human PrPSc, indicating that it corresponds to a novel human prion strain.

Our findings suggest that CWD prions have the capability to infect humans, and that this ability depends on CWD strain adaptation, implying that the risk for human health progressively increases with the spread of CWD among cervids.

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<http://www.bellinghamherald.com/2010/08/19/1578605/outdoors-cwd-state-list-grows.html>

FALL, 2010

OUTDOORS: CWD state list grows by two

[Colorado, Illinois, Kansas, Nebraska, New Mexico, New York, North Dakota, South Dakota, Utah, West Virginia, Virginia, Wisconsin and Wyoming plus the Canadian provinces of Alberta and Saskatchewan are now on the North American CWD list and those are ranks that the state of Washington does not want to join.

MAY 2010 - SOCIETY FOR NEUROSCIENCE -

http://www.sfn.org/index.aspx?pagename=brainBriefings_10_proteinfolding

ALZHEIMER'S, PARKINSON'S, ALS, HUNTINGTON'S, etc. ALL THE SAME PROTEIN MISFOLDING/PRION DISEASE AS KURU, BSE, CJD (Creutzfeldt Jakob)

Alzheimer's, Huntington's, and Parkinson's are some of the most common brain diseases — each causing a unique form of progressive brain cell death. However, they may not be so different after all. New research suggests these and many other neurological diseases may be versions of the same basic disorder: a breakdown in the body's ability to fold proteins into their correct shapes. Based on these findings, brain researchers are hoping for a common treatment for these conditions, using new kinds of drugs that prevent misfolding or minimize harm done to the cell.

What if many of the most common brain disorders were all different versions of the same basic disease? At first glance, this seems ridiculous. Huntington's disease, Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis (ALS) have widely varying symptoms, affect different parts of the brain, and respond to different treatments.

However, a look under the microscope tells a different story. In each of these disorders, brain cells accumulate clusters of misfolded proteins — perhaps the best known are the Lewy bodies found in people with Parkinson's, the plaques of a protein called amyloid-beta seen in Alzheimer's patients, or the armies of misfolded proteins called prions in "mad cow" disease. Neuroscientists are finding increasing evidence that these clumps, rather than being a result of disease, may be a root cause.

Research also suggests these clumps develop from the same essential source — a breakdown in the body's system for ensuring proteins fold into their correct shapes. This theory of "protein misfolding diseases" is leading to:

- Better explanations for how many brain diseases begin, spread, and worsen.
- Potential new, universal methods of treating many disorders by reducing the amount of protein misfolding or by breaking up misfolded proteins.

"However, this system sometimes becomes overwhelmed. In the early 1980s, researchers identified misfolded proteins called prions that cause a number of rare brain disorders, such as kuru, bovine spongiform encephalopathy ("mad cow" disease), and Creutzfeldt-Jakob disease. This unprecedented finding led many to wonder, could misshapen proteins be the root cause of other brain diseases?

Brain researchers have now discovered that many brain diseases feature protein folding problems. In Parkinson's patients, alpha-synuclein forms clumps known as Lewy bodies. Alzheimer's sees tau tangles form inside brain cells and amyloid plaques accumulate near them. In Huntington's, the nucleus becomes gummed up with clusters formed by an abnormal version of the huntingtin protein, and in ALS, the proteins superoxide dismutase and TD-43 accumulate in the body and projections of nerve cells. "

click on link for rest of
article: http://www.sfn.org/index.aspx?pagename=brainBriefings_10_proteinfolding

.....
<http://precedings.nature.com/documents/4847/version/1/files/npre20104847-1.pdf>

Version 4

Without magic bullets: the biological basis for public health interventions against protein folding disorders

Rodrick Wallace, Ph.D. Division of Epidemiology

The New York State Psychiatric Institute

September 1, 2010

"The diseases range from prion illnesses like Creutzfeld-Jakob disease, in addition to amyloid-related dysfunctions like Alzheimer's, Huntington's and Parkinson's diseases, and type 2 diabetes. Misfolding disorders include emphysema and cystic Fibrosis."

6/23

In addition, they argue, there are unexplored similarities between Alzheimer's and prion diseases, that is, the analogies between prion and A aggregates could be broader than initially suspected."

Given the eight-fold symmetry of the amyloid fiber, say versions A ! H, then the simplest `frangibility code' is the set of identical pairings: fAA;BB; :::; GG;HHg, **producing eight different possible structures and their reproduction by**

fragmentation. More complex prion symmetries, or the possibility of combinatorial recombination, would allow a much richer structure, producing quasi-species, in the sense of Collinge and Clarke (2007). Permitting different sequence lengths or explicitly identifying different sequence orders would vastly enlarge what Collinge has characterized as a 'cloud' of possibilities, in the case of prion diseases. Indeed, classic studies by Bruce and Dickinson (1987) found 15 or more different prionstrains in a mouse model.

Recent work on prions appears to support something of Maury's hypothesis. Li et al. (2010) find that infectious pri-ons, mainly what is called PrPSc, a spectrum of sheet-rich conformers of the normal host protein PrPC, undergo Darwinian evolution in cell culture. In that work, prions show the evolutionary hallmarks: they are subject to mutation, as evidenced by heritable changes of their phenotypes, and to selective amplification, as found by the emergence of distinct populations in different environments

Figure 4, from Li et al. (2010), shows a prion energy landscape similar to figure 1. This suggests the possibility of characterizing the underlying topology of a 'prion reproduction code', in the sense of the sections above. One might speculate that prions and prion diseases represent fossilized remains of Maury's prebiotic amyloid world.

http://en.wikipedia.org/wiki/Beta_amyloid **ALZHEIMER'S –INFECTIOUS**
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[\[edit\]](#) Antimicrobial Properties

A recent study assessing the antimicrobial properties of amyloid-beta suggests that current theories regarding its role in Alzheimer's disease may be incorrect. In vitro assays demonstrated significant antimicrobial abilities against eight clinically relevant organisms, in several cases exceeding the potency of known antimicrobial peptide LL-37. If amyloid-beta is, in fact, a component of the [innate immune system](#), then Alzheimer's may be an infectious disease caused by a previously unidentified microorganism.^[18]

<http://english.peopledaily.com.cn/90001/90782/90880/6976115.html>

Alzheimer's may be "infectious" among spouses: study

21:51, May 06, 2010 🔍 + -

U.S. researchers have found that seniors whose spouses have Alzheimer's or another form of dementia face an increased risk of dementia themselves.

Such a risk is six times higher than for other husbands and wives, according to researchers at Utah State University.

The study was published on Wednesday in the Journal of the American Geriatrics Society.

The findings were based on analysis of 2,442 people (1,221 married couples), aged 65 and older, in Utah.

The participants were dementia-free at the start of the study. During 12 years of follow-up, 125 husbands and 70 wives developed dementia, and both the husband and wife developed dementia in 30 couples.

After adjusting for a number of factors, the researchers found that people with a spouse who developed dementia were six times more likely to develop dementia themselves than people whose spouses never had dementia. Men had a higher risk than women. Older age was also significantly associated with dementia risk.

"Future studies are needed to determine how much of this association is due to caregiver stress compared to a shared environment," said study leader Dr. Maria Norton at the university.

"On the positive side, the majority of individuals with spouses who develop dementia did not themselves develop dementia, therefore more research is needed to explore which factors distinguish those who are more vulnerable."

"Given the significant public health concern of Alzheimer's disease and other dementias, and the upcoming shift in population age composition, continued research into the causes of dementia is urgent," Norton said.

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<http://www.ncbi.nlm.nih.gov/pubmed/20502038>

[Neurodegener Dis.](#) 2010;7(4):272-8. Epub 2010 May 27.

A new story about an old guy: is Alzheimer's disease infectious?

[Reis HJ](#), [Mukhamedyarov MA](#), [Rizvanov AA](#), [Palotás A](#).

Laboratório de Neurofarmacologia, Departamento de Farmacologia, Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais (ICB-UFMG), Belo Horizonte, Brazil.

Abstract

Protein aggregation and amyloid fibril deposits in the central nervous system are characteristic features of more than 2 dozens of pathologic conditions. The various peptides thought to underlie these disorders have striking structural and functional similarities. The main difference between them at the molecular level is whether they are endogenously produced particles, exogenously transmitted infectious agents, or both. These similarities and novel approaches to their transmissibility are discussed in this review-based hypothesis.

2010 S. Karger AG, Basel.

PMID: 20502038 [PubMed - in process]

<http://www.americangeriatrics.org/press/id:665>

Strictly Embargoed Until 00.01 Hours (EST) Wednesday, May 5, 2010

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Medicalnews@wiley.com

Spouses of Dementia Sufferers Have a Six-Fold Increased Risk of Dementia Onset

Husbands Appear at Higher Risk Than Wives

.....
<http://betaamyloidcjd.blogspot.com/2009/06/alzheimers-disease-is-transmissible.html>

<http://www.guardian.co.uk/science/2009/jun/07/alzheimers-transmission-mice-dementia-research>

Sunday, June 7, 2009

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ALZHEIMER'S DISEASE IS TRANSMISSIBLE

Mice injected with Alzheimer's cast new light on dementia

Alok Jha guardian.co.uk, Sunday 7 June 2009 19.11 BST

”Scientists have found that harmful tangles of proteins that cause diseases such as Alzheimer's can be transmitted from one brain to another, spreading and causing damage after being injected into the brains of mice. The researchers stressed, however, that Alzheimer's was not contagious and said it could not be caught, for example, through blood transfusions “

“This research in mice does not show that tau pathology is contagious or it can spread easily from mouse to mouse - what it has revealed is how tau tangles spread within brain tissues of individual mice,” he said. “It suggests that tangles of proteins that build up in the brain to cause symptoms could have some contagious properties within brain tissue but not between mice that haven't been injected with tissue from another mouse and certainly not between people.” Though they are also bits of protein, tau tangles do transmit in the same way as prions, the proteins that cause diseases such as vCJD and mad cow disease by destroying brain tissue, because they cannot be passed easily between individuals. “

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<http://www.whiteowlconspiracy.com/2010/10/can-alzheimers-be-transmitted-in-humans.html>

Saturday, October 23, 2010

Can Alzheimer's be transmitted in humans through blood transfusion?



(Medical Daily) Researchers have found that Alzheimer's may be transmitted in humans through blood, but further investigations needs to be done as the initial study was done on mice.

A study conducted by Lary Walker at Emory University and Mathias Jucker at the University of Tübingen and their colleagues, the findings have indicated that brain plaques that resemble Alzheimer's are formed in mice when the protein that is responsible for this disease is injected into their bellies.

It was not so long ago (the year 2006) that the same group of researchers found that they could trigger Alzheimer-like plaques in healthy mice that were injected with samples of plaque from other mice.

In their second experiment, the group had developed beta-amyloid protein in substantial quantities from genetically modified mice (similar to the plaques formed in Alzheimer's) which they extracted from these mice when they were two years old, and injected it into the lining of the abdomen of transgenic mice. On the other hand, another set of mice were injected with healthy brain tissue.

In comparing the two groups after a period of seven months, researchers found that the mice injected with healthy brain tissue had normal brains while those injected with tissue that had beta-amyloid protein had developed plaques very similar to those found in people with Alzheimer's.

And since the beta-amyloid was injected into their stomachs, caused the plaque in their brains, one important question has been asked: Can Alzheimer's be transmitted in humans through blood transfusion?

<http://www.microbiologybytes.com/blog/2006/12/11/alzheimers-disease-and-prions/>

12/11/06

Alzheimer's Disease and Prions (amyloidosis infectious ?)

It has previously been believed that degenerative diseases such as Alzheimer's and Parkinson's diseases differ from prion diseases in that they are non-infectious. This conclusion was made after a number of experiments failed to show that post-mortem brain tissue samples from disease victims failed to transmit the disease to experimental animals (unlike prion diseases, where brain and other tissues are clearly infectious).

The clear difference between non-infectious amyloid diseases and infectious prion diseases just became a lot murkier with the publication of a recent paper in the journal Science (Exogenous induction of cerebral beta-amyloidogenesis is governed by agent and host. Meyer-Luehmann M, et al. Science. 2006 313: 1781- 1784). **By injecting amyloid-containing brain extracts from people with Alzheimer's disease into the brains of a strain of transgenic mice are predisposed to develop an Alzheimer's-like condition due to overproduction of the amyloid precursor protein, the researchers were able to induce similar pathological conditions in the animals**

When they denatured or depleted the amyloid protein in the extracts with antibodies, the ability of the extract to cause disease was reduced or abolished. In addition, immunization of the host animal against the amyloid protein also prevented transmission of the condition. Most strikingly of all, the phenotype of the disease induced in experimental animals depended on both the host and the source of the agent, suggesting the existence of polymorphic amyloid strains with varying biological activities. This is highly reminiscent of prion strains, and has never been observed before.

There is currently no evidence that amyloid diseases are transmissible between humans in the same sense as prion diseases, but these similarities between the two clearly related types of disease could shed light on the origins of Alzheimer's disease, which is poorly understood.

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Science 12 November 2010:

Vol. 330, no. 6006, pp. 918 - 919

[Prev](#) | [Table of Contents](#) | [Next](#)

DOI: 10.1126/science.1198314

Perspectives

Medicine:

Prion-Like Behavior of Amyloid- β

Jungsu Kim and David M. Holtzman

Can certain neurodegenerative diseases be transmitted between humans by an infectious agent? The discovery that protein particles called prions can enter healthy mammals, including humans, and trigger a cascade of endogenous protein misfolding associated with bovine spongiform encephalopathy ("mad cow disease") and Creutzfeldt-Jakob disease, certainly demonstrates this in prion diseases.

Remarkably, neuronal proteins such as tau, α -synuclein, and polyglutamine aggregates, which are causally implicated in the neurodegenerative disorders Alzheimer's disease, Parkinson's disease, and Huntington's disease, respectively, can be released from donor cells and taken up by neighboring acceptor cells. Moreover, treatment with exogenous misfolded neuronal proteins, such as tau, can trigger the misfolding and aggregation of their properly folded endogenous counterparts in host cells and animals (1). Besides prions, there is yet no evidence that other neurodegenerative diseases associated with protein misfolding are transmissible between humans by an infectious agent. But on page 980 in this issue, Eisele *et al.* (2) report that peripherally injected (outside the brain) mouse brain lysates containing aggregates of amyloid- β (A β)—the peptide that induces the formation of debilitating brain plaques in Alzheimer's disease—causes plaque-associated pathological changes in the brains of recipient mice. This has implications for a pathogenic mechanism reminiscent of prion transmission.

