



## Women's Brain Project

An international non-profit organization  
advocating for women's brain  
and mental health

[womensbrainproject.com](http://womensbrainproject.com)



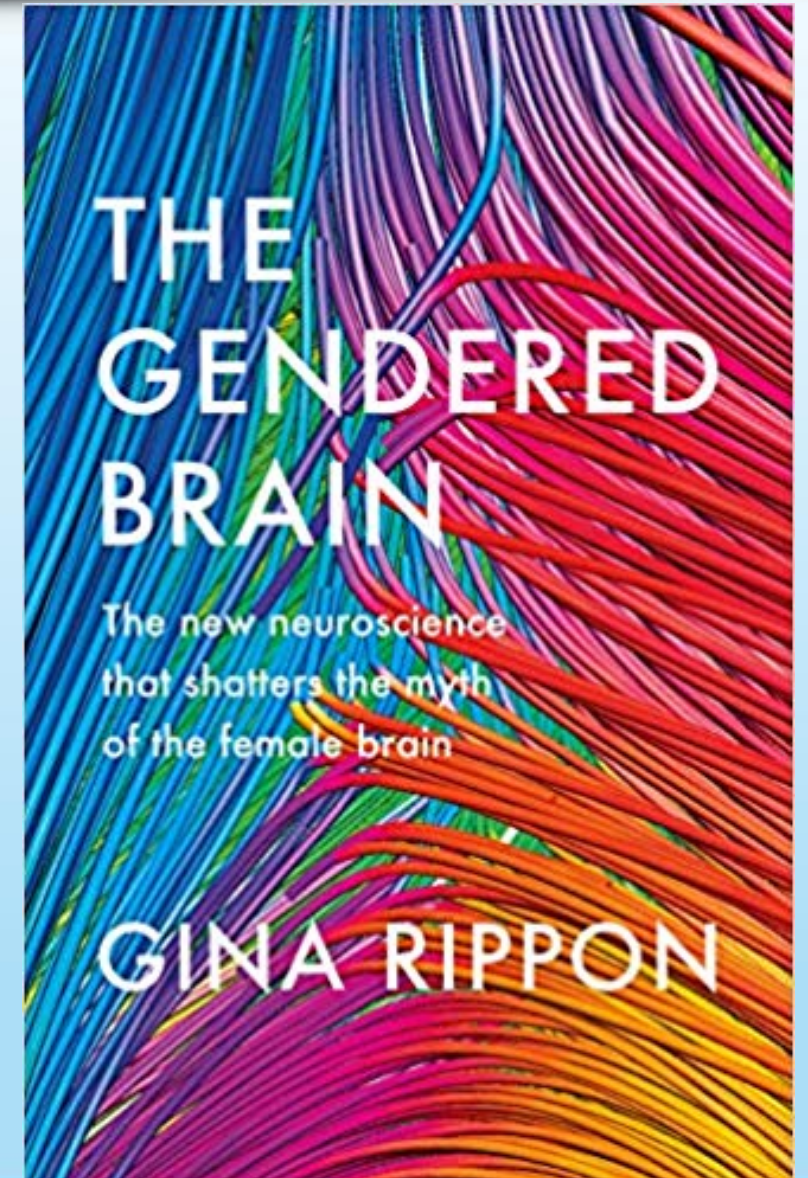


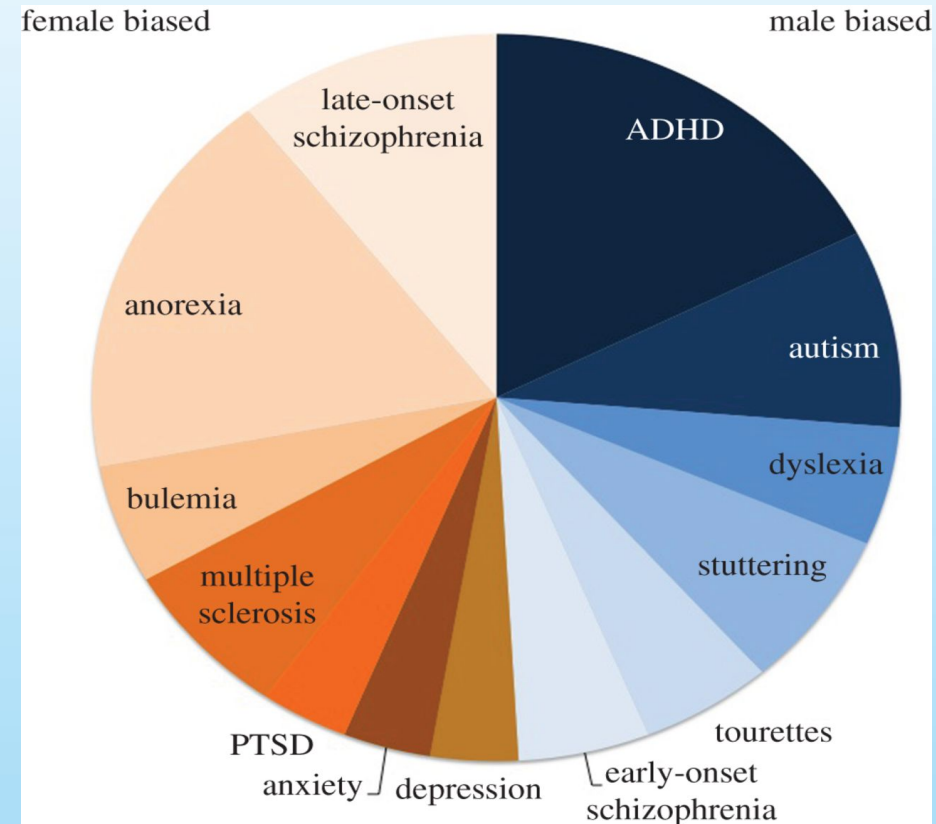
# **Sex and gender differences in Alzheimer's disease. An update from the Women's Brain Project**

*Maria Teresa Ferretti, PhD*

*Co-founder and Chief Scientific Officer, Women's Brain Project*

*[www.womensbrainproject.com](http://www.womensbrainproject.com)*





Dementia  
 Some brain tumors  
 Migraine  
 Depression  
 NMDA encephalitis  
 ...

