

John Q. Trojanowski: Insights and Impact

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I. Neuropathology Champion

The Clinicopathologic Correlation ca. 1900

"...near the end of the century, clinicopathological correlation was reaching the limits of its explanatory possibilities."

"contemporary clinical research should not be founded on the "dead house" science of pathology that had characterized the previous generation, but on the active, progressive science of physiology."

Alzheimer's Disease Case #6

COMMENT:

The numbers with senile plaques and neurofibrillary tangles in this case exceed established controls for any age and are most consistent with the diagnosis of Senile Dementia of Alzheimer type. Congophilia of blood vessels reflected by positive Thioflavin-S flouresence is a commonly associated microscopic finding. The findings in midbrain: mild pigmentary incontinence, few Lewy bodies and few globose tangles are of uncertain significance.

MICROSCOPIC DIAGNOSIS: Senile Dementia of Alzheimer type 930 - 7.9X

SEC/JQT/pk 2/11/86

Sidney E. Croul, M.D.

John Q. Trojanowski, M.D.

National Institute on Aging–Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease

Bradley T. Hyman^a, Creighton H. Phelps^b, Thomas G. Beach^c, Eileen H. Bigio^d, Nigel J. Cairns^{e,f}, Maria C. Carrillo^g, Dennis W. Dickson^h, Charles Duyckaertsⁱ, Matthew P. Frosch^j, Eliezer Masliah^{k,l}, Suzanne S. Mirra^m, Peter T. Nelsonⁿ, Julie A. Schneider^{o,p,q}, Dietmar Rudolf Thal^r, Bill Thies^g, John Q. Trojanowski^s, Harry V. Vinters^{t,u}, Thomas J. Montine^{v,*} Alzheimer's & Dementia 8 (2012) 1–13



Department of Pathology and Laboratory Medicine 1981 - T982



The Molecular Pathology of Alzheimer's Disease

Dennis J. Selkoe Center for Neurologic Diseases Harvard Medical School Brigham and Women's Hospital Boston, Massachusetts 02115 "...since the quantitative depolymerization of PHFs has not been reported, one cannot yet be certain whether proteins besides tau are intrinsic constituents of these abnormal fibers."

α-Synuclein inLewy bodies

Maria Grazia Spillantini, Marie Luise Schmidt, Virginia M.-Y. Lee John Q. Trojanowski, Ross Jakes, Michel Goedert





Ubiquitinated TDP-43 in Frontotemporal Lobar Degeneration and Amyotrophic Lateral Sclerosis

Manuela Neumann,^{1,11}* Deepak M. Sampathu,¹* Linda K. Kwong,¹* Adam C. Truax,¹ Matthew C. Micsenyi,¹ Thomas T. Chou,² Jennifer Bruce,¹ Theresa Schuck,¹ Murray Grossman,^{3,4} Christopher M. Clark,^{3,4} Leo F. McCluskey,³ Bruce L. Miller,⁶ Eliezer Masliah,⁷ Ian R. Mackenzie,⁸ Howard Feldman,⁹ Wolfgang Feiden,¹⁰ Hans A. Kretzschmar,¹¹ John Q. Trojanowski,^{1,4,5} Virginia M.-Y. Lee^{1,4,5}†







The Value of Pathology: Current Views

"Could they represent merely superfluous junk? Well, perhaps the "patho-" is correct, but to date, there is no "physiology" to substantiated this claim." (*Published in Annals of Neurology in 2007*)

COMMENT:

The numbers with senile plaques and neurofibrillary tangles in this case exceed established controls for any age and are most consistent with the diagnosis of Senile Dementia of Alzheimer type. Congophilia of blood vessels reflected by positive Thioflavin-S flouresence is a commonly associated microscopic finding. The findings in midbrain: mild pigmentary incontinence, few Lewy bodies and few globose tangles are of uncertain significance. MICROSCOPIC DIAGNOSIS: Senile Dementia of Alzheimer type 9.30-7.9.XSEC/JQT/pk 2/11/86 Sidney E. Croul, M.D.



 TDP-43 since 2006: 3454 publications from 11,467 authors

- Publications 1400+
- Co-authors 5187
- H-index 246
 - Tony Fauci 231
 - Stephen Hawking 128
- Top 10 most cited neuroscientist

II. What is Alzheimer's Disease?

Journal of Neuropathology and Experimental Neurology Copyright © 1997 by the American Association of Neuropathologists Vol. 56, No. 10 October, 1997 pp. 1095-1097

Editorial on Consensus Recommendations for the Postmortem Diagnosis of Alzheimer Disease from the National Institute on Aging and the Reagan Institute Working Group on Diagnostic Criteria for the Neuropathological Assessment of Alzheimer Disease

BRADLEY T. HYMAN, MD, PHD, AND JOHN Q. TROJANOWSKI, MD, PHD





doi:10.1093/brain/awy146

A JOURNAL OF NEUROLOGY

BRAIN 2018: 141; 2181-2193 2181

Neurodegenerative disease concomitant proteinopathies are prevalent, age-related and APOE4-associated







Robinson JL, et al., Brain 141: 2181-2193, 2018

III. How do we diagnose AD?

Cerebrospinal Fluid Biomarker Signature in Alzheimer's Disease Neuroimaging Initiative Subjects

Leslie M. Shaw, PhD,¹ Hugo Vanderstichele, PhD,² Malgorzata Knapik-Czajka, PhD,¹ Christopher M. Clark, MD,³ Paul S. Aisen, MD,⁴ Ronald C. Petersen, MD,⁵ Kaj Blennow, MD, PhD,⁶ Holly Soares, PhD,⁷ Adam Simon, PhD,⁸ Piotr Lewczuk, MD, PhD,⁹ Robert Dean, MD,¹⁰ Eric Siemers, MD,¹⁰ William Potter, MD,⁸ Virginia M.-Y. Lee, PhD,¹ John Q. Trojanowski, MD, PhD,¹ and the Alzheimer's Disease Neuroimaging Initiative







In vivo detection of amyloid plaques in a mouse model of Alzheimer's disease

Daniel M. Skovronsky*, Bin Zhang*, Mei-Ping Kung⁺, Hank F. Kung⁺⁺, John Q. Trojanowski*, and Virginia M.-Y. Lee*§





IV. What dictates disease progression?

Pathological α-Synuclein Transmission Initiates Parkinson-like Neurodegeneration in Nontransgenic Mice

Kelvin C. Luk, Victoria Kehm, Jenna Carroll, Bin Zhang, Patrick O'Brien, John Q. Trojanowski, Virginia M.-Y. Lee*







JQT Highlights

- Paired helical filaments are made of tau protein
- Lewy bodies contain alpha-synuclein
- TDP-43 forms inclusions in FTLD and ALS
- Autopsy-confirmed CSF biomarkers
- Neurodegenerative disease PET biomarkers
- Alzheimer's disease and related dementias are multi-proteinopathies
- Co-morbid neurodegenerative disease pathologic change
- Cell-to-cell transmission of neuropathologic change









IN LOVING MEMORY JOHN Q. TROJANOWSKI, MD, PHD leader • mentor • friend





