<http://www.sciencemag.org/cgi/content/full/330/6006/889-q> ++

Science 12 November 2010:

Vol. 330. no. 6006, p. 889

[Prev](#) | [Table of Contents](#) | [Next](#)

DOI: 10.1126/science.330.6006.889-q

This Week in Science

Infectious Amyloid?

Patients with Alzheimer's disease have characteristic lesions in the brains associated with masses of polymerized protein called β -amyloid. Recently, evidence from mouse models of Alzheimer's disease shows that brain extracts containing β -amyloid can "infect" otherwise healthy animals when injected directly into their brains. Eisele *et al.* (p. 980, published online 21 October; see the Perspective by [Kim and Holtzman](#)) extend these findings to show that when mice are injected in other parts of their bodies with similar brain extracts after several months, they also develop amyloidosis within their brains.

E-mail: holtzman@neuro.wustl.edu

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<http://www.barchester.com/Healthcare-News/Dementia-charity-funds-protein-research/376/3754>

Dementia charity funds protein research

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Healthcare News

13/10/2010

University of Leeds scientists have received funding to research dementia proteins. A grant has been given to scientists at the University of Leeds to begin a major study into the development of dementia.

The researchers have been awarded £244,926 courtesy of the Alzheimer's Research Trust, which has collected the money from numerous supporter donations.

This research will investigate the relationship between

two proteins - amyloid and prion. Amyloid is known to be a factor in the onset of Alzheimer's disease, but it is not known why it attaches to prion before inflicting its damage.

[Infectious Alzheimer's disease? Roland Riek. News and Views. Nature 444, 429-431 2006.](#)

.....

<http://www.nature.com/nature/journal/v444/n7118/full/444429a.html>

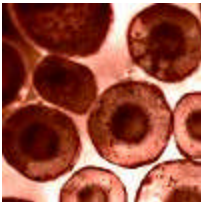
Nature **444**, 429-431 (23 November 2006) | doi:10.1038/444429a;
Published online 22 November 2006

Search Pubmed for

Roland Riek

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Membrane-associated Protein Expression



Cell biology: Infectious Alzheimer's disease?
Roland Riek¹

Top of page

Abstract

Accumulation of organized, self-polymerizing protein aggregates is a hallmark of Alzheimer's disease and infectious prion diseases. The similarities between these conditions may be even closer than that.

Amyloid fibrils are malicious. These insoluble, highly organized protein aggregates are associated with devastating disorders such as Alzheimer's and Parkinson's diseases, type II diabetes and the prion (proteinaceous infectious particle) diseases that include Creutzfeldt–Jakob and mad cow diseases¹.

Roland Riek is in the Department of Structural Biology, Salk Institute for Biological Studies, 10010 North Torrey Pines Road, La Jolla, California 92037, USA.

Email: riek@salk.edu

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Published March 2010

<http://www.plospathogens.org/article/info:doi%2F10.1371%2Fjournal.ppat.1000800>

Fatal Transmissible Amyloid Encephalopathy: A New Type of Prion Disease Associated with Lack of Prion Protein Membrane Anchoring

Bruce Chesebro^{1*}, Brent Race¹, Kimberly Meade-White¹, Rachel LaCasse¹, Richard Race¹, Mikael Klingeborn¹, James Striebel¹, David Dorward², Gillian McGovern³, Martin Jeffrey³

1 Laboratory of Persistent Viral Diseases, Rocky Mountain Laboratories, National Institute of Allergy and Infectious Diseases, Hamilton, Montana, United States of America, **2** Electron Microscopy Section, Research Technology Branch, Rocky Mountain Laboratories, National Institute of Allergy and Infectious Diseases, Hamilton, Montana, United States of America, **3** VLA (Lasswade), Penicuik, Scotland, United Kingdom

Brain tissue of transgenic mice had high amounts of infectivity, and histopathology showed dense amyloid PrPres plaque deposits without gray matter spongiosis. In contrast, infected non-transgenic mice had diffuse non-amyloid PrPres deposits with significant gray matter spongiosis. Brain graft studies suggested that anchored PrPsen expression was required for gray matter spongiosis during prion infection.

Furthermore, electron and light microscopic studies in infected transgenic mice demonstrated several pathogenic processes not seen in typical prion disease, including cerebral amyloid angiopathy and ultrastructural alterations in perivascular neuropil. These findings were similar to certain human familial prion diseases as well as to non-prion human neurodegenerative diseases, such as Alzheimer's disease.

Sent: Saturday, May 15, 2010 12:33 PM

Subject: alz 2010 UK PRION DISORDERS: AD PD CJD & Motor Neurone Disease - PROTEIN CANCERS - metals manganese copper aluminum mercury -pesticides

http://drmyhill.co.uk/wiki/Prion_disorders:_Alzheimer's_Disease:_Parkinson's_Disease:_Creutzfeldt-Jacob's_Disease_%26_Motor_Neurone_Disease

Prion disorders: Alzheimer's Disease; Parkinson's Disease; Creutzfeldt-Jacob's Disease & Motor Neurone Disease

From DoctorMyhill

We are currently seeing an epidemic of these conditions - the number of people suffering from it is increasing fast. Not my words but the words of Professor Colin Pritchard, professor of epidemiological medicine at Southampton University. They are an inevitable part of Western lifestyles and diets high in sugar and refined carbohydrate. Indeed Alzheimer's has been dubbed "Diabetes of the brain".

What are prion disorders?

I have no difficulty with the concept of prion disorders. **I think of prion disorders as protein cancers.** Prions are proteins which are normally present in the body and perform essential functions. However, if they come into contact with a particular toxin or heavy metal or

another twisted prion (rotten apple effect), then they too twist and distort. When they twist in such a way that they cannot be broken down by the body enzyme systems, they cause problems because the body cannot break them down so it dumps them. Pathologically this is known as amyloid. This results in deposition of these indigestible proteins and this can be anywhere in the body.

.....

alzheimer's PRUSINER AGUZZI STRITTMATTER - prions & amyloid beta plaques in neural tissue

<http://www.sociocide.com/forums/showthread.php?t=54993>

Prions complicit in Alzheimer's disease Supposedly harmless version plays a role in neuron malfunction

By [Laura Sanders](#)

[March 28th, 2009: Vol.175 #7](#) (p. 10)

Text Size

Not only did Prusiner establish a protein-based mechanism for the disease, but two years later he also purified the protein involved. Toxic prions were discovered to be an evil doppelganger of a naturally occurring protein, which purpose is unknown, but thought to have a basis in the maintenance of memory and certain stem cells. The toxic protein is misfolded and by nature of its poor shape induces similar proteins to bind and form insoluble clumps of protein called amyloid-beta plaques in neural tissue. This could explain its apparent ability to reproduce without a set of nucleic acid instructions and its long latency period.

Recent research has connected these plaques with a wide range of diseases, including the big one: Alzheimer's disease. Researchers Adriano Aguzzi and Stephen Strittmatter have published a study of the damaging effects of smaller, semi-soluble plaques on neurons in mice. They showed that the prion proteins are necessary for the damaging effects of the semi-soluble plaques. "Researchers removed the prion protein middleman from mice and examined brain slices. When the team washed A-beta oligomers* over the brain slices, the oligomers no longer had an effect on cell activity in the hippocampus." In a similar study, other researchers got the same results using an antibody primed to block the section of prion protein that binds to the A-beta oligomer. Without the prion proteins the damaging effects of the disease weren't seen. "Blocking prion protein binding may be a new therapeutic target for Alzheimer's disease. Get rid of the prion

protein middleman, or its ability to bind A-beta oligomers, and get rid of the disease, said Strittmatter. "

“Prion protein, notorious for causing the brain-wasting mad cow and Creutzfeldt-Jakob diseases, may also be a coconspirator in Alzheimer’s disease, a new study in mice suggests.

In mad cow and Creutzfeldt-Jakob diseases, misshapen prion proteins do the damage. But the new paper, appearing February 26 in Nature, offers evidence that the harmless version of the prion protein assists the amyloid-beta protein responsible for brain cell death in Alzheimer’s disease.

“It’s pretty sensational,” comments Adriano Aguzzi, a neuropathologist at the University of Zurich. “What’s tremendously electrifying is that prion protein may be a genetic sensor for extremely toxic, small concentrations of A-beta.”

A-beta proteins can travel alone or in groups in the brain. On their own, A-beta proteins are harmless. Massive, insoluble clumps of A-beta, known as plaques, are probably harmless, too, says study coauthor Stephen Strittmatter, a neuroscientist at Yale University. These plaques may be a gravestone marker of dead brain cells but are probably not the killer. Instead, smaller, soluble clumps of 50 to 100 A-beta proteins, known as oligomers, are the most likely suspect, Strittmatter says.

Earlier studies have shown that mice with A-beta oligomers can’t remember how to get through a maze as quickly as mice without A-beta oligomers. Such oligomers prevent cross-talk between certain brain cells in the hippocampus of mice, which helps explain the loss of learning and memory functions in Alzheimer’s disease.

But how these A-beta oligomers cause cellular mayhem is a mystery. The oligomers are toxic to cells at very low concentrations, so it’s likely that specific proteins are exquisitely tuned to recognize the A-beta proteins. “What’s been unclear is if A-beta acts on cells directly or if it acts through cell surface receptors, where it maybe corrupts the cell in some way,” comments Lennart Mucke, a neuroscientist from the Gladstone Institute of Neurological Disease in San Francisco and the University of California, San Francisco, who wrote a commentary in the same Nature issue.

Strittmatter and his colleagues searched for proteins embedded in the outer membrane of cells that might sense the dangerous amyloid-beta oligomers. After screening 225,000 possible mouse proteins, only one

specifically grabbed on to the human form of A-beta: the prion protein. The protein bound to oligomers but not to single A-beta proteins.

The role of harmless prion protein, which is prevalent in the brain and peripheral tissues of healthy people and animals, has been a mystery. “Everybody and his brother have been trying to find the normal function of prion protein,” Aguzzi says.

Earlier reports suggest that the protein may help maintain the brain’s white matter and brain cell formation, and may have a role in sensing smells. Even so, Aguzzi says, the matter is far from settled. “I never had the feeling that we’ve come to the bottom of [prion protein’s] function,” Aguzzi says. But prion protein’s new job as an A-beta oligomer sensor may shed light on how A-beta proteins can damage brain cells.

In the new study, researchers removed the prion protein middleman from mice and examined brain slices. When the team washed A-beta oligomers over the brain slices, the oligomers no longer had an effect on cell activity in the hippocampus. The researchers got the same results when an antibody blocked the 11 amino acids of prion protein required for A-beta binding: no harmful A-beta effects. These “striking” results make the case that prion proteins are crucial for A-beta–induced damage, Mucke says.

Blocking prion protein binding may be a new therapeutic target for Alzheimer’s disease. Get rid of the prion protein middleman, or its ability to bind A-beta oligomers, and get rid of the disease. “In many ways it may be better than addressing A-beta levels,” which are difficult to reduce completely, Strittmatter says.

The research is in very early stages. “Every new discovery raises more questions than it answers,” Mucke says, and these findings are no exception. Researchers don’t yet know if prion protein and A-beta interact similarly in human Alzheimer’s disease, or if blocking the connection between prion protein and A-beta is effective or safe in humans.

“How A-beta makes neurons sick was a black box,” Strittmatter says. “This research helps us understand the first step of the process.””

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<http://www.stanford.edu/group/pandegroup/folding/FoldingFAQ.pdf>

Folding@Home is based at Stanford University and Stanford University Medical School and is funded by the National Institutes of Health and the National Science Foundation

*What are proteins and why do they "fold"? Proteins are biology's workhorses -- its "nanomachines." Before proteins can carry out their biochemical function, they remarkably assemble themselves, or "fold." The process of protein folding, while critical and fundamental to virtually all of biology, remains a mystery. **Moreover, perhaps not surprisingly, when proteins do not fold correctly (i.e. "misfold"), there can be serious effects, including many well known diseases, such as Alzheimer's, Mad Cow (BSE), CJD, ALS, and Parkinson's disease.***

*What happens if proteins don't fold correctly? Diseases such as Alzheimer's disease, cystic fibrosis, BSE (Mad Cow disease), an inherited form of emphysema, and even many cancers are believed to result from protein misfolding. **When proteins misfold, they can clump together ("aggregate"). These clumps can often gather in the brain, where they are believed to cause the symptoms of Mad Cow or Alzheimer's disease.***

<http://www.pnas.org/content/106/31/12571.extract>

AUGUST 4, 2009

Is Parkinson's disease a prion disorder?

1. [C. Warren Olanow](#)^{a,1} and
2. [Stanley B. Prusiner](#)^b

This Article

1. Published online before print July 28, 2009, doi:
10.1073/pnas.0906759106 *PNAS August 4, 2009 vol. 106*
no. 31 12571–12572

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^bInstitute for Neurodegenerative Diseases and Department of Neurology, University of California, San Francisco, CA 94143

In this issue of PNAS, Desplats et al. (1) demonstrate that nerve cells that overexpress tagged α -synuclein can transmit the protein to neural stem cells in both in vitro and in vivo models. This important study could explain the remarkable finding that human embryonic dopamine nerve cells implanted into the striatum of patients with Parkinson's disease (PD) develop PD pathology with loss of dopamine markers and classic Lewy bodies (2, 3). It also provides insight into how α -synuclein pathology might sequentially spread throughout the nervous system in PD.

PD is an age-related, neurodegenerative disease that affects approximately one million persons in the United States. Pathologically, the disease is characterized by a loss of dopamine neurons in the substantia nigra pars compacta coupled with proteinaceous inclusions in nerve cells and terminals, known as Lewy bodies and Lewy neurites, respectively. PD pathology is also known to affect nondopamine neurons in the upper and lower brainstem, olfactory system, cerebral hemisphere, spinal cord, and autonomic nervous system. The cause of cell death in PD is not known, **but proteolytic stress with the accumulation of misfolded proteins has been implicated (4).**

That the aberrant accumulation of proteins might feature in the pathogenesis of PD is a reasonable posit, given that Lewy bodies, the hallmark of the disease, are composed of a variety of aggregated proteins. Among these, α -synuclein has attracted particular attention. α -Synuclein is a 140-aa synaptic protein that is unstructured in aqueous buffers, but adopts an α -helical-rich conformation when bound to membranes (5), and can acquire a β -sheet-rich structure that readily polymerizes into fibrils when present in high concentration or in a mutant form (6). ...

Dr. Stanley Prusiner won the The Nobel Prize in Physiology or Medicine 1997

"for his discovery of Prions - a new biological principle of infection"

.....