Parkinson disease  
 ALS  
 Schizophrenia  
 Autism  
 Midlife stroke  
 ...



## THE GENDERED BRAIN

The new neuroscience  
that shatters the myth  
of the female brain

GINA RIPPON



nature

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CORRESPONDENCE · 30 APRIL 2019

## Account for sex in brain research for precision medicine

Maria Teresa Ferretti , Antonella Santucci-Chadha & Harald Hampel



In her review of Gina Rippon's book *The Gendered Brain*, Lise Eliot uses the term "neurosexism" to describe the "myth" of brain differences in men and women (*Nature* **566**, 453–454; 2019). Although the field is indeed rife with misinterpretation and methodological flaws, that is no justification for dismissing sex differences in neuroscience (see also R. Voskuhl and S. Klein *Nature* **568**, 171; 2019).

 [PDF version](#)

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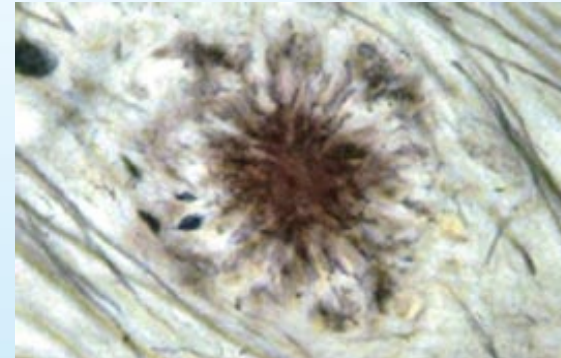
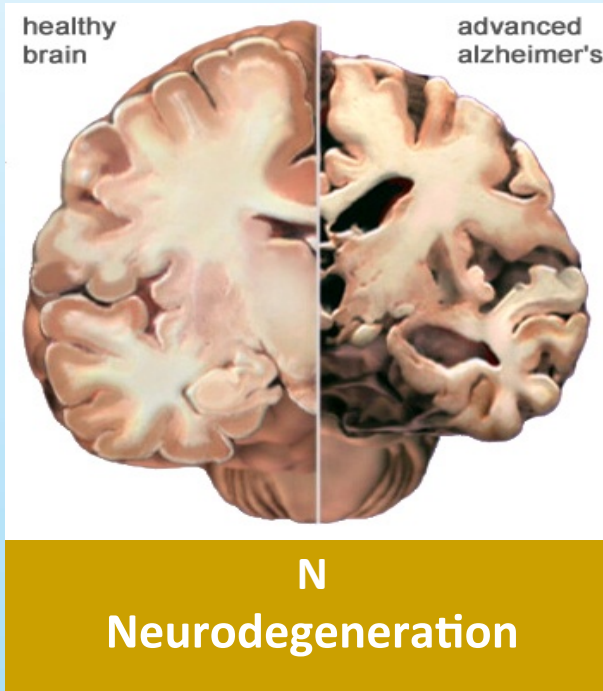
1. Sex differences and mechanistic insights
2. Sex differences and disease presentation