<http://www.biotechniques.com/news/Size-matters-in-prion-diseases-say-researchers/biotechniques-305962.html>

When prions enter a mammalian brain, they can cause a variety of neurodegenerative diseases such as Parkinson's disease.

Size matters in prion diseases, say researchers

11/15/2010

Julie Manoharan

Researchers have found a wide variation in the size of prion aggregates, creating heterogeneity in prion populations.



Researchers at Brown University have found that it is not the amount of prion aggregates, but the size of those aggregates that determines the severity of prion diseases. The findings suggest that certain aggregate sizes may be preferable to others, and shed light on prion transmission.

Prions are misfolded proteins—often protein-based infectious agents—that perpetuate that misfolded state in other proteins in an organism. **When prions enter a mammalian brain, they can cause a variety of neurodegenerative diseases such as Parkinson's disease.**

<http://opa.yale.edu/news/article.aspx?id=7579>

Prions, Not Plaques, Cause Memory Loss in Mice With Alzheimer's

Published: May 20, 2010



New Haven, Conn. — Prion proteins appear to be the key culprit in the loss of memory in mice with brains riddled with plaques associated with Alzheimer's Disease, Yale scientists report.

The findings reported in the Journal of Neuroscience show that common cellular prion proteins – not the beta amyloid plaques themselves – are needed to produce the cognitive impairments associated with Alzheimer's.

“Cellular prion protein is the essential mediator in Alzheimer's that leads to memory dysfunction and reduced survival in mice,” said [Stephen Strittmatter](#), the Vincent Coates Professor of Neurology, professor of neurobiology and senior author of the study.

Scientists have long debated whether the plaques associated with Alzheimer's caused the devastating dementia that is the hallmark of the disease or were simply a side-effect of the disease process. The latter view has been supported by autopsy results that show the presence of Alzheimer-like plaques in brains of individuals who had suffered no memory loss or cognitive impairment.

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• <http://www.newsmax.com/FastFeatures/vegetarian-meat-diet-eat/2010/11/19/id/377642>

How Eating Less Red Meat Can Change Your Life

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Friday, 19 Nov 2010 04:24 PM

Article Font Size [+](#) [-](#)

Let's take a look at the risks associated with eating red meat:

1. Eating red meat increases the chance of early death. People who consume four ounces or more of red meat everyday, have a 30 percent increased chance of dying due to heart problems and cancer. Processed meats also seem to double the risk.

2. There is a very strong probability that Mad Cow Disease, which is caused by prions (infectious proteins) found in meat, is responsible for the increased incidence of Alzheimer's disease. Although there is no proof, researchers have stated that many cases of Mad Cow Disease in humans might have been misdiagnosed as Alzheimer's disease over the last few years.

3. The saturated fat content in meat is also responsible for a higher incidence of heart disease, atherosclerosis, and arteriosclerosis.

28 year old man with iCJD and Alzheimer's – 23 year incubation

<http://jnnp.bmj.com/content/77/3/413.abstract>

J Neurol Neurosurg Psychiatry 2006;77:413-416 doi:10.1136/jnnp.2005.070805

Short report

Alzheimer-type neuropathology in a 28 year old patient with iatrogenic Creutzfeldt-Jakob disease after dural grafting

[M Preusser](#)¹,

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[E Gelpi](#)^{1,2},

[M Eiler](#)³,

[G Broessner](#)⁴,

[E Schmutzhard](#)⁴,

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Received 27 April 2005

Accepted 9 August 2005

Revised 24 June 2005

Abstract

We report the case of a 28 year old man who had received a cadaverous dura mater graft after a traumatic open skull fracture with tearing of the dura at the age of 5 years.

A clinical suspicion of Creutzfeldt-Jakob disease (CJD) was confirmed by a brain biopsy 5 months prior to death and by autopsy, **thus warranting the diagnosis of iatrogenic CJD (iCJD) according to WHO criteria.** Immunohistochemistry showed widespread cortical depositions of disease associated prion protein (PrP^{Sc}) in a synaptic pattern, and western blot analysis identified PrP^{Sc} of type 2A according to Parchi *et al.*

Surprisingly, we found Alzheimer-type senile plaques and cerebral amyloid angiopathy in widespread areas of the brain. Plaque-type and vascular amyloid was immunohistochemically identified as deposits of beta-A4 peptide. CERAD criteria for diagnosis of definite Alzheimer's disease (AD) were met in the absence of neurofibrillar tangles or alpha-synuclein immunoreactive inclusions. There was no family history of AD, CJD, or any other neurological disease, and genetic analysis showed no disease specific mutations of the prion protein, presenilin 1 and 2, or amyloid precursor protein genes.

This case represents (a) the iCJD case with the longest incubation time after dural grafting reported so far, (b) the youngest documented patient with concomitant CJD and Alzheimer-type neuropathology to date, (c) the first description of Alzheimer-type changes in iCJD, and (d) the second case of iCJD in Austria. Despite the young patient age, the

Alzheimer-type changes may be an incidental finding, possibly related to the childhood trauma

SWEDISH STUDY – IATROGENIC TRANSMISSION OF sCJD (question: Considering the present Alzheimer’s Disease (AD) epidemic in US (5.3 million victims, new one every 70 seconds,) – could iatrogenic transmission be a pathway of risk for AD ?)

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2790765/>

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Neuroepidemiology. 2008 November; 31(4): 229–240.
Published online 2008 October 9. doi: [10.1159/000163097](https://doi.org/10.1159/000163097).

Excerpts:

“Methods

From Danish and Swedish registries we selected 167 definite and probable sCJD cases (with onset between 1987 and 2003) and 3,059 controls (835 age-, sex-, and residence-matched, and 2,224 unmatched). Independent of case/control status, surgical histories were obtained from National Hospital Discharge Registries. Surgical procedures were categorized by body system group and lag time to onset of sCJD. Exposure frequencies were compared using logistic regression”

“Surgery of various body systems, including peripheral vessels, digestive system and spleen, and female genital organs, was significantly associated with increased sCJD risk.”

“Conclusions

A variety of major surgical procedures constitute a risk factor for sCJD following an incubation period of many years. A considerable number of sCJD cases may originate from health care-related accidental transmission.” Overall, the present study indicates that a considerable proportion of sCJD may constitute a health care-related disorder, accidentally transmitted during surgery. While this has been suggested before [7,8,9,10], the present study is unique because of the unbiased assessment of exposure histories for decades before disease onset, randomly chosen controls, and strict lag time measurement.

What then are the potential implications for public health?

To conclude, we provide evidence to indicate that surgery, acting with long incubation periods, has constituted a risk factor for sCJD in Sweden and Denmark. The associations may have implications for precautionary measures and surveillance.”

“

http://www.upi.com/Science_News/2010/03/08/New-form-of-prion-disease-discovered/UPI-39271268070249/

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New form of prion disease discovered
Published: March. 8, 2010 at 12:44 PM

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- [Scientists convert proteins into prions](#)

http://www.upi.com/Science_News/2010/02/08/Scientists-convert-proteins-into-prions/UPI-96651265642305/

Scientists convert proteins into prions

Published: Feb. 8, 2010 at 10:18 AM

COLUMBUS, Ohio, Feb. 8 (UPI) -- U.S. scientists say they have converted normal protein into a prion -- an abnormal protein that causes brain disease in humans, sheep and cows.

"The major thing we showed in this study is that the infectious agent in these diseases is truly a misfolded protein," said Ma. "We folded recombinant mouse prion protein into its normal shape, then converted it into a different conformation and showed that when it infected an animal, it caused full-blown prion disease."

- ['Lifeless' prions able to evolve](#)
- [Study finds origins of prion disease gene](#)
- [Prion diseases cause iron imbalance](#)

BETHESDA, Md., March 8 (UPI) -- U.S. scientists say they've discovered a new form of prion disease that damages brain arteries and might lead to new Alzheimer's disease therapies.

*The researchers at the National Institute of Allergy and Infectious Diseases studying how prions -- infectious protein particles -- destroy the brain said they observed a new form of the disease that doesn't cause the sponge-like brain deterioration typically seen in prion diseases. **Instead, it resembles a form of human Alzheimer's disease, cerebral amyloid angiopathy, that damages brain arteries.***

"The study results ... are similar to findings from two newly reported human cases of the prion disease Gerstmann-Straussler-Scheinker syndrome," the NIH said, adding **the finding represents a new mechanism of prion disease brain damage, according to Dr. Bruce Chesebro, chief of the Laboratory of Persistent Viral Diseases at the institute's Rocky Mountain Laboratories.**

Prion diseases -- also known as transmissible spongiform encephalopathies -- include mad cow disease, in cattle; scrapie in sheep; sporadic Creutzfeldt-Jakob disease in

humans and chronic wasting disease in deer, elk and moose. All primarily damage the brain.

The findings in the study that involved laboratory **mice indicate prion diseases can be divided into two groups: those with plaques that destroy brain blood vessels and those without plaques that lead to the sponge-like damage to nerve cells, Chesebro said.**

Scientists from the Veterinary Laboratories Agency in Scotland also participated in the study that is reported in the journal PLoS Pathogens.

<http://followmehere.com/tag/neuroscience/> MARCH 28, 2010

Prions Complicit In Alzheimer's Disease

Posted by FmH under Uncategorized | Tags: [Alzheimer's](#), [neuroscience](#), [prions](#) |

Amyloid plaques in Alzheimer's brain tissue

This may be a blockbuster finding:

"Prion protein, notorious for causing the brain-wasting mad cow and Creutzfeldt-Jakob diseases, may also be a coconspirator in Alzheimer's disease, a new study in mice suggests.

In mad cow and Creutzfeldt-Jakob diseases, misshapen prion proteins do the damage. But the new paper, appearing February 26 in Nature, offers evidence that the harmless version of the prion protein assists the amyloid-beta protein responsible for brain cell death in Alzheimer's disease."

The prion protein — a role for which in the brain has been a headscratcher for neuroscientists — acts as the middleman in

amyloid-beta binding to the cell membrane. This may hint at a new therapeutic strategy for Alzheimer's prevention.

'Get rid of the prion protein middleman, or its ability to bind A-beta oligomers, and get rid of the disease. "In many ways it may be better than addressing A-beta levels," which are difficult to reduce completely, [one of the investigators] says.' via [Science News](#).

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http://www.basqueresearch.com/berria_irakurri.asp?Berri_Kod=2685&hi
zk=1
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Saturday, April 24, 2010

[New connection between Alzheimer's and prionic illnesses discovered](#)

2010/4/23

New connection between Alzheimer's and prionic illnesses discovered

Researchers at the Basque Country's CIC bioGUNE Centre for Cooperative Research and the University of Texas Medical School at Houston (USA) have discovered the existence of a new interaction between Alzheimer's disease and prionic pathologies, fundamentally caused by the incorrect folding of proteins involved in such illnesses. The study has also been published in the Journal of Neuroscience.

The research, led by investigators at CIC bioGUNE and the University of Texas Medical School in Houston, was based on the premise that, despite the diversity of clinical symptoms associated with illnesses related to misfolding of proteins, there exists a great similarity which suggests that many of these ailments could have a significant relation at a mechanistic molecular level.

The principal aim of the study was to analyse the interaction of the incorrect folding of proteins involved in Alzheimer's disease and in prionic diseases.

To this end, prions were inoculated into transgenic rats used as a model for Alzheimer's disease, in which amyloid plaques are developed

The results showed a dramatic acceleration and exacerbation in both pathologies.

Concretely, the clinical signs of the prion illness in the transgenic rats appeared much more rapidly with the resulting increase in levels of incorrectly folded prionic protein in the brain. Likewise, a notable increase was observed in the deposits of the amyloid plaques so characteristic of Alzheimer's disease.

Histological and biochemical study showed the physical association between the two incorrectly folded proteins in the brain and in vitro experiments showed that incorrect folding of the proteins may be favoured heterologically **(i.e. the prionic protein favours incorrect folding of the Alzheimer plaque-forming protein) in vitro.**

This suggests, as a conclusion, a deep interaction between Alzheimer's disease and the prionic pathologies involved in the process of folding of proteins and could be a significant risk factor in the development of a second pathology.

This research may well have important implications for understanding the origin and progress of illnesses in which this phenomenon of the misfolding of proteins is involved.

The techniques used are common to both pathologies - prionic illnesses and Alzheimer's disease -, such as the inoculation of animal models, as well as histopathological and immunohistochemical studies, biochemical studies and studies of the in vitro replication of proteins.

Prionic illnesses

Prions are pathogenic agents responsible for transmissible spongiform encephalopathies (TSEs), also known as prionic illnesses. TSEs belong to the group of mortal neurodegenerative diseases that affect human beings and animals and for which there is currently no available therapy. These conditions may have a number of different origins: hereditary, sporadic (supposedly spontaneous) and infectious.

Scrapie, the disease affecting sheep and goats, is probably the oldest prionic illness.

Nevertheless, BSE (Bovine Spongiform Encephalopathy) is that which caught the attention of the public most, given its involvement in the generation of a new illness amongst humans and its proven transmission to most other species. Then there is the Creutzfeldt Jacob disease which, while having an annual rate of 1-2 cases per million inhabitants, it is still the big unknown, especially in the sporadic cases the origin of which is a mystery. In the Basque Country, a somewhat unusual situation exists, as it concentrates many of the total number of cases throughout the world of fatal familial insomnia, a human prionic illness of genetic origin.

Prions are probably one of the most intriguing pathogenic agents in nature, as its supposed composition relating it to a single protein and the appearance of clearly differentiated strains give them an unparalleled scientific value. Their replication mechanism similar to what could well be the development of diseases such as Alzheimer's or Parkinson's, amongst others, make them a unique pathogen. But, if to this we add that we do not yet know what a prion is, it makes it an irresistible object for study for researchers such as those at the Prions Laboratory of at the Proteomic Unit at CIC bioGUNE.

http://www.basqueresearch.com/berria_irakurri.asp?Berri_Kod=2685&hizk=I

.....
<http://alzheimers.infopop.cc/eve/forums/a/tpc/f/770108781/m/599300743>

NEW FORM OF PRION DISEASE – BRAIN DAMAGE SIMILAR TO AD - [Gerstmann-Straussler-Scheinker syndrome]

Posted March 10, 2010 10:00 PM
From Yahoo

Prion Disease in Mice May Help Advance Alzheimer's Research

FRIDAY, March 5 (HealthDay News) -- U.S. researchers have discovered a new form of **prion disease that doesn't act like related illnesses, such**

as mad cow disease, but instead causes brain damage similar to that produced by Alzheimer's disease.