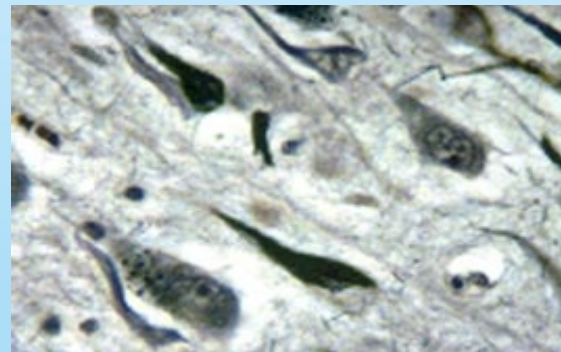
# Dementia





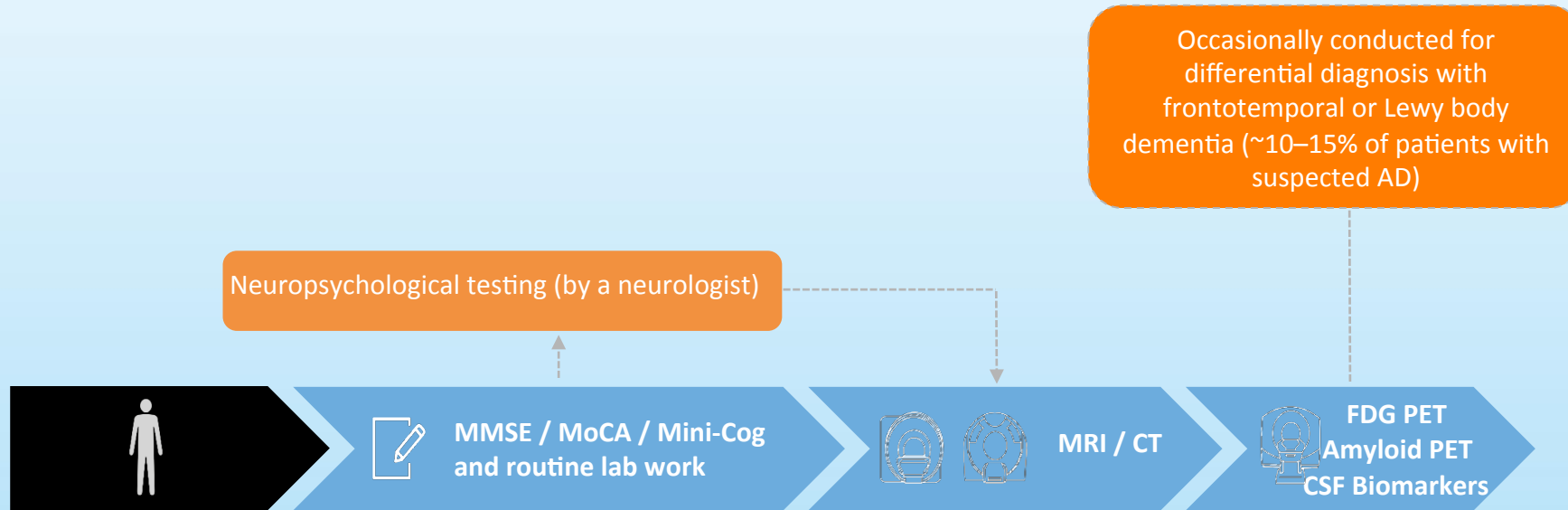


**A**  
Amyloid plaques

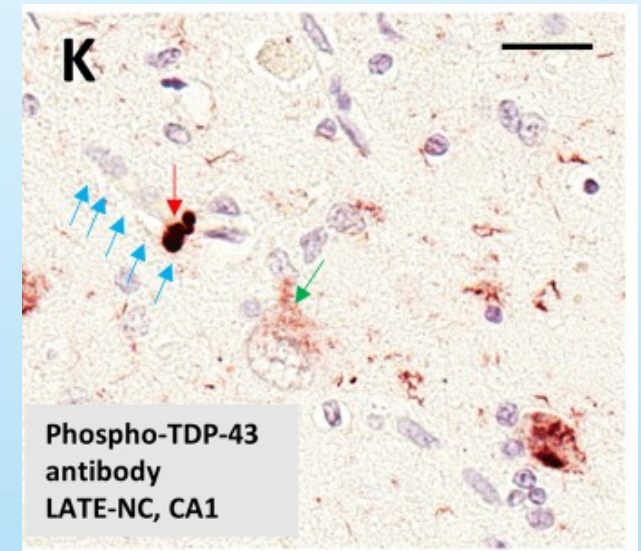
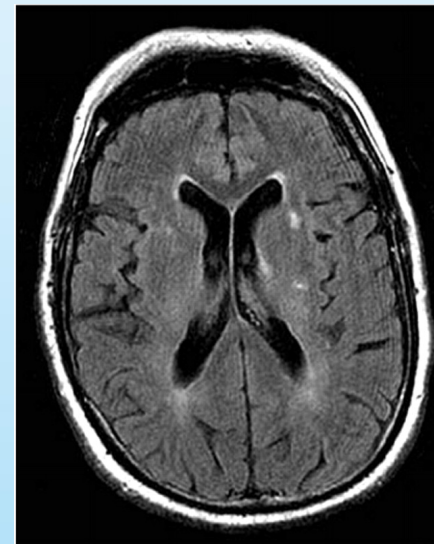
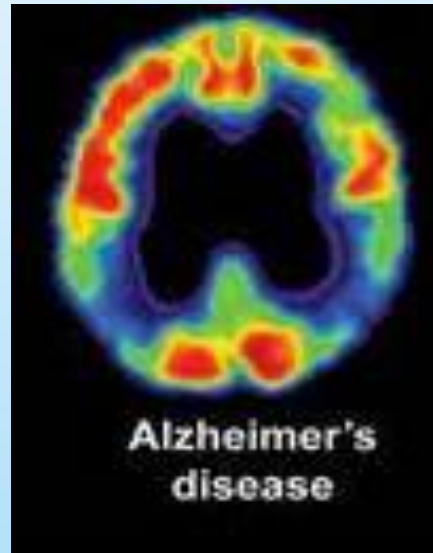
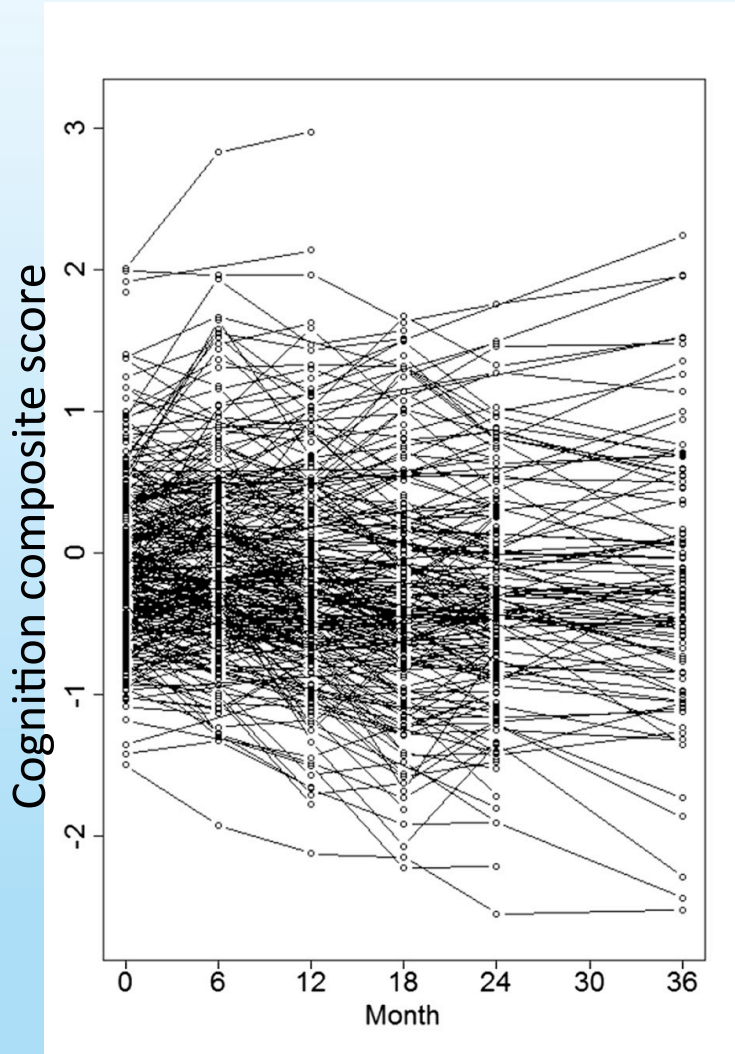


**T**  
Tau neurofibrillary tangles

# Current diagnostic pathway of AD



- CSF, cerebrospinal fluid; CT, computerised tomography; FDG, fluorodeoxyglucose; MMSE, Mini Mental State Examination; MoCA, Montreal Cognitive Assessment; MRI, magnetic resonance imaging; PET, positron-emission tomography



# Dementia disproportionately affects women

## WOMEN AND DEMENTIA IN EUROPE

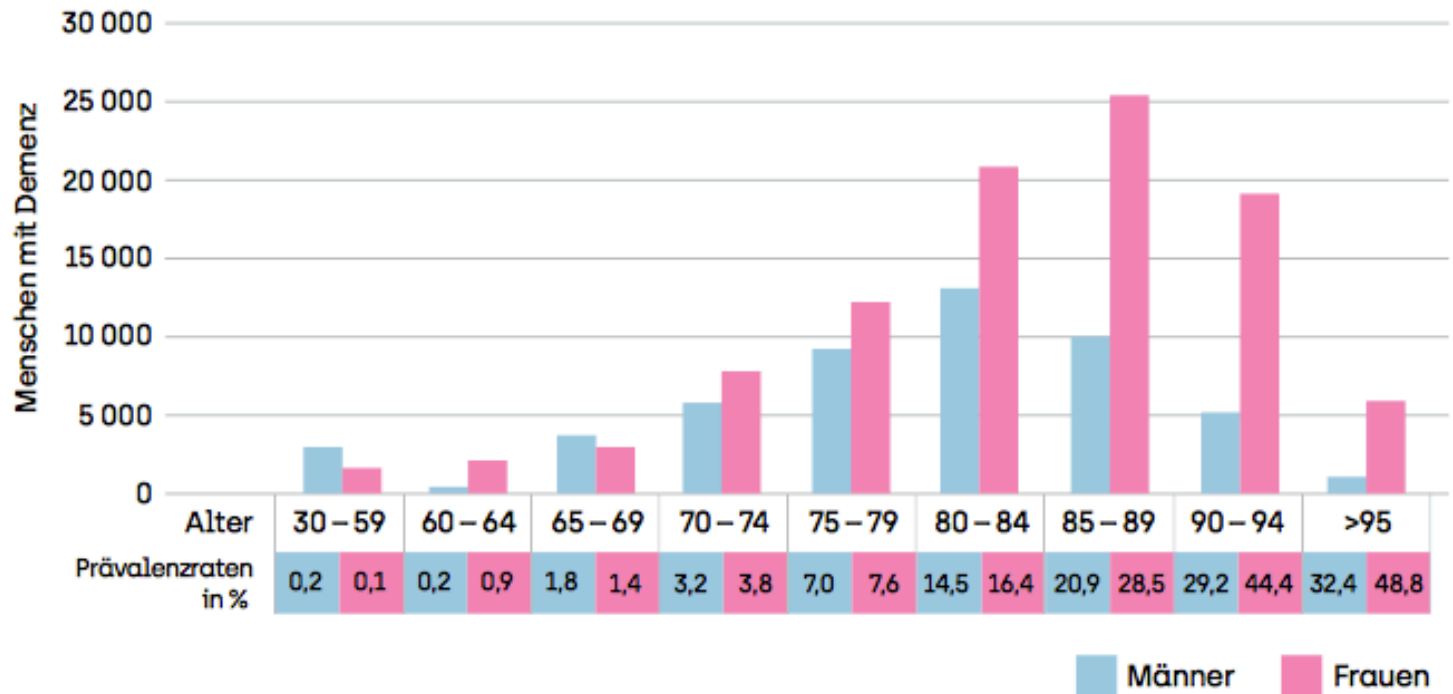
### POSITION PAPER

*Addressing the Disproportionate Burden of Dementia on Women*

Table 3. The frequency of dementia in Europe (EU-28) according to sex

Country	Men	Women
Austria	45,938	99,494
Belgium	62,972	128,309
Bulgaria	37,851	72,042
Croatia	20,394	46,682
Cyprus	4,333	6,917
Czech Republic	45,532	97,778
Denmark	29,715	55,847
Estonia	5,469	16,252
Finland	29,287	62,945
France	375,843	799,113
Germany	517,136	1,054,968
Greece	75,392	126,375
Hungary	43,636	105,291
Ireland	17,895	31,574
Italy	414,975	857,341
Latvia	8,902	26,812
Lithuania	12,567	34,768
Luxembourg	2,327	4,662
Malta	1,878	3,423
Netherlands	83,247	162,314
Poland	150,371	350,721
Portugal	62,260	120,266
Romania	90,484	179,820
Slovakia	17,834	40,774
Slovenia	9,324	22,711
Spain	280,149	538,197
Sweden	60,479	112,656
United Kingdom	360,581	677,210
<b>Total</b>	<b>2,866,771</b>	<b>5,835,262</b>

## / Anzahl Menschen mit Demenz nach Alter



[https://www.alzheimer-schweiz.ch/fileadmin/dam/Alzheimer\\_Schweiz/de/Publikationen-Produkte/Zahlen-Fakten/2018-CH-zahlen-fakten.pdf](https://www.alzheimer-schweiz.ch/fileadmin/dam/Alzheimer_Schweiz/de/Publikationen-Produkte/Zahlen-Fakten/2018-CH-zahlen-fakten.pdf)