It is not yet clear what the finding may mean for humans because the disease was found in mice, the study authors noted in the report published online March 5 in PLoS Pathogens.

However, the disease does seem to be similar to two newly reported cases of the prion disease known as Gerstmann-Straussler-Scheinker syndrome, according to the researchers from the U.S. National Institute of Allergy and Infectious Diseases (NIAID).

Prion diseases cause a number of unusual killer diseases, including mad cow disease, sporadic Creutzfeldt-Jakob disease and a kind of fatal insomnia, according to background information in a news release from NIAID.

In the new study, the researchers examined mice that were genetically engineered to process prion proteins in a unique way. Then they exposed them to a prion disease known as scrapie.

The mice didn't develop holes in the brain like those typically caused by prion diseases. Instead, they developed plaques that resembled a form of human Alzheimer's disease.

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feces may transmit fatal cheetah disease ++

<http://www.scientificamerican.com/article.cfm?id=feces-may-transmit-cheetah-disease>

A fatal, Alzheimer's-like disease that attacks cheetahs' internal organs and has impeded breeding of the cats in captivity may be spread by their feces. Researchers from Japan and China report in the journal *Proceedings of the National Academy of Sciences USA* that the disease, AA amyloidosis, was transmitted to

mice exposed to fecal proteins from a cheetah that died of it.

Thanks to inbreeding, cheetahs have greater susceptibility to diseases such as AA amyloidosis, which is among a group of disorders characterized by the accumulation tangles of misfolded protein called amyloid fibrils. Other diseases in the group include Alzheimer's and type 2 diabetes in humans as well as the prion (infectious protein) diseases such as scrapie in sheep, bovine spongiform encephalopathy (aka mad cow disease) and chronic wasting disease in deer and elk. In cheetahs amyloid fibrils build up in the spleen and liver, typically following an inflammatory stomach disease.

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<http://www.nsf.gov/pubs/2007/nsf0701/pdf/06.pdf>

P. 4

Determining the molecular structure of fibrils, a feat that had eluded researchers for decades, will ultimately help medical researchers understand and devise treatments for the more than two dozen human diseases associated with fibrils, including Alzheimer's, Parkinson's, and Huntington's diseases, as well as so-called prion diseases like mad cow.

http://www.madcow.org/Alzheimer_cjd.html#Dementia

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Dementia associated with a 216 base pair insertion in the prion protein gene

Duchen LW; Poulter M; Harding AE
Brain 116 (Pt 3): 555-67 (1993)

We report the clinical and neuropathological findings in a patient with a 216 base pair insertion in the prion protein (PrP) gene. She died aged 57 years after a 2.5-year illness characterized by falls, axial rigidity, myoclonic jerks and progressive dementia. There was no history of affected relatives. The pathological changes consisted of the deposition in cerebellum, basal ganglia and cortex of small plaques composed of variable amounts of amyloid and degenerative material which was associated with a marked macrophage reaction. The amyloid deposits in the cerebellum and basal ganglia gave a positive immunoperoxidase staining reaction for PrP.

In some places plaques bore a resemblance to senile neuritic plaques and in the hippocampus there were abundant typical neuritic plaques giving positive staining reactions for beta-amyloid protein and tau protein, but not PrP. There were few neurons bearing neurofibrillary tangles.

This is the first report of the neuropathological changes associated with this particular abnormality of the PrP gene and it seems to demonstrate a transition between the pathology of prion disease and that of Alzheimer's disease. The importance of PrP gene analysis to the understanding of neurodegenerative diseases is stressed.

Alzheimer's disease and CJD: overlap of pathogenic mechanisms.

DeArmond SJ

Curr Opin Neurol 6: 872-81 (1993)

This article compares beta-amyloid precursor protein (beta-APP) disorders exemplified by Alzheimer's disease (AD), with prion protein (PrP) disorders, exemplified by Creutzfeldt-Jakob disease (CJD) in humans and scrapie in animals. Although there are obvious differences in the etiology and pathogenesis of both sets of disorders, a remarkable number of similarities exist.

Both sets of disorders are characterized clinically by age-related sporadic and familial diseases. In both, an abnormal form of a neuronal membrane protein appears to play a key role in the pathogenesis: beta-A4 peptide in AD and PrPCJD in CJD. **Both beta-A4 and PrPCJD are amyloidogenic. Neuritic plaques characteristic of AD were once thought to be exclusively associated with beta-A4 amyloid; however, some pedigrees with familial prion disease produced neuritic plaques with PrP amyloid cores.**

Finally, beta-APP accumulation in skeletal muscle has been implicated in the age-related muscle disorder, inclusion body myositis. A similar myopathy has recently been discovered in transgenic mice expressing high levels of normal PrP. These similarities suggest that what is learned about one set of disorders may be applicable to the other.

<http://betaamyloidcjd.blogspot.com/2010/08/transcellular-spread-of-cytosolic.html>

Dr. Adriano Aguzzi, et als

The Transcellular Spread of Cytosolic Amyloids, Prions, and Prionoids

EXCERPTS

“There is mounting evidence (Clavaguera et al., 2009; Frost et al., 2009; Ren et al., 2009; Desplats et al., 2009; Luk et al., 2009) suggesting that the events sketched above, far from being confined to science-fiction and prion diseases (whose incidence in humans is

just z1/106/year), may underlie highly prevalent human diseases of the brain and many other organs.'

“Some prionoids may soon qualify for an upgrade to prion status. At least in select settings, amyloid A (AA) amyloidosis may exist as a truly infectious disease based on a self-propagating protein”

Furthermore, AA seeds are excreted with the feces, and AA amyloidosis is endemic in populations of cheetah (Zhang et al., 2008). It is therefore tantalizing to suspect that amyloid may entertain the complete life cycle of an infectious agent, including transmission by the orofecal and hematogenous route—similarly to enteroviruses and, perhaps, scrapie prions.

Alzheimer’s disease (AD) has long been suspected to be a transmissible disease, but these suspicions have never materialized in epidemiological studies. On the other hand, Mathias Jucker and Lary Walker observed that injection of the Ab peptide from human AD brains induced robust and convincing aggregation of Ab in transgenic mice overexpressing the Ab precursor protein, APP (Kane et al., 2000; Meyer-Luehmann et al., 2006). Jucker’s finding raises an epistemologically significant question: if aggregation depends on the introduction of seeds and on the availability of the monomeric precursor, and if amyloid represents the primordial state of all proteins (Chiti and Dobson, 2006), wouldn’t all proteins—under appropriate conditions— give rise to prionoids in the presence of sufficient precursor?

<http://emedicine.medscape.com/article/1168941-overview>

Prion-Related Diseases

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“NFTs are an essential feature of Alzheimer disease, but are also observed in other neurodegenerative conditions.”

“Cerebral amyloid angiopathy (CAA) is also an essential feature of Alzheimer disease. Both these variants of prionoses further link the pathogenesis of Alzheimer disease and the prion-related diseases.”

<http://www.sciencemag.org/cgi/content/short/326/5958/1337>

Science 4 December 2009:

Vol. 326, no. 5958, pp. 1337 - 1339

DOI: 10.1126/science.326.5958.1337

News Focus

Neurodegeneration:

Could They All Be Prion Diseases?

Greg Miller

Misfolded proteins called prions are the cause of several neurodegenerative disorders in humans and other animals. A recent flurry of papers has revived interest in the idea that such mechanisms may play a role in an even wider range of neurodegenerative disorders, including two of the most dreaded scourges of old age: Alzheimer's and Parkinson's diseases.

Such diseases almost certainly aren't contagious like true prion diseases are, at least in ordinary circumstances, but they may propagate through the nervous system in much the same way. Evidence from recent animal studies suggests that many of the misfolded proteins thought to play a central role in a wide range of neurodegenerative disorders can, like prions, "seed" the misfolding and aggregation of their normally folded kin. In some cases, these pathological protein clusters appear to propagate from cell to cell. Such a mechanism could help explain several puzzles—such as why some neurodegenerative disorders tend to spread from one part of the nervous system to another in a characteristic pattern, and why some researchers have found pathological protein deposits in fetal stem cells transplanted into the brains of Parkinson's patients.

<http://emedicine.medscape.com/article/1168941-overview>

Prion-Related Diseases

Author: Tarakad S Ramachandran, MBBS, FRCP(C), FACP, Professor of Neurology, Clinical Professor of Medicine, Clinical Professor of Family Medicine, Clinical Professor of Neurosurgery, State University of New York Upstate Medical University; Chair, Department of Neurology, Crouse Irving Memorial Hospital

Coauthor(s): Arun Ramachandran, State University of New York Upstate Medical University

[Contributor Information and Disclosures](#)

Updated: Sep 21, 2009

<http://emedicine.medscape.com/article/1168941-overview>

Background

The prion diseases are a large group of related neurodegenerative conditions, which affect both animals and humans.¹ Included are Creutzfeldt-Jakob disease (CJD) and Gerstmann-Sträussler-Scheinker (GSS) in humans, bovine spongiform encephalopathy (BSE, or "mad cow disease") in cattle, chronic wasting disease (CWD) in mule deer and elk, and scrapie in sheep. These diseases all have long incubation periods but are typically rapidly progressive once clinical symptoms begin. All prion diseases are fatal, with no effective form of treatment currently; however, increased understanding of their pathogenesis has recently led to the promise of effective therapeutic interventions in the near future. . . .

"Prion diseases are unique in that they can be inherited, they can occur sporadically, or they can be infectious. The infectious agent in the prion disease is composed mainly or entirely of an abnormal conformation of a host-encoded glycoprotein called the prion protein. The replication of prions involves the recruitment of the normally expressed prion protein, which has mainly an alpha-helical structure, into a disease-specific conformation that is rich in beta-sheet. . . . snip . . .

- - “The prominent involvement of the brainstem often leads to symptoms suggestive of olivopontocerebellar degeneration. The pattern of inheritance is autosomal dominant and is caused by mutations of the PrP gene. The neuropathology of GSS is remarkable in that extensive and invariable amyloid deposition occurs, in addition to the typical spongiform change, gliosis, and neuronal loss.
 -
 - Interestingly, in several kindreds of GSS, extensive neurofibrillary tangle (NFT) formation is found.⁵³ **NFTs are an essential feature of Alzheimer disease, but are also observed in other neurodegenerative conditions.**
 -
 - **Another variation of autosomal dominantly inherited human prionosis has been termed prion protein congophilic angiopathy (ie, prion protein cerebral amyloid angiopathy [PrP-CAA]), which is characterized by cerebral vessel amyloid deposition and the presence of NFT.⁵⁴ Cerebral amyloid angiopathy (CAA) is also an essential feature of Alzheimer disease. Both these variants of prionoses further link the pathogenesis of Alzheimer disease and the prion-related diseases.”**

25th Feb 2009 ALZHEIMER'S - PRION CAUSES AMYLOID PLAQUE BUILD UP -
 JOURNAL - NATURE
 J. Lauren et al (2009) Nature vol 457, p 1128 to 1132

<http://www.thenakedscientists.com/HTML/content/news/news/1635/>

Alzheimer's prion protein clue

More than 20 million people around the world are affected by Alzheimer's disease, a degenerative brain condition that is currently incurable. We know that many of the effects of the disease are due to the buildup of a protein called amyloid-beta, which makes lumps, called plaques, in the brain.

But until now it hasn't been clear exactly how amyloid protein starts to build up in brain cells, or the root cause of the illness. But **this week, scientists in the US have discovered that the buildup of amyloid might be aided by a rogue protein – the prion protein** cells in the brain and helping to grow new neurons. **But sometimes PrP is found in a different shape, or conformation, and this is where the trouble starts, as it causes severe problems in the brain. It's high levels of the bad form of PrP that lead to CJD**

The prion protein, PrP, is found in many different cells and sits in the membrane that surrounds cells. Normally, it does a useful job helping brain cells to respond to changes in the environment around them, as well as controlling the immune.

Writing in this week's edition of the journal Nature, the researchers discovered that amyloid-beta can stick to the normal form of the prion protein, and this might be what causes amyloid to build up in brain cells. Importantly, they discovered that little groups of amyloid are more likely to stick to the prion protein than single amyloid molecules, suggesting that it's important for building up amyloid plaques, and could be a key step in Alzheimer's.

The scientists went on to look at samples of mouse brains, particularly looking at the hippocampus – the part of the brain that's involved in learning and memory, which is badly affected in Alzheimer's. They found that in brain samples from normal mice, the buildup of amyloid protein blocked a process called long term potentiation – which is basically how the brain builds memory. But in samples from mice that lacked the prion protein, amyloid didn't cause problems with long term potentiation. **So this shows that the prion protein is a key link in the chain.**

This discovery is pretty exciting because it gives us a new angle for Alzheimer's treatments. **Perhaps if researchers could develop drugs that block the interaction between amyloid and the prion protein, this might be potential way to prevent the plaques building up, or reduce their effects on the brain.**

But there's a lot we don't know. For example, we don't know if the prion protein changes shape once it has stuck to amyloid – does it stay in the normal conformation, or change to the bad version? And it's clear that the prion protein isn't the whole story, because if you get rid of the prion proteins altogether, you only reduce the binding of amyloid to brain cells by about 50%. But it's certainly a good start, and an exciting new lead for future research.

References

- J. Lauren et al (2009) Nature vol 457, p 1128 to 1132

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<http://www.lifeinitaly.com/node/16574>

PROTEIN ROLE IN ALZHEIMER'S

NEW ITALIAN STUDY CONFIRMS PROTEIN ROLE IN ALZHEIMER'S

(ANSA) - Rome, January 14, 2010 - **A team of Italian scientists has confirmed the critical role played by a group of amino acids in the brains of Alzheimer's disease patients, according to a new study. The research looked at the impact of amyloid beta amino acid chains, thought to be the main component responsible for plaque build-ups in the brain of those suffering from the disease.**

Although scientists have long known of the role these amino acids play in Alzheimer's, the research by the Mario Negri Institute of Milan explored the link between beta amyloid proteins and prion proteins, which cause mad cow disease (BSE) and its human variant Creutzfeldt-Jakob disease (CDJ).

The team first applied small soluble aggregates of the beta amyloid protein, similar to those found in Alzheimer's patients onto the brain of laboratory animals. The application of these aggregates, known as oligomers, was found to cause selective memory loss among the animals, the report authors noted.

http://scienceblogs.com/notrocketscience/2009/02/fishing_expedition_reveals_unexpected_link_between_alzheimer.php

Fishing expedition reveals unexpected link between Alzheimer's and prion diseases

Category: Brain • Medicine & health • Mental Health • Neuroscience

Posted on: February 25, 2009 1:00 PM, by Ed Yong

Alzheimer's disease is the most common form of dementia in the world, affecting more than 26 million people. Creutzfeldt-Jacob disease (CJD), another affliction is far less common, but both conditions share many of the same qualities. They are fatal within a few years of diagnosis, they are incurable and they involved the crippling degeneration of the brain's neurons. **Now, a group of Yale researchers have discovered that the two diseases are also linked by a pair of critical proteins.**

Look into the brain of someone with Alzheimer's disease and you will see large, insoluble "plaques" sitting between nerve cells. They consist of a protein fragment (or "peptide") called amyloid-beta, accumulating in its thousands. These plaques are a hallmark of the disease, but even before they have formed, amyloid-beta peptides have already begun to cluster in small soluble groups. Even at this stage, they can impair memory, degrading the connections between separate neurons.

Juha Lauren wanted to work out how exactly clusters of amyloid-beta wreak havoc in neurons before they form plaques. In particular, he was after the identity of its molecular accomplices. Many proteins work their will in a cell by attaching to other proteins called receptors. To see if amyloid-beta does the same, Lauren's team went fishing for receptors.

They created a synthetic version of the amyloid-beta peptide and connected it to a molecule called biotin - these were their hooks. Lauren lowered them into a massive pool of different proteins found in the brains of mice; if one of those was a receptor for amyloid-beta, it should take the bait and stick to it. As a rod, he used beads covered in a molecule called avidin, which sticks very strongly to biotin. The beads attracted biotin, which was stuck to amyloid-beta, which was in turn bound to its receptor.

From hundreds of thousands of proteins, their fishing trips pulled out just one that stuck to amyloid-beta, and it's a familiar one - the prion protein. Incorrectly folded versions of this protein (PrP^{Sc}) are the culprits behind diseases like CJD, mad cow disease and scrapie. And now it seems that the normal, correctly folded version (PrP^C) plays a role in Alzheimer's disease too, by acting as the receptor for amyloid-beta. It's the accomplice through which amyloid-beta clusters work their damaging effects on neurons.

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<http://www.sciencemag.org/cgi/content/abstract/302/5646/814>

Science 31 October 2003:

Vol. 302. no. 5646, pp. 814 - 818

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DOI: 10.1126/science.1087348

Review

Games Played by Rogue Proteins in Prion Disorders and Alzheimer's Disease

Adriano Aguzzi^{1*} and Christian Haass^{2*}

The incidence of Alzheimer's disease (AD) and that of prion disorders (PrD) could not be more different. One-third of octogenarians succumb to AD, whereas Creutzfeldt-Jakob disease typically affects one individual in a million each year. **However, these diseases have many common features impinging on the metabolism of neuronal membrane proteins: the amyloid precursor protein APP in the case of AD, and the cellular prion protein PrP^C in PrD. APP begets the A β peptide, whereas PrP^C begets the malignant prion protein PrP^{Sc}. Both A β and PrP^{Sc} are associated with disease, but we do not know what triggers their accumulation and neurotoxicity. A great deal has been learned, however, about protein folding, misfolding, and aggregation; an entirely new class of intramembrane proteases has been identified; and unsuspected roles for the immune system have been uncovered. There is reason to expect that prion research will profit from advances in the understanding of AD, and vice versa.**

¹ Institute of Neuropathology, University Hospital of Zurich, Schmelzbergstrasse 12, CH-8091 Zurich, Switzerland.

² Department of Biochemistry, Adolf-Butenandt-Institute, Laboratory for Alzheimer's and Parkinson's Disease Research, Ludwig-Maximilians-University, Schillerstrasse 44, Munich, Germany.

Adriano Aguzzi Stephen Strittmatter

<http://mednews.wustl.edu/news/page/normal/15213.html>

Family's inherited condition links prion diseases, Alzheimer's

By Michael Purdy

Dec. 8, 2009 -- A laboratory connection between Alzheimer's disease and brain-wasting diseases such as the human form of mad cow disease has moved into the clinic for what is believed to be the first time, manifesting itself in the brains of patients with a rare inherited disorder.

In three cases from an Illinois family, researchers at Washington University School of Medicine in St. Louis report that brain regions harmed by an inherited form of Creutzfeldt-Jakob disease (CJD) also have amyloid plaques identical to those found in the same brain areas in Alzheimer's patients.

The finding adds to other, earlier evidence suggesting that the misfolded protein believed to cause CJD, known as a prion, appears to play a role in the Alzheimer's disease process.

"This interplay between amyloid and the prion protein raises questions about whether these diseases are really all that different, and whether there are common pathways involved in both conditions that can provide an avenue for new treatments," says lead author Nupur Ghoshal, M.D., Ph.D., an investigator at Washington University's Alzheimer's Disease Research Center (ADRC).

Ghoshal's research, published in Archives of Neurology, began with the autopsy of a patient who died from inherited CJD more than two decades ago after being followed clinically by senior author John C. Morris, M.D., now the Harvey A. and Dorismae Hacker Friedman Distinguished Professor of Neurology and director of the ADRC. The autopsy revealed not only the expected brain changes inflicted by CJD but also amyloid brain plaques, even though the patient was younger than the age at which Alzheimer's typically occurs.

CJD and other spongiform encephalopathies rapidly plunge patients into dementia, causing death in a few months to years. They have been associated with rare genetic mutations typically found in a handful of ethnic groups that includes some Jewish sects and some Eastern European lineages. In recent decades, sporadic cases of CJD-like diseases have been associated with

consumption of brain and spinal tissues from cows with a brain-wasting condition called mad cow disease. These cases helped spur development of a theory that a misfolded protein known as a prion causes inherited and transmissible forms of diseases like CJD.

Healthy organisms normally make the prion protein, which in its regular configuration contributes in a yet-to-be-identified way to the function of nerve cells. Researchers believe misfolded copies of the prion protein can cause other nearby copies of the protein to misfold, triggering a harmful chain reaction that leads to conditions like CJD.

Ghoshal's analysis showed that the amyloid detected in the initial CJD patient's autopsy was the same type found in the brains of patients with Alzheimer's. The amyloid appeared in regions of the brain most often harmed by CJD and Alzheimer's disease.

DR. CLAUDIO SOTO
April 5-7, 2010

<http://alznews.org/Library/InfoManage/Zoom.asp?InfoID=7586&RedirectPath=Add&FolderID=1419&SessionID={FF77EAF3-C1B1-4FE4-B01F-F8B005316270}&InfoGroup=Main&InfoType=Article>

Amyloid and Prions - Co-Conspirators in Disease?

(Source: Alzheimer Research Forum) - Many neurodegenerative diseases involve a common pattern of protein misfolding, aggrega for neurons. But what do the different proteins, and their deadly pathways, have in common?

Claudio Soto, PhD, and colleagues at the University of Texas Medical School looked at the B amyloid of Alzheimer's disease (AD) and the prion protein that causes transmissible spongiform encephalopathy, the only protein misfolding disease known to be contagious in people. They injected infective prions into an AD mouse model, and found an exacerbation of pathology and an accelerated onset of disease. In addition, each protein cross-seeded aggregation of the other in vitro. The study has implications for understanding protein-folding diseases in general, and raises the question of whether protein misfolds may be more widely transmissible than we think.

Go to full story: alzforum.org tion, and toxicity. Though the proteins vary for each disease, the outcome results in a bad end

<http://science-education.nih.gov/home2.nsf/Educational+Resources/Resource+Formats/Online+Resources/+High+School/D07612181A4E785B85256CCD0064857B>

Prions: Puzzling Infectious Proteins
Ruth Levy Guyer, Ph.D.

Sometimes a scientific discovery shakes the confidence of scientists, making them question whether they truly understand nature's "ground rules." . . . snip . . .

"Now researchers are coming around, albeit reluctantly, to accepting the shocking fact that naked proteins can be infectious. "More than one protein chemist has declared this to be insane-- and yet this is precisely what is implied by a growing number of studies" was the way one news article put it (1)." . . . snip . . .

*"Standard procedures for grinding up carcasses were altered in the 1970s, **and the new processing methods seem not to have been adequate for destroying scrapie prions. The cattle were exposed, through the offal, to sheep prions, and the prions eventually established themselves in their cow hosts. Later, they adapted further, infecting cells of people who had eaten hamburgers from prion-bearing cows.**" . . . snip . . .*

"At the moment, CJD and only a handful of other human diseases have clear links to prions. But it is likely that prions will turn out to be the agents of a variety of currently enigmatic diseases in which brain cells are destroyed and the nervous system deteriorates. Alzheimer's disease and Parkinson's disease are two prime candidates.

So, a couple new ground rules now seem to govern infectious diseases. The first is that naked proteins--prions--can be infectious and can cause infectious diseases. The second and potentially more troubling is that, like other infectious agents, prions can jump species' barriers and cause deadly diseases in humans.

Recently, and for the first time known, two farmers with mad cows in their herds died of CJD.” . . . snip . . .

“Gerstmann-Straussler-Scheinker Syndrome (GSSS)

*This disease was linked to two mutations in the prion gene in 1989. PrP^{Sc} fragments accumulate in the brain in structures called plaques. **In Alzheimer's disease, similar plaques develop, but they are composed of fragments of a different protein (7).**”*

.....

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2646838/?tool=pmcentrez>

AGGREGATED, WILD-TYPE PRION PROTEIN CAUSES NEUROLOGICAL DYSFUNCTION AND SYNAPTIC ABNORMALITIES

Roberto Chiesa,¹ Pedro Piccardo,^{2,3} Emiliano Biasini,^{1,4} Bernardino Ghetti,² and David A. Harris⁴

[INFECTIVITY AND PATHOGENICITY]

There is evidence that in prion disorders, as well as in other neurodegenerative diseases, neurotoxicity is induced by small, β -rich oligomers, rather than by large amyloid polymers. For example, we previously found that transgenic mice expressing mouse PrP carrying a 9-octapeptide insertion (PG14) associated with an inherited prion disease accumulate in their brains a weakly aggregated, β -sheet-rich form of the mutant protein ([Chiesa et al., 1998](#); [Chiesa et al., 2000](#)). This form is highly neurotoxic, but differs from PrP^{Sc} because it lacks detectable infectivity ([Chiesa et al., 2003](#); [Biasini et al., 2008a](#)). A biochemically similar pathogenic form of misfolded PrP was also found in Tg(MoPrP-P101L) mice, which overexpress the mouse PrP homologue of the P102L mutation linked to Gerstmann-Sträussler-Scheinker (GSS) disease ([Nazor et al., 2005](#)), and in transgenic mice expressing the mouse PrP homologue of the D178N/V129 mutation linked to familial CJD ([Dossena et al., 2008](#)). **There is now abundant evidence that small, misfolded oligomers of A β play a crucial pathogenic role in Alzheimer's disease, possibly by damaging synaptic structure or impairing synaptic**

function ([Haass and Selkoe, 2007](#)). **Similar aggregates are likely to be involved in other, non-infectious neurodegenerative disorders, including Huntington's disease, Parkinson's disease, and tauopathies** ([Friedhoff et al., 1998](#); [Lashuel et al., 2002](#); [Marchut and Hall, 2006](#)).

We now report that an aggregated, neurotoxic PrP isoform is spontaneously produced in transgenic mice expressing high levels of wild-type PrP. These mice develop a neurodegenerative syndrome characterized clinically by tremor and paralysis of the hind limbs, and neuropathologically by coarse PrP deposits and dramatic synaptic alterations in the cerebellar molecular layer. **The phenotype of these mice defines a new neurodegenerative illness caused by aggregation of wild-type PrP. Our results support the concept that infectivity and pathogenicity are distinct features of abnormal PrP, underscoring the similarity between prion diseases and non-transmissible neurodegenerative disorders of protein conformation.**

<http://blog.bioasis.ca/?p=2361>

[Bioasis Technologies Inc.](#)

The Science of Melanotransferrin (p97)

The Relationship Between Alzheimer's, Parkinson's, and Huntington's Disease

by Henry on December 10, 2009

"We have discovered a compelling new therapeutic approach for Parkinson's disease, which we expect will allow our scientists – as well as those at pharmaceutical and biotech companies – to pursue innovative new drugs that will treat and perhaps even cure this disorder," says Aleksey Kazantsev, PhD, director of MGH-MIND Drug Discovery Laboratory, who led the Science study.

“Since the same sort of aggregation of misfolded proteins has been reported in Huntington’s and Alzheimer’s diseases – as well as Lewy body dementia, which also involves alpha-synuclein deposits – we plan to test this approach in those conditions as well.”

From: [Dorothy Kraemer](#)
To: cjdnews@yahoogroups.com
Sent: Saturday, April 04, 2009 10:43 AM
Subject: [CJDNEWS] Fw: [CJDVoice] Under-reported Dementia Deaths Raises Questions About Accuracy Of Mortality Statistics

This under-reporting on death certificates is not just a problem with CJD patients. I can't believe these numbers!

<http://www.sciencedaily.com/releases/2008/12/081210171914.htm>

Under-reported Dementia Deaths Raises Questions About Accuracy Of Mortality Statistics

ScienceDaily (Dec. 16, 2008) — Deaths due to dementia and Alzheimer's disease are underreported on death certificates, according to a study conducted by Hebrew SeniorLife's Institute for Aging Research (IFAR), raising concerns about the accuracy of mortality statistics based on these documents.

According to the National Center for Health Statistics (NCHS), which derives its data from death certificates, **Alzheimer's disease, the most common form of dementia, is the fifth leading cause of death among Americans over age 65.** Dementia is the loss of mental capacities—thinking, memory, reasoning and decision making, among others—that interferes with a person's daily functioning

<http://www.sfgate.com/cgi-bin/article.cgi?f=/c/a/2009/02/25/MNC7164VHL.DTL>
February 2009

The latest in a recent flurry of clues on the workings of Alzheimer's

disease comes from Yale University researchers who found a link between the disorder and the prion protein, which can cause mad cow disease and other maladies.

The Yale team found that the prion protein, whose normal function is to maintain brain health, may contribute to nerve damage if it becomes entangled with a protein fragment that scientists consider a chief suspect as a cause for Alzheimer's disease.

That suspect fragment, the amyloid beta peptide, builds up in the gluey plaques in the brain that are a characteristic sign of Alzheimer's, a progressive neurodegenerative disease. The amyloid peptide seems to stick to the prion protein, block its benign effects and interfere with learning and memory, the Yale group said in a paper published today in the journal Nature.