# Gateway to precision medicine



nature  
REVIEWS

NEUROLOGY

Review Article | Published: 09 July 2018

## Sex differences in Alzheimer disease — the gateway to precision medicine

Maria Teresa Ferretti , Maria Florencia Iulita, Enrica Cavedo, Patrizia Andrea Chiesa, Annemarie Schumacher Dimech, Antonella Santuccione Chadha, Francesca Baracchi, H el ene Girouard, Sabina Misoch, Ezio Giacobini, Herman Depypere, Harald Hampel & for the Women's Brain Project and the Alzheimer Precision Medicine Initiative

*Nature Reviews Neurology* **14**, 457–469 (2018) | [Download Citation](#) ↓



# Sex and gender differences in Alzheimer's disease



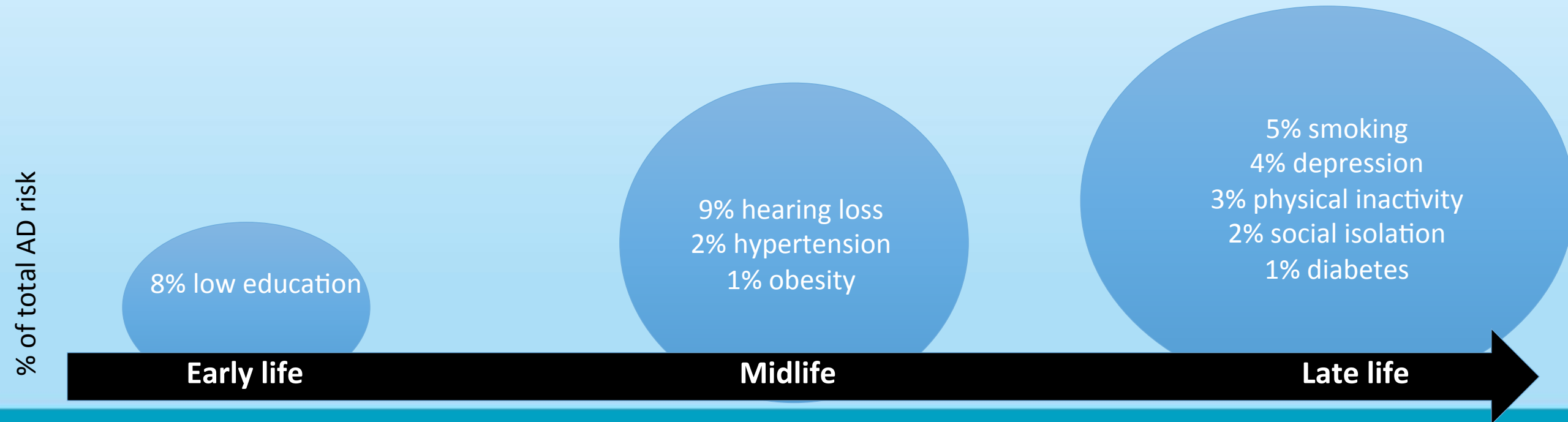


: ApoE, apolipoprotein E; DMT, disease-modifying therapy  
Livingston G, et al. Lancet 2017;390:2673–734.

35% of Alzheimer risk is **modifiable**

Higher risk of AD in women is debated by the experts, but

**Sex and gender affect modifiable risk factors**



## Potential female-specific risk factors:

- Early menopause
- Hypertensive complications during pregnancy
- Pregnancies
- Migraine

Journal of Alzheimer's Disease 71 (2019) 353–360  
DOI 10.3233/JAD-190581  
IOS Press 353

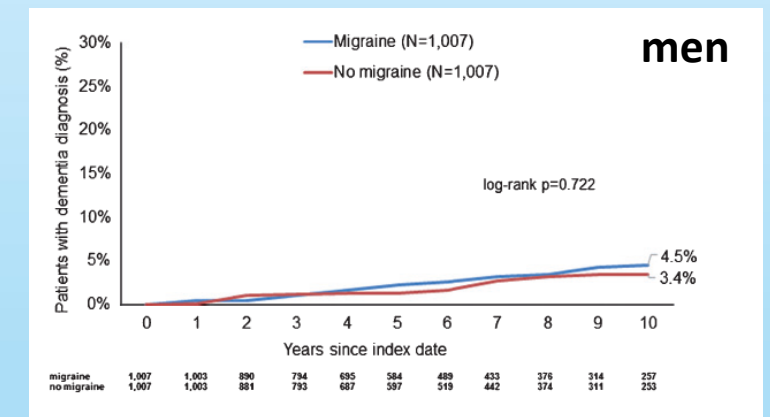
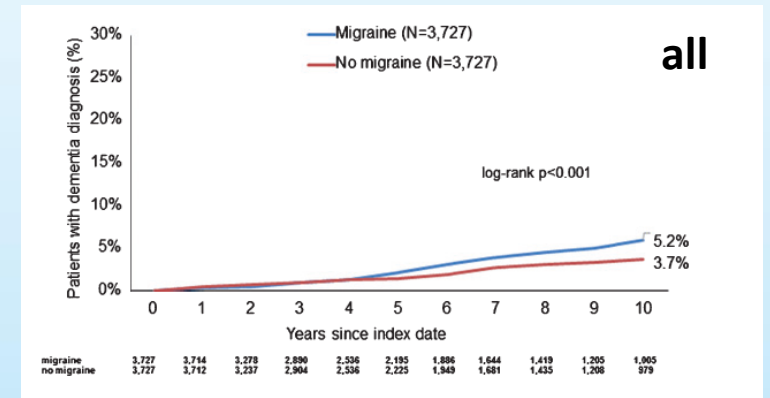
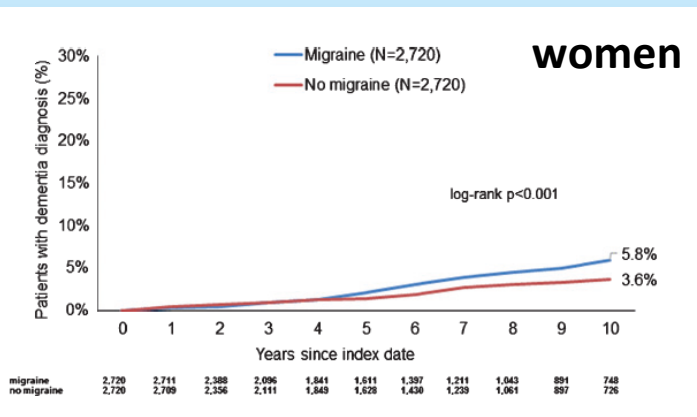
### Association between Migraine Headaches and Dementia in more than 7,400 Patients Followed in General Practices in the United Kingdom