Published online first JULY 22, 2008

[Free Abstract](#) [Article \(References\)](#) [Article \(PDF 280 KB\)](#)

Original Paper

Association between Deposition of Beta-Amyloid and Pathological Prion Protein in Sporadic Creutzfeldt-Jakob Disease

Laura Debatin^a, Johannes Streffer^b, Markus Geissen^c, Jakob Matschke^c, Adriano Aguzzi^a, Markus Glatzel^{a, c}

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[Address of Corresponding Author](#)

 **Key Words**

- Sporadic Creutzfeldt-Jakob disease
- Alzheimer's disease
- Deposition of β -amyloid
- Prion protein

 **Abstract**

Background: Alzheimer's disease (AD) and prion diseases such as sporadic Creutzfeldt-Jakob disease (sCJD) share common features concerning their molecular pathogenesis and neuropathological presentation and the coexistence of AD and CJD in patients suggest an association between the deposition of the proteolytically processed form of the amyloid precursor protein, β -amyloid ($A\beta$), which deposits in AD, and the abnormal form of the prion protein, PrP^{Sc} , which deposits in sCJD.

Methods:

We have characterized sCJD patients (n = 14), AD patients (n = 5) and nondemented controls (n = 5) with respect to the deposition of PrP^{Sc} and $A\beta$ morphologically, biochemically and genetically and correlated these findings to clinical data.

Results: sCJD-diseased individuals with abundant deposits of $A\beta$ present with a specific clinicopathological profile, defined by higher age at disease onset, long disease duration, a genetic profile and only minimal amounts of PrP^{Sc} in the cerebellum.

Conclusion: The co-occurrence of pathological changes typical for sCJD and AD in combination with the inverse association between accumulation of $A\beta$ and PrP^{Sc} in a subgroup of sCJD patients is indicative of common pathways involved in the generation or clearance of $A\beta$ and PrP^{Sc} in a subgroup of sCJD patients.

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http://www.nih.gov/news/research_matters/march2009/03092009alzheimers.htm

March 9, 2009

Non-Infectious Prion Protein Linked to Alzheimer's Disease
The prion protein, notorious for causing fatal neurodegenerative disorders such as Creutzfeldt-Jakob disease and mad cow disease, may also be an accomplice in Alzheimer's disease, according to a new study. In this case, it's not the infectious misfolded prion protein causing the problem but the cellular form, whose function is relatively unknown.

A region of amyloid plaque in the brain of a person with Alzheimer's disease. Image courtesy of Medical Microscopy Sciences, Cardiff University School of Medicine. All rights reserved by Wellcome Images.

Alzheimer's disease is marked by clumps of protein fibers called amyloids that accumulate into "plaques" around nerve cells in the brain, leading to the progressive loss of function. The main protein fragment found in these plaques, amyloid- β peptide, is created by the improper cleavage of a protein called amyloid precursor protein (APP). **Over time, amyloid- β peptides transform into small clusters known as oligomers, which then develop into the long, sticky fibers that form plaques around brain cells. Scientists are uncertain if amyloid- β oligomers act directly or through cell surface receptors to affect thinking and decision-making, but most agree that they're toxic to brain.**

A team of scientists led by Dr. Stephen Strittmatter at Yale University reasoned that if there were cell surface receptors on brain cells that bound amyloid- β oligomers, they might play a role in altering nerve cell function. Their search for these proteins was supported by NIH's National Institute of Neurological Disorders and Stroke (NINDS), National Institute of Drug Abuse (NIDA) and the NIH Medical Scientist Training Program.

.....
<http://www.npr.org/templates/story/story.php?storyId=101145687>

Mad Cow And Alzheimer's Have Surprising Link

by [Jon Hamilton](#)

February 25, 2009

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text size [A](#) [A](#) [A](#)

February 25, 2009

Scientists have discovered a surprising link between Alzheimer's disease and mad cow disease. It turns out both diseases involve something called a prion protein.

The finding, which appears in the journal Nature, could explain one of the great mysteries in Alzheimer's disease: How components of the plaques that form in patient's brains are able to damage brain cells. It also could point the way to new treatments for the disease.

"It's very exciting," says Lennart Mucke, director of the Gladstone Institute of Neurological Disease and a professor of neurology and neuroscience at the University of California, San Francisco. "The study shines the light on a very unexpected component."

Mucke was not involved in the study, but wrote an article that accompanied it in Nature.

In mad cow disease, and a similar human condition called new variant Creutzfeldt-Jakob disease, prion proteins fold into an abnormal shape that appears to cause degeneration of the brain and spinal cord. Prion diseases can be transmitted by eating the brain or spinal cord of a sick animal.

In Alzheimer's, prion proteins appear to play a different role, says Stephen Strittmatter, one of the new study's authors and the Vincent Coates Professor of Neurology at Yale University School of Medicine.

Strittmatter says there's no evidence the prion proteins fold into an abnormal shape or actually cause Alzheimer's. Instead, they

seem to interact with early stage plaques in the brain in a way that allows those plaques to damage brain cells.

Strittmatter's team made the discovery after looking at hundreds of thousands of molecules that occur naturally in the brain. The prion protein turned out to be the best at interacting with a protein called amyloid-beta, which is what forms the plaques in Alzheimer's

"At first they said, 'No that can't be,'" Strittmatter says. "It's too bizarre that these two diseases would share this common protein."

But he says it seemed less strange when they considered that both diseases affect brain cells and cause dementia.

"Once you start thinking about the details," Strittmatter says, "there are so many shared similarities that it actually begins to make a lot of sense."

After showing that the amyloid-beta from plaque could interact with prion protein, the researchers needed to demonstrate that the combination could harm brain cells.

So the Yale team exposed mouse brain tissue to small clusters of amyloid-beta.

In tissue from normal mice, which contains non-infectious prion proteins, the amyloid interfered with brain cells' ability to communicate.

Then, the team took a slice of tissue from a special mouse whose brain contained no prion protein.

"That slice no longer responded," Strittmatter says. "It carried out completely normal functions."

No prion protein, no problem.

It's still unclear exactly how prion proteins allow amyloid beta to affect brain cells. And the study certainly doesn't suggest that prion proteins cause Alzheimer's.

But Mucke says if prion proteins work the same way in people as in mice, the new research could lead to a drug that would

prevent Alzheimer's by keeping prion proteins from interacting with amyloid-beta.

Mucke says finding such a drug could happen relatively quickly because scientists already have spent so many years studying mad cow disease.

"We know a great deal about the biochemistry and biology of prion protein," he says, "which should really facilitate the development of drugs."

ALABAMA MAD COW g-h-BSEalabama

In this study, we identified a novel mutation in the bovine prion protein gene (Prnp), called E211K, of a confirmed BSE positive cow from Alabama, United States of America. This mutation is identical to the E200K pathogenic mutation found in humans with a genetic form of CJD. This finding represents the first report of a confirmed case of BSE with a potential pathogenic mutation within the bovine Prnp gene. We hypothesize that the bovine Prnp E211K mutation most likely has caused BSE in "the approximately 10-year-old cow" carrying the E221K mutation.

Enderlein's Endobiont and Prusiner's Prion

http://www.darkfieldtraining.com/main/page_lectures_articles_prion_end_obiont_in_live_blood.html

"Latest research by Prusiner's institute and other researchers around the world indicates Diabetes Type II, Parkinson's disease, Alzheimer's disease and Motor Neuron disease to be prion related diseases (1, 2, 3). "

References:

(1) *Stanley B. Prusiner – Prion Biology and Diseases*

(2)

<http://www.sciencedaily.com/releases/2007/04/070430102021.htm>

[

["Alzheimer', Parkinson's, Type II Diabetes Are Similar At The Molecular Level

ScienceDaily (May 4, 2007) — Alzheimer's disease, Parkinson's disease, type II diabetes, the human version of mad cow disease and other degenerative diseases are more closely related at the molecular level than many scientists realized, an international team of chemists and molecular biologists reported April 29 in the online version of the journal Nature (print version to follow)."]

UCLA (2007, May 4). Alzheimer's, Parkinson's, Type II Diabetes Are Similar At The Molecular Level. *ScienceDaily*. Retrieved November 27, 2010, from <http://www.sciencedaily.com/releases/2007/04/070430102021.htm>

(3) <http://www.universityofcalifornia.edu/news/article/9140>

http://webcache.googleusercontent.com/search?q=cache:KU_DjkCNamIJ:www.scu.edu/cas/enrichment/prusiner.cfm+STANLEY+PRUSINER,+ALZHEIMER'S+IS+A+PRION+DISEASE&cd=7&hl=en&ct=clnk&gl=us

The Scourge of Alzheimer's and Parkinson's and Prion Diseases
Dr. **Stanley Prusiner**, Nobel Prize-winning neurologist, biochemist, teacher, and expert in neurodegenerative diseases, looks at some of the greatest challenges facing neurological research today.

"Remarkably, the more common neurodegenerative diseases like **Alzheimer's** and Parkinson's diseases have been found over the past two decades to be, like the **prion** diseases, disorders of protein processing.'

<http://www.ahaf.org/aboutahaf/structure/board.html>

**American Health Assistance Foundation Board of Directors
Honorary Member Stanley B. Prusiner, M.D.**

There are similarities between the loss of brain function in prion diseases and in Alzheimer's disease. Both prions and beta-amyloid, respectively, are natural human proteins that, under certain conditions, can form harmful deposits in the brain. Dr. Prusiner's dedication to understanding how prion disease begins and develops may one day lead to a treatment and cure for Alzheimer's disease

**

<http://www.sciencemag.org/site/feature/data/prusiner/245.xhtml>

Prion Diseases and the BSE Crisis

Stanley B. Prusiner

Understanding how PrP^C unfolds and refolds into PrP^{Sc} not only has implications for interfering with the pathogenesis of prion diseases, but may open new approaches to deciphering the causes of and developing effective therapies for the more common neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis (ALS). In addition, two different stable metabolic states in yeast and one in a fungus have been ascribed to prion-like changes in protein conformation ([106-108](#)). Indeed, the expanding list of prion diseases and their novel modes of pathogenesis (Table [1](#)), as well as the unprecedented mechanisms of prion propagation and information transfer (Table [4](#)), indicate that much more attention to these fatal disorders of protein conformation is urgently needed.



EMBARGOED FOR RELEASE
Thursday, June 2, 2005
2:00 p.m. ET

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Variant Prion Protein Causes Infection But No Symptoms

Finding Could Have Implications for Alzheimer's Disease

Abnormal prion proteins are little understood disease agents involved in causing horrific brain-wasting diseases such as Creutzfeldt-Jacob disease in people, mad cow disease in cattle and chronic wasting disease in deer and elk. Now, new research suggests that a variant form of abnormal prion protein — one lacking an “anchor” into the cell membrane — may be unable to signal cells to start the lethal disease process, according to scientists at the Rocky Mountain Laboratories (RML), part of the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health.

(Scrapie)

*“Subsequent electron microscopic examinations at UCSD, however, confirmed that they produced amyloid fibrils, an abnormal form of prion protein, and that they even had brain lesions. More remarkably, according to Dr. Chesebro, **the diseased brain tissue resembled that found in Alzheimer's disease rather than in scrapie.**”*

*“There was so much about this research that surprised us and gave us ideas to pursue,” says Dr. Chesebro. “First, the mice didn't get sick. That's very significant. **Second, the dense accumulations of scrapie plaque in the brain resembled the plaque seen in Alzheimer's, but it wasn't toxic,**” which **might support more recent concepts about plaque in Alzheimer's patients.** **“Previously, most researchers thought plaques were the toxic component of Alzheimer's that kills neurons, and many treatments focus on removing the plaques. But what if the plaques are inert, as they were in this research? What if only small clumps are toxic?”**”*

Prion Diseases

Stephen J. DeArmond and Stanley B. Prusiner

"Molecular genetics has led to the discovery of new prion disorders. PRNP gene codon 198 and 217 mutations (21, 42) have been found in a unique form of GSS in which Alzheimer's disease-like neuropathological changes, including neuritic plaques and neurofibrillary tangles, are associated with deposition of PrP amyloid plaques and not the β A4 peptide (31, 32, 68). **These unique pedigrees raise questions about the relationship of the β A4 peptide deposition and senile plaques in Alzheimer's disease and suggest that there is an overlap of pathogenic mechanisms in Alzheimer's disease and prion diseases "**

<http://www.ncbi.nlm.nih.gov/pubmed/11593450>

[Huntington disease phenocopy is a familial prion disease.](#)

Huntington disease phenocopy is a familial prion disease. Moore RC, Xiang F, Monaghan J, Han D, Zhang Z, Edström L, Anvret M, **Prusiner SB.** ...

www.ncbi.nlm.nih.gov/pubmed/11593450 -

<http://www.sciencedaily.com/releases/2008/09/080929212926.htm>

IDIOPATHIC BRAINSTEM NEURONAL CHROMATOLYSIS – IBNC – A NEW PRION DISEASE IN CATTLE (and new idiopathic prion diseases in sheep, deer and in man ?)

"We've shown for the first time that prion protein is somehow involved in IBNC," says Jeffrey, "In this disease, there is an association with abnormally high levels of a prion protein in the brain but clearly this PrP is in a different form to that involved in BSE and CJD. This may have implications for diagnosis and recognition of typical forms of BSE as well as the related diseases in sheep, deer and in man."

[question: it is possible that cattle with IBNC that are tested for BSE may come up negative for BSE and be passed into the food supply, even though they may actually have IBNC ?]

<http://www.ucop.edu/research/publications/pdf/NIHatUC.pdf>

*The Emerging Epidemic: Alzheimer's
Disease in an Aging Population*

Many researchers suspect prions will eventually be implicated in Alzheimer's disease. Far more research needs to be done to identify the exact mechanisms of the prion diseases. There may be more Nobel prizes to come.

<http://betaamyloidcjd.blogspot.com/2010/08/transcellular-spread-of-cytosolic.html>

**[AMYLOIDS AND PRIONOIDS-
AGGREGATING PRIONOPATHIES]**

Sunday, August 8, 2010

**The Transcellular Spread of Cytosolic Amyloids,
Prions, and Prionoids**

Adriano Aguzzi1,* and Lawrence Rajendran2,* 1Institute of Neuropathology, University Hospital of Zurich, Schmelzbergstrasse 12, CH-8091 Zurich, Switzerland 2Systems and Cell Biology of Neurodegeneration, Psychiatry Research, University of Zurich, CH-8008 Zurich, Switzerland *Correspondence:

“Recent reports indicate that a growing number of intracellular proteins are not only prone to pathological aggregation but can also be released and “infect” neighboring cells. Therefore, many complex diseases may obey a simple model of propagation where the penetration of seeds into hosts determines spatial spread and disease progression. We term these proteins prionoids, as they appear to infect their neighbors just like prions—but how can bulky protein aggregates be released from cells and how do they access other cells? The widespread existence of such prionoids raises unexpected issues that question our understanding of basic cell biology.” . . . snip . . .

“Through ingenuity and technology, you may then discover that the infectious agent is exceedingly simple and homogeneous, that it lacks informational nucleic acids, and that it is generated both by ordered aggregation of an intrinsic precursor and by appositional growth of extrinsically added seeds. Your discovery will earn you the Intergalactic Nobel Prize, yet two crucial questions remain unanswered: how do the crystals transfer between individuals, and what can be done to prevent this from happening? “ . . . snip . . .

“There is mounting evidence (Clavaguera et al., 2009; Frost et al., 2009; Ren et al., 2009; Desplats et al., 2009; Luk et al., 2009) suggesting that the events sketched above, far from being confined to science-fiction and prion diseases (whose incidence in humans is just 1/106/year), may underlie highly prevalent human diseases of the brain and many other organs.”

“The unifying characteristics of all these diseases is the aggregation of proteins into highly ordered stacks, henceforth termed “amyloids” irrespective of their size. Since PrPSc undoubtedly fulfills the latter definition of amyloid, one is led to wonder whether the prion principle may be much more pervasive than previously appreciated and whether many more diseases of unknown cause may eventually turn out to rely on prion-like propagation (Table 1, upper panel). Even more intriguingly, a number of proteins appear to exert normal functions when arranged in highly ordered stacks that are similar to amyloids and to prionoids (Table 1, lower panel).”

“There is one crucial difference between bona fide prion diseases and all other amyloids and prion-like phenomena hitherto described in uni- and pluricellular organisms (Table 1). Prions are infectious agents, transmissible between individuals, and tractable with microbiological techniques—including, e.g., titer determinations. Even if certain amyloids of yeast and mammals appear to infect neighboring molecules and sometimes neighboring cells, they do not propagate within communities, and none of them were found to cause macroepidemics such as Kuru and bovine spongiform encephalopathy. We have therefore termed these self-aggregating proteins “prionoids” (Aguzzi, 2009), since the lack of microbiological transmissibility precludes their classification as true prions.”

“Some prionoids may soon qualify for an upgrade to prion status. At least in select settings, amyloid A (AA) amyloidosis may exist as a truly infectious disease based on a self-propagating protein. AA amyloid consists of orderly aggregated fragments of SAA protein, whose deposition can damage many organs of the body. Somewhat bizarrely, AA aggregation is also present in the liver of force-fed geese, hence contributing to the pathophysiology of foie gras (Solomon et al., 2007). AA seeds can induce amyloidosis upon transfer of white blood cells (Sponarova et al., 2008). Furthermore, AA seeds are excreted with the feces, and AA amyloidosis is endemic in populations of cheetah (Zhang et al., 2008). It is therefore tantalizing to suspect that amyloid may entertain the complete life cycle of an infectious agent, including transmission by the orofecal and hematogenous route—similarly to enteroviruses and, perhaps, scrapie prions.“

“Alzheimer’s disease (AD) has long been suspected to be a transmissible disease, but these suspicions have never materialized in epidemiological studies. On the other hand, Mathias Jucker and Lary Walker observed that injection of the Ab peptide from human AD brains induced robust and convincing aggregation of Ab in transgenic mice overexpressing the Ab precursor protein, APP (Kane et al., 2000; Meyer-Luehmann et al., 2006). Jucker’s finding raises an epistemologically significant question: if

aggregation depends on the introduction of seeds and on the availability of the monomeric precursor, and if amyloid represents the primordial state of all proteins (Chiti and Dobson, 2006), wouldn't all proteins— under appropriate conditions— give rise to prionoids in the presence of sufficient precursor? “

“The wave of these recent reports on the prion-like behavior of disparate pathogenic proteins raises many more questions than it answers. Here we have highlighted a number of open issues related to mechanisms of cell-to-cell spread of prionoids. The resolution of such issues may constitute the first step toward the development of rational strategies aimed at blocking transcellular propagation. There is justified hope that the latter may decelerate the progression of pathology and, consequently, help toward fighting the devastating outcome of aggregation proteinopathies. “

[http://www.cell.com/neuron/abstract/S0896-6273\(09\)01006-X](http://www.cell.com/neuron/abstract/S0896-6273(09)01006-X)

<http://esciencenews.com/articles/2008/09/29/is.there.more.prion.protein.mad.cow.disease>

Is there more to prion protein than mad cow disease?

Published: Monday, September 29, 2008 - 18:28 in [Biology & Nature](#)

Prion protein, a form of protein that triggers BSE, is associated with other brain diseases in cattle, raising the possibility of a significant increase in the range of prion disease. Publishing their findings in the open access journal BMC Veterinary Research, scientists have detected changes in the production and accumulation of the prion protein in the brains of cattle with a rare neurodegenerative disorder. Martin Jeffrey of the Veterinary Laboratories Agency led a research team that tested *15 brains of cattle with idiopathic brainstem neuronal*

chromatolysis and hippocampal sclerosis (IBNC). They are the first group to show that the brains of animals with this disease accumulate prion protein (PrP), the protein that misfolds to cause BSE and which, when transmitted to humans through the food chain, can cause the deadly Variant Creutzfeldt-Jakob disease

IBNC is a rare neurological disease of adult cattle. It was first characterised in 1988 following laboratory tests from cattle suspected of having BSE. Although IBNC has some clinical similarities to BSE, the brains of affected cattle do not have the neuronal vacuolation (lesions) typical of BSE.

Further laboratory tests suggest that the misfolded form of PrP, which accumulates in the brains of BSE cases, is not present in IBNC cases. Commercial BSE testing kits did not detect the telltale, BSE-inducing form of PrP either. However, the presence of increased levels of PrP was detected.

"We've shown for the first time that prion protein is somehow involved in IBNC," says Jeffrey, "In this disease, there is an association with abnormally high levels of a prion protein in the brain but clearly this PrP is in a different form to that involved in BSE and CJD. This may have implications for diagnosis and recognition of typical forms of BSE as well as the related diseases in sheep, deer and in man.

Source: [BioMed Central](#)

[More than 5 million have Alzheimer's in U.S. - Alzheimer's Disease ...](#)

updated 6:15 p.m. ET March 18, 2008. WASHINGTON - An estimated 5.2 million Americans have Alzheimer's disease, and it could steal the minds of one out of ... www.msnbc.msn.com/id/23697160/ - 49k - [Cached](#) - [Similar pages](#) - [Note this](#)

- Canada

<http://www.healthdepartment.com/alzheimers-disease/interview-mad-cow-and-misdiagnosed-alzheimers-disease-4541.html>

VIDEO Interview – Mad Cow and Misdiagnosed Alzheimer’s Disease

Interview with Colm Kelleher author of “Brain Trust: The Hidden Connection Between Mad Cow and Misdiagnosed Alzheimer’s Disease” recorded November 16, 2004. video about 1 hour long – well worth the time

.....

THE RELATIONSHIP BETWEEN THE ALZHEIMERS EPIDEMIC AND CJD ??

<http://www.thebukowskiagency.com/DyingForAHamburger.htm>

Absolutely impossible, insisted British health authorities, that mad cow disease could be transmitted to humans through infected beef. Yet less than a decade later, hundreds of people (including recent victims in Saskatchewan and Florida) who ate infected beef have died of Creutzfeldt-Jakob disease (CJD), with perhaps hundreds of thousands more at risk for developing the disease. Could the same scenario hold true for Alzheimer’s disease?

Before about 1900 Alzheimer’s disease did not exist, or if it did, was so rare as not to be noticed. We know that as long as people have been keeping records, they have inventoried diseases. But just over a hundred years ago, Alzheimer’s disease was unknown, and most people did not know anyone who exhibited the symptoms of dementia that are now all too familiar to the families and friends of victims.

Alzheimer’s disease (AD) now afflicts 15 million people around the world, including 250,000 Canadians and 4.5 million

Americans. One in 10 persons over 65 and nearly half of those over 85 have the disease. More significantly, the number of people with dementia is expected to increase steadily over the next 25 years: in Canada, 10,000 new cases of AD are diagnosed each year – 27 cases per day.

***Dying for a Hamburger* presents strong evidence that Alzheimer's disease is caused by the same agent that causes mad cow disease (bovine spongiform encephalopathy, or BSE), variant Creutzfeldt-Jakob disease (vCJD), and a host of other neurodegenerative diseases called transmissible spongiform encephalopathies (TSEs). *Dying For a Hamburger* now presents compelling evidence that Alzheimer's disease has become epidemic due to modern meat-packing practices.**

The link between eating processed meat and Alzheimer's disease unfolds as a remarkable narrative, one of the most fascinating stories in modern medicine. The tale involves cannibals, both two- and four-legged, one Nobel Prize winner who is a convicted paedophile, and another who is reputed to be one of the most disliked men in academic medicine.

***Dying for a Hamburger* is a medical story, a detective story, a story of bureaucratic bungling, and a story of the rise of an epidemic that has already created extraordinary public health, social, and economic implications. With baby boomers fast heading towards their sixth decade, our society will soon experience far-reaching consequences of the AD epidemic – in the work force, government, health care, medicine, business, and industry – in the next twenty years. This is a story that affects all of us.**

.....
http://www.sciencecodex.com/brain_plaques_in_healthy_individuals_linked_to_increased_alzheimers_risk

Brain plaques in healthy individuals linked to increased Alzheimer's risk

Posted On: December 14, 2009 - 9:30pm

St. Louis, Dec. 10, 2009 — Scientists have long assumed that amyloid brain plaques found in autopsies of Alzheimer's patients are harmful and cause Alzheimer's disease. But autopsies of people with no signs of mental impairment have also revealed brain plaques, challenging this theory.

Now, for the first time, researchers at Washington University in St. Louis have shown that brain plaques in apparently healthy individuals are associated with increased risk of diagnosis with Alzheimer's disease years later.

In two studies published this month in *Archives of Neurology*, scientists report that volunteers with brain plaques were more likely to have declining scores on annual cognitive tests, to show signs of shrinkage in a key brain area affected by Alzheimer's and to eventually be diagnosed with the disease

"We don't have enough data yet to definitively say that people who scan positive for these brain plaques have presymptomatic Alzheimer's disease, but something is clearly going on that does not bode well for the health of their aging brains," says John C. Morris, the Harvey A. and Dorismae Hacker Friedman Distinguished Professor of Neurology and director of Washington University's Alzheimer's Disease Research Center (ADRC) and the Friedman Center for Aging.

Morris and others at the ADRC have previously found evidence that Alzheimer's disease harms the brain for years prior to typical diagnosis. They are pushing for earlier diagnosis as an essential step to successful treatment of Alzheimer's disease, but to do that they first have to seek earlier indicators of disease and then wait years to see if people with the indicators later develop symptomatic Alzheimer's.

According to Morris, the new papers are early and encouraging indicators that scientists are on track to pushing back the time at which diagnosis can be made. "We only have a very small number of subjects to date, but what we're learning so far has been consistent with our predictions," he says.

The new studies were made possible by the development of an imaging agent, Pittsburgh Compound B (PiB), that lets scientists use positron emission tomography scans to detect amyloid plaques in living brains for the first time. Prior to PiB, clinicians could only verify the presence of brain plaques during autopsies. PiB scanning of ADRC research participants is directed by Mark Mintun, M.D., vice chair for research in radiology and professor of radiology at the University's Mallinckrodt Institute of Radiology.

Martha Storandt, Ph.D., professor of psychology and of neurology, led one of the studies, which compared a variety of factors in plaque-positive and plaque-negative subjects.

"One of the main things we wanted to know was whether people who scanned positive for brain plaques scored abnormally low on cognitive tests," she says. "They didn't, but when we looked at their annual testing records over a period of years, we saw that the scores of the plaque-positive group were declining, while those of the plaque-negative group were not."

http://www.alzheimersanddementia.org/webfiles/images/journals/jalz/JALZ_739.pdf

Saturday, March 22, 2008

10 Million Baby Boomers to have Alzheimer's in the coming decades

2008 Alzheimer's disease facts and figures

Alzheimer's Association*

Abstract Alzheimer's disease is the seventh leading cause of all deaths in the United States and the fifth leading cause of death in Americans older than the age of 65 years. More than 5 million Americans are estimated to have Alzheimer's disease. Every 71 seconds someone in America develops Alzheimer's disease; by 2050 it is expected to occur every 33 seconds.

During the coming decades, baby boomers are projected to add 10 million people to these numbers.

.....

ALZHEIMER'S DISEASE (AD) AND sporadic CREUTZFELDT JAKOB DISEASE (sCJD) – THE SAME PRION DISEASE? (Most of the research cited below which indicates AD and sCJD are frequently mistaken one for the other – is from late 1980s to early 2000s and came out before scientists stated in 2009 that AD is a prion disease. Also, the incredible magnitude of the AD epidemic was not obvious back then.)

[Alzheimer's and CJD](#)

A clinical series with 13% of Alzheimer actually CJD diagnosed with dementia were actually dying from Creutzfeldt-Jakob disease (**Boller**, 1989). ...

www.mad-cow.org/Alzheimer_cjd.html - 33k - [Cached](#) - [Similar pages](#) - [Note this](#)

[More Evidence Mad Cow Same As CJD And Alzheimer's](#)

I have posted some data below on **CJD** and **Alzheimer's** that you may find **Boller**

F. Cognitive deficits and clinical diagnosis of **Alzheimer's** disease. ...

www.rense.com/general34/cjmd.htm - 123k - [Cached](#) - [Similar pages](#) - [Note this](#)

[Alzheimer's And CJD Scientifically Linked](#)

The most common misdiagnosis of **CJD** is **Alzheimer's** disease (**Harrison**, 1991). ...

Boller, F., O. L. Lopez, and J. Moossy. "Diagnosis of Dementia. ...

www.rense.com/general46/alz.html - 20k - [Cached](#) - [Similar pages](#) - [Note this](#)

[Alzheimer's and CJD](#)

A clinical series with 13% of **Alzheimer** actually **CJD** 3 out of 12 "**Alzheimer**" patients actually died from a spongiform encephalopathy (**Teixeira**, 1995). ...

www.mad-cow.org/Alzheimer_cjd.html - 33k - [Cached](#) - [Similar pages](#) - [Note this](#)

[Could Mad Cow Disease Already be Killing Thousands of Americans ...](#)

[55] Neither **CJD** nor **Alzheimer's** can be conclusively diagnosed without a brain 67

Teixeira, F., et al. "Clinico-Pathological Correlation in Dementias. ...

www.commondreams.org/views04/0107-07.htm - 43k - [Cached](#) - [Similar pages](#) - [Note this](#)

[Alzheimer's And CJD Scientifically Linked](#)

The most common misdiagnosis of **CJD** is **Alzheimer's** disease (**Harrison**, 1991). ...