Karel Kostev<sup>a,\*</sup>, Jens Bohlken<sup>b</sup> and Louis Jacob<sup>c</sup>

<sup>a</sup>Epidemiology, IQVIA, Frankfurt, Germany

<sup>b</sup>Institut für Sozialmedizin, Arbeitsmedizin und Public Health (ISAP), Medizinische Fakultät der Universität Leipzig

<sup>c</sup>Faculty of Medicine, University of Versailles Saint-Quentin-en-Yvelines, Montigny-le-Bretonneux, France





ARTICLES

## Better verbal memory in women than men in MCI despite similar levels of hippocampal atrophy

Erin E. Sundermann, PhD  
Anat Biegon, PhD  
Leah H. Rubin, PhD  
Richard B. Lipton, MD  
Wenzhu Mowrey, PhD  
Susan Landau, PhD  
Pauline M. Maki, PhD  
For the Alzheimer's Disease Neuroimaging Initiative

**ABSTRACT**

**Objective:** To examine sex differences in the relationship between clinical symptoms related to Alzheimer disease (AD) (verbal memory deficits) and neurodegeneration (hippocampal volume/intracranial volume ratio [HpVR]) across AD stages.

**Methods:** The sample included 379 healthy participants, 694 participants with amnesic mild cognitive impairment (aMCI), and 235 participants with AD and dementia from the Alzheimer's Disease Neuroimaging Initiative who completed the Rey Auditory Verbal Learning Test (RAVLT). Cross-sectional analyses were conducted using linear regression to examine the interaction between sex and HpVR on RAVLT across and within diagnostic groups adjusting for age, education, and APOE ε4 status.

**Results:** Across groups, there were significant sex × HpVR interactions for immediate and dela

Sundermann et al., *Neurology* 2016

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October 09, 2019 ARTICLE

## Sex-specific norms for verbal memory tests may improve diagnostic accuracy of amnesic MCI

Erin E. Sundermann, Pauline Maki, Anat Biegon, Richard B. Lipton, Michelle M. Mielke, Mary Machulda, Mark W. Bondi, for the Alzheimer's Disease Neuroimaging Initiative

First published October 9, 2019, DOI: <https://doi.org/10.1212/WNL.00000000000008467>

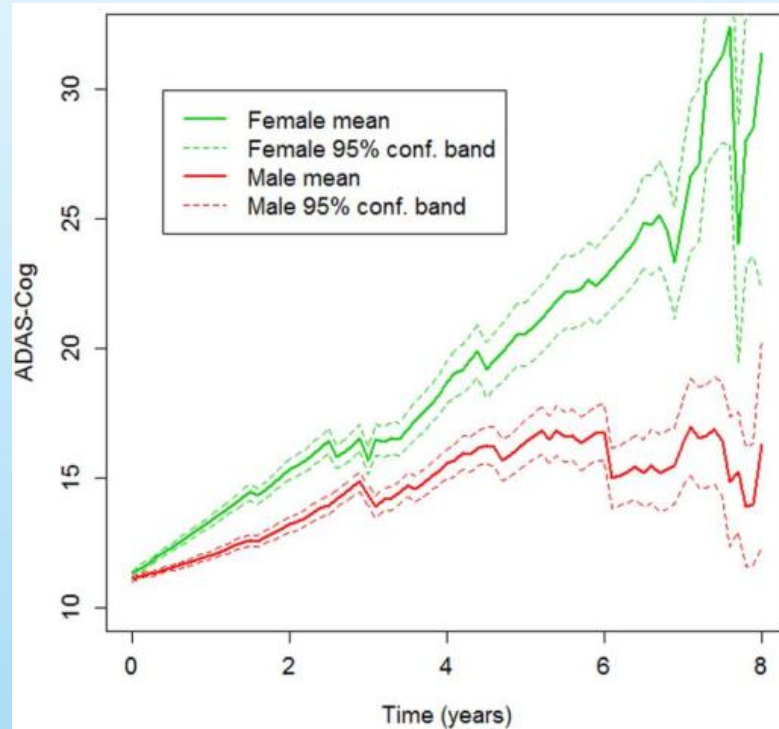
	Women with aMCI, n (%)	Men with aMCI, n (%)	$\chi^2$ Test, p value
<b>aMCI classified via conventional diagnostic criteria</b>	120 (26)	239 (45)	38.5, <0.001
<b>aMCI classified via sex-specific diagnostic criteria</b>	165 (36)	184 (35)	0.25, 0.66

Abbreviation: aMCI = amnesic mild cognitive impairment.

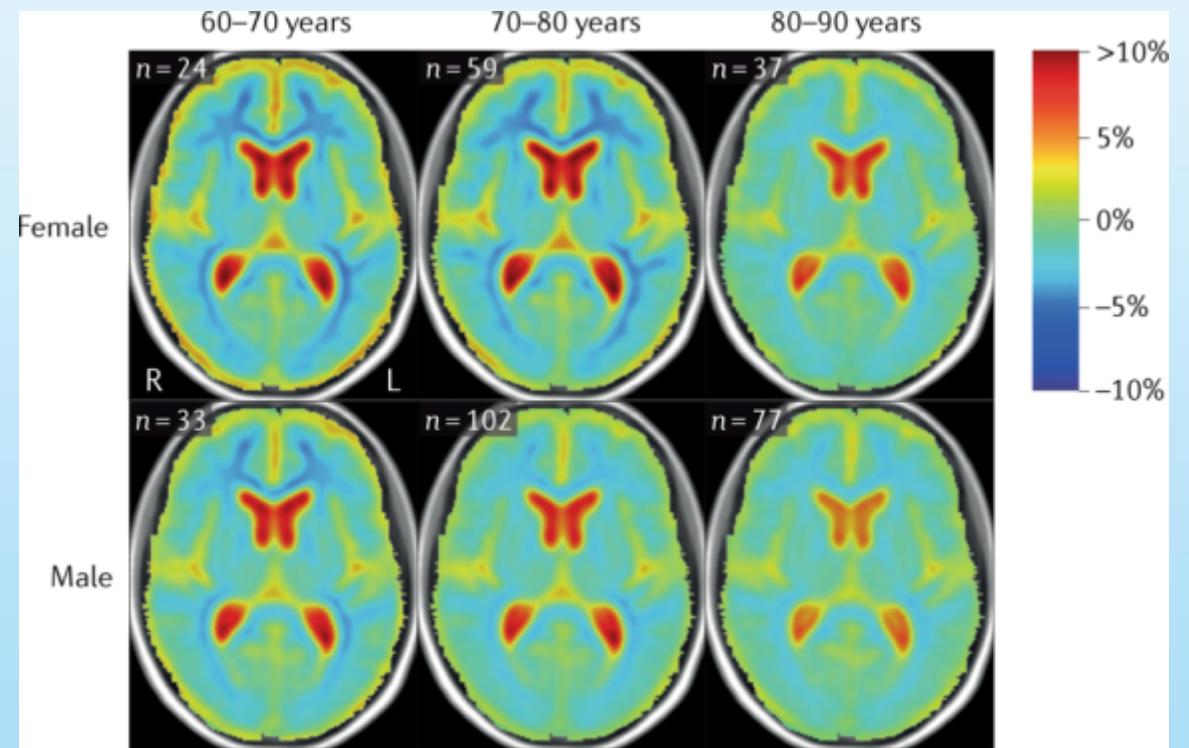
# Faster disease progression in women



2x faster cognitive decline



Faster brain shrinkage (darker blue)



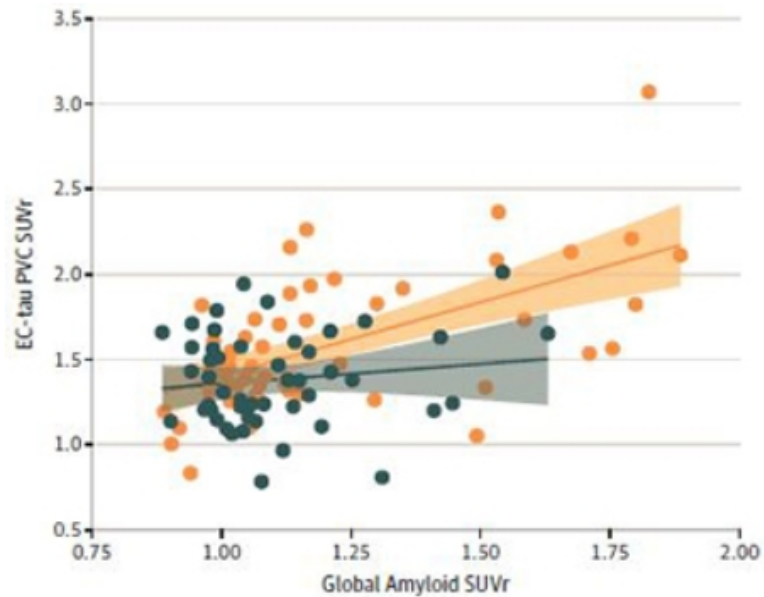


## Amyloid and Regional Tau Deposition Measured By Positron Emission Tomography in Clinically Normal Older Adults

Rachel F. Buckley, PhD<sup>1,2,3,4</sup>; Elizabeth C. Mormino, PhD<sup>5</sup>; Jennifer S. Rabin, PhD<sup>6</sup>; et al

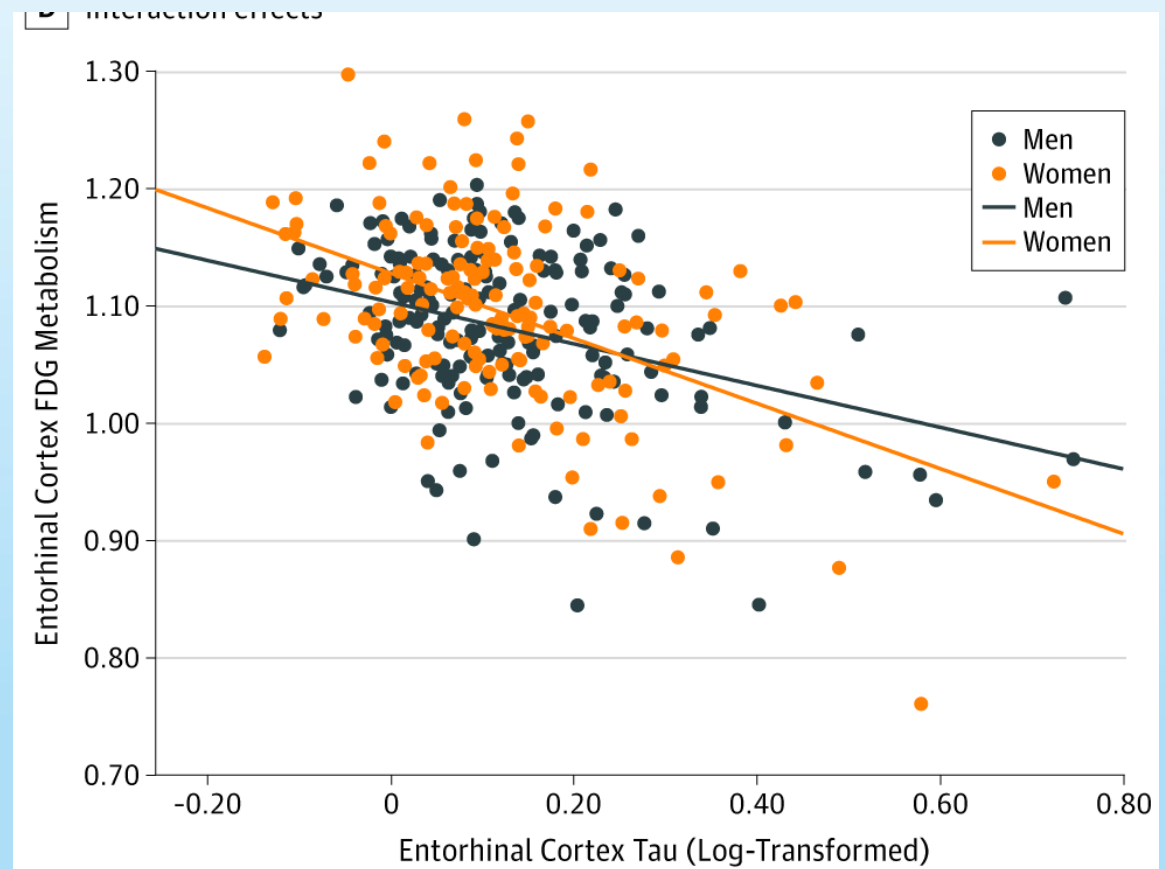
» Author Affiliations | Article Information