... patients actually died from a spongiform encephalopathy (**Teixeira**, 1995). ...

www.rense.com/general46/alz.html - 20k - [Cached](#) - [Similar pages](#) - [Note this](#)

http://www.mad-cow.org/Alzheimer_cjd.html

The true prevalence of prion diseases in this or any other country remains a mystery (Harrison, 1991). Compounding the uncertainty, autopsies are rarely performed on atypical dementias (Harrison, 1991), **because medical professionals fear infection** (Altman, 1996a). The officially reported rate in this country is less than 1 case in a million people per year (World, 1996). An informal survey of neuropathologists, however, registered a theoretical range **of 2-12% of all dementias as actually CJD** (Harrison, 1991). And hundreds of thousands of Americans suffer from severe dementias every year (Brayne, 1994; United, 1995). Two other studies average about a 3% CJD rate among dementia patients (Mahendra, 1987; Wade, 1987). **A preliminary 1989 University of Pennsylvania study showed that 5% of patients diagnosed with dementia were actually dying from Creutzfeldt-Jakob disease (Boller, 1989). It would**

seem CJD is seriously underdiagnosed at present (Harrison, 1991).

[More than 5 million have Alzheimer's in U.S. - Alzheimer's Disease ...](#)

updated 6:15 p.m. ET March 18, 2008. WASHINGTON - An estimated 5.2 million Americans have Alzheimer's disease, and it could steal the minds of one out of ... www.msnbc.msn.com/id/23697160/ - 49k - [Cached](#) - [Similar pages](#) - [Note this](#)

5% x 5.2 MILLION = 260,000

ALZHEIMER'S = between 2 and 25% actually have sCJD

The statistical incidence of CJD cases in the United States has been revised to reflect that there is one case per 9000 in adults age 55 and older. Eighty-five percent of the cases are sporadic, meaning there is no known cause at present.

<http://www.cjdfoundation.org/fact.html>
.....

“Human victims of sCreutzfeldt Jakob Disease (CJD) are also shedding infectious prions into public sewers, to end up in both Class B and Class A sludge compost. Between 2 and 25% of the 4.5 million cases of Alzheimer's Disease and senile dementia victims in the US are actually infected with sporadic CJD. (Manuelidis, et al, 1989; Bendixen, 1996; Boller, et al, 1989, 1995; Harrison, 1991; Teixeira, 1995; Warren, et al, 2005) “

The hidden incidence of CJD

http://www.mad-cow.org/jan_11_98_news.html#hidden

Dr. Birgitte Bendixen, assistant professor in the University of Iowa College of Medicine's Department of Neurology has been quoted as stating in 1996

'When we do autopsies, we find that five of every 100 people who have been diagnosed with Alzheimer's had CJD,'

.....

<http://brain.oxfordjournals.org/cgi/content/full/128/9/20>

16

Brain biopsy in dementia

J. D. **Warren**¹, J. M. Schott¹, N. C. Fox¹, M. Thom², T. Revesz^{2,3}, J. L. Holton^{2,3}, F. Scaravilli², D. G. T. Thomas⁴, G. T. Plant⁵, P. Rudge⁵ and M. N. Rossor^{1,5}

Brain biopsy has an uncertain role in the diagnosis of dementia. Here we report a retrospective analysis of 90 consecutive cerebral biopsies undertaken for the investigation of dementia in adults at a tertiary referral centre between 1989 and 2003. In most cases (90%), biopsy consisted of a right frontal full thickness resection of cortex, white matter and overlying leptomeninges. Fifty-seven per cent of biopsies were diagnostic: the most frequent diagnoses were Alzheimer's disease (18%), Creutzfeldt–Jakob disease (12%) and inflammatory disorders (9%).

Creutzfeldt-Jakob Disease (CJD) affects both men and women worldwide usually between the ages of 50 to 75 years. The officially stated mortality rate is one to two deaths per one million population per year. However, this figure appears to be an understatement as CJD is often misdiagnosed. A study performed at the University of Pittsburgh showed over 5% of Alzheimer's patients were actually CJD victims
<http://www.zarcrom.com/users/alzheimers/odem/cjd1.html>

In a study by Yale University researchers found that 13% of Alzheimers patients were found upon autopsy to actually have CJD. (Dr. Laura Manuelidis, et al http://www.cyber-dyne.com/~tom/Alzheimer_cjd.html#clinical

Teixeira, et al, found 3 out of 12 AD patients were really suffering from CJD. (25%) Teixeira, F., et al. "Clinico-Pathological Correlation in Dementias." *Journal of Psychiatry and Neuroscience* 20 (1995): 276-282.

“ . . . a study at the University of Pittsburgh, in which autopsies were done on 54 demented patients diagnosed as having probable or possible Alzheimer's or some other dementia (but not CJD), found 3 cases (or 5.5%) of CJD among the 54 studied (**Boller et al., 1989**).

Furthermore, research by Dr. Laura Manuelidis, head of neuropathology at Yale University found that as many as 13% of Alzheimer patients actually die of CJD. (*Alzheimer Disease and Associated Disorders*, Vol 3 Nos 1-2 1989).

The American Council on Science and Health estimates there are 5 million Alzheimer victims in the United States.

<http://www.acsh.org/publications/booklets/alzheimers2002.html>

Using the lower figure of 5%, this means there may be up to 250,000 victims of CJD/prion disease in the US at the present time. Thus, there could be a **hidden CJD epidemic**. (See accompanying file on CJD which notes several clusters and victims under 55 years of age.)

Prions have been found in the blood and urine of CJD victims. (Gabizon, et al, 2001; Reichl, et al 2002). Undertakers and medical facilities routinely discharge CJD infected blood and body fluids into public sewers. (Yale; UC Davis, CDC)

Prions can cross the intestinal barrier by riding piggyback on ferritin, a protein normally absorbed by the intestine. Because ferritin shares considerable homology across species, these data suggest that PrP^{Sc}-associated proteins, in particular ferritin, may facilitate PrP^{Sc} uptake in the intestine from distant species, leading to a carrier state in humans. (Singh, et al 2004)

“ . . . enteric infection at early as well as later stages of (CJD) disease, and regardless of the route of agent entry, implicates potential environmental spread by fecal matter.” (Radebold, et al 2001)

.....
<http://www.jbc.org/content/279/22/23661.abstract>

A Pitfall in Diagnosis of Human Prion Diseases Using Detection of Protease-resistant Prion Protein in Urine

CONTAMINATION WITH BACTERIAL OUTER MEMBRANE PROTEINS*

Abstract

Because a definite diagnosis of prion diseases relies on the detection of the abnormal isoform of prion protein (PrP^{Sc}), it has been urgently necessary to establish a non-invasive diagnostic test to detect PrP^{Sc} in human prion diseases. To evaluate diagnostic usefulness and reliability of the detection of protease-resistant prion protein in urine, we extensively analyzed proteinase K (PK)-resistant proteins in patients affected with prion diseases and control subjects by Western blot, a coupled liquid chromatography and mass spectrometry analysis, and N-terminal sequence analysis

“Instead, discrete protein bands with an apparent molecular mass of \approx 37 kDa were detected in the urine of many patients affected with prion diseases and two diseased controls. Although these proteins also gave strong signals in the Western blot using a variety of anti-PrP antibodies as a primary antibody, we found that the signals were still detectable by incubation of secondary antibodies alone, i.e. in the absence of the primary anti-PrP antibodies”

DR. JOEL PEDERSEN, ET AL, UNIV. OF WISCONSIN – PRIONS IN SEWAGE SLUDGE:

<http://pubs.acs.org/doi/abs/10.1021/es703186e>

Here, we report the results of experiments examining the partitioning and persistence of PrP^{TSE} during simulated wastewater treatment processes including activated and mesophilic anaerobic sludge digestion. **Incubation with activated sludge did not result**

in significant PrP^{TSE} degradation. PrP^{TSE} and prion infectivity partitioned strongly to activated sludge solids and are expected to enter biosolids treatment processes.

Note: Prions have been found in the muscles, blood, urine and feces of human and animal victims of prion diseases.

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Russian study

NEURODEGENERATIVE DISEASES Review

Neurodegenerative Dis 2010;7:272–278

DOI: 10.1159/000309659

Received: January 20, 2010

Accepted after revision: March 26, 2010

Published online: May 27, 2010

A New Story about an Old Guy:

Is Alzheimer's Disease Infectious?

Helton J. Reis a Marat A. Mukhamedyarov

bAlbert A. Rizvanov cAndrás Palotás d

“That this happened, as well as how the novel assumption that less virulent strains of prion proteins or similar peptides or even smaller particles such as AP or -synuclein – by a yet unknown mode of transmission – cause neurodegeneration in the cholinergic or dopaminergic systems and form senile plaques or Lewy bodies in the disease postulated and eventually called AD or PD, should come as a surprise to no one. Although the question of AD infectivity remains an early-stage hypothesis and further evidence will be required to reach conclusions, be aware that we might catch Alzheimer's dementia from our neighbors and spread it along to cause an ‘infectious neurodegenerative’ epidemic ...’

(email hshields@worldpath.net for e-copy of this Russian study)

<http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=17965932>

[Cell Mol Neurobiol.](#) 2007 Nov;27(7):943-57. Epub 2007 Oct 27.

Role of cyclin-dependent kinase 5 N(Cdk5) in the neurodegenerative process triggered by amyloid-Beta and prion peptides: implications for Alzheimer's disease and prion-related encephalopathies.

[Lopes JP](#), [Oliveira CR](#), [Agostinho P](#).

Faculty of Medicine, Center for Neuroscience and Cell Biology, Biochemistry Institute, University of Coimbra, 3004, Coimbra, Portugal.

Tau hyperphosphorylation, amyloid plaques, and neuronal death are major neuropathological features of Alzheimer's disease (AD) and Prion-related encephalopathies (PRE).** Cyclin-dependent kinase 5 (Cdk5) is a serine/threonine kinase, active in post-mitotic neurons, where it regulates survival and death pathways. Overactivation of Cdk5 is conferred by p25, a truncated fragment of the p35 activator formed upon calpain activation. Cdk5 deregulation causes abnormal phosphorylation of microtubule-associated protein tau, leading to neurodegeneration. **In this work we investigated the involvement of Cdk5 in the neurodegeneration triggered by amyloid-beta (Abeta) and prion (PrP) peptides, the culprit agents of AD and PRE.** As a work model, we used cultured rat cortical neurons treated with Abeta 1-40 and PrP 106-126 synthetic peptides. The obtained data show that apoptotic neuronal death caused by both the peptides was in part due to Cdk5 deregulation. After peptide treatment, p25 levels were significantly enhanced in a pattern consistent with the augment in calpain activity. Moreover, Abeta 1-40 and PrP 106-126 increased the levels of tau protein phosphorylated at Ser202/Thr205. Cdk5 (roscovitine) and calpain (MDL28170) inhibitors reverted tau hyperphosphorylation and prevented neuronal death caused by Abeta 1-40 and PrP 106-126. **This study demonstrates, for the first time, that Cdk5 is involved in PrP-neurotoxicity. Altogether, our data suggests that Cdk5 plays an active role in the pathogenesis of AD and PRE.

PMID: 17965932 [PubMed - indexed for MEDLINE]

DR. MURRAY WALDMAN, TORONTO MEDICAL EXAMINER, DYING FOR
HAMBURGERS ALZHEIMERS EPIDEMIC

<http://www.canada.com/calgary/calgaryherald/news/story.html?id=73024452-8ee6-477b-8e60-d96c145abe72>

Ranchers, scientists air beef over book

Jim Farrell

CanWest News Service

Sunday, April 11, 2004

A major Canadian publisher is likely to add to the woes of the beef industry by releasing a book that blames hamburgers for an "epidemic of Alzheimer's disease."

Dr. Murray Waldman, a coroner with the City of Toronto and co-author of the McClelland and Stewart book, *Dying for a Hamburger: modern meat processing and the epidemic of Alzheimer's disease*, charges hamburger is the main source of prions, which trigger Alzheimer's.

Prions, a type of malformed protein found in the brains of infected animals and humans, are credited as the cause of mad cow disease, several cases of which have been linked to Canadian cattle, and its human form, variant Creutzfeldt-Jakob disease. The book is slated for release in the next two weeks.

But Canada's leading expert on prions said Waldman doesn't know what he is talking about. Alzheimer's isn't a prion disease, said Dr. David Westaway of the University of Toronto; experiments have shown it isn't transmissible.

An epidemiologist whose studies are quoted in the book says Waldman and co-author Marjorie Lamb misinterpreted his findings.

"There's no evidence of Alzheimer's being a prion-caused disease," said epidemiologist Dr. Hugh Hendrie of the University of Indiana. "Pathologically, Alzheimer's and variant Creutzfeldt-Jakob disease don't look the same at all."

The executive vice-president of the Canadian Cattleman's Association has heard of Waldman's theory and knows about his forthcoming book. Dennis Laycraft hopes readers and beef consumers will dismiss Waldman's theory.

"There are a lot of theories out there but we have to trust in the intelligence of the reading public," Laycraft said.

Reached by phone Saturday, Waldman insisted his science is strong. There is no contradiction between what is in his book and what Westaway says, Waldman claimed.

"I never said that Alzheimer's is transmissible or that it is a prion disease. What I am saying is that Alzheimer's is caused by prions, that prions set in motion a chain of events and there are some fairly good articles to prove that."

It is only the prions, not Alzheimer's that are transmissible, Waldman said. Those prions merely set the stage for non-transmissible Alzheimer's

In its 270 pages, *Dying for a Hamburger* surveys the history of dementia from the ancient to the modern world, cannibalism in New Guinea, Europe's mad cow disaster, the nature of prions, the beef-rich diets of North Americans, the beef-restricted diets of people in West Africa, the meatless diets of India and modern meat-packing practices. Waldman argues that because processed meat and hamburger from many cows can end up in a single package, a single prion-infected cow among millions of slaughtered cows can infect multiple humans.

A century ago, that couldn't happen because meat from a single animal was kept separate from the meat of other animals. Cows also weren't fed protein additives made from the remains of other cows, so prion diseases weren't transmitted from one cow to another.

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