JAMA Neurol. Published online February 4, 2019. doi:10.1001/jamaneurol.2018.4693



*Faster Tau Accumulation? The more amyloid in the brain, the more tau tangles in entorhinal cortices of cognitively normal women (orange) compared to men (gray). [Courtesy of © 2019 American Medical Association. All rights reserved.]*

Women displayed greater tau-mediated metabolic dysfunction than men (Ramanan et al., JAMA Neurology 2019)



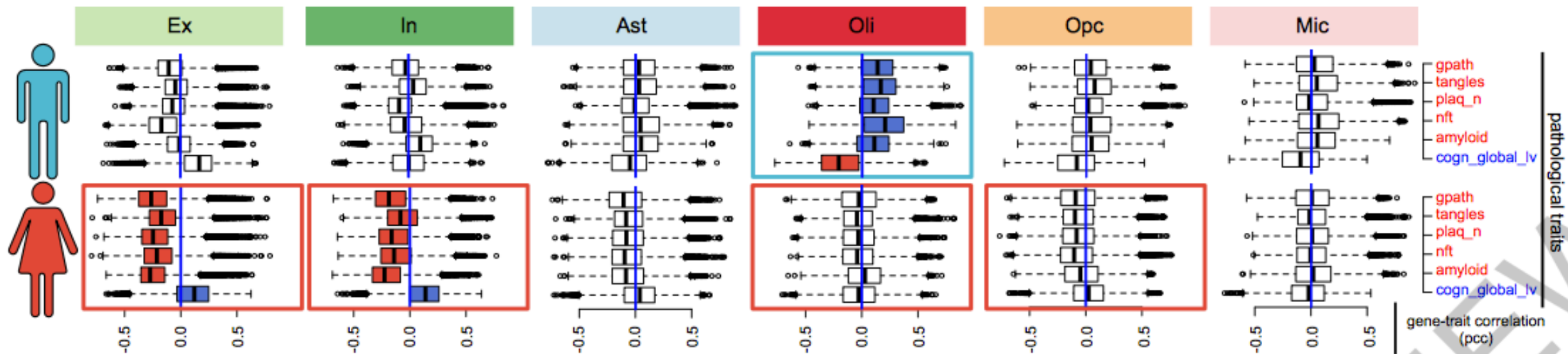


nature  
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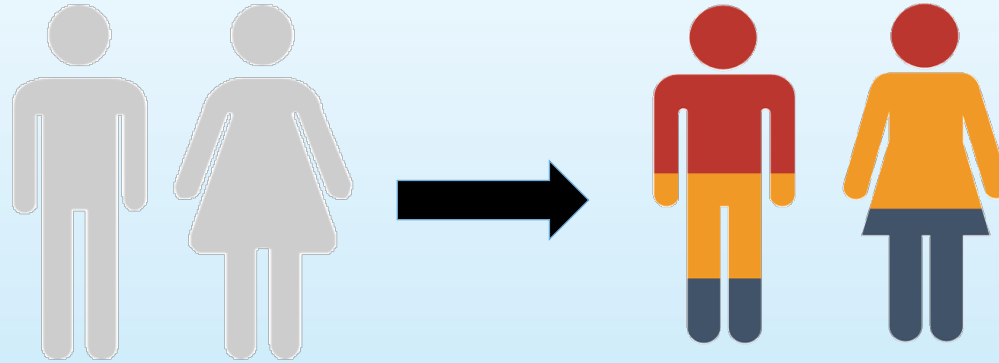
## Single-cell transcriptomic analysis of Alzheimer's disease

Hansruedi Mathys, Jose Davila-Velderrain, Zhuyu Peng, Fan Gao, Shahin Mohammadi, Jennie Z. Young, Madhvi Menon, Liang He, Fatema Abdurrob, Xueqiao Jiang, Anthony J. Martorell, Richard M. Ransohoff, Brian P. Hafler, David A. Bennett, Manolis Kellis & Li-Huei Tsai

Nature (2019) | [Download Citation](#)



Moving from  
'one size fits all'  
medicine....



...to Precision Medicine

## Sex-sensitive

- Preventative campaigns
- Early diagnosis
- Treatment
- In **Clinical trial design**
- In **preclinical research**

# Meet the WBP Team!



III Women's Brain Forum, Zurich, September 18<sup>th</sup>-19<sup>th</sup> 2020