

ONSET OF TUBEROUS SCLEROSIS COMPLEX ASSOCIATED NEUROPSYCHIATRIC DISORDER (TAND)

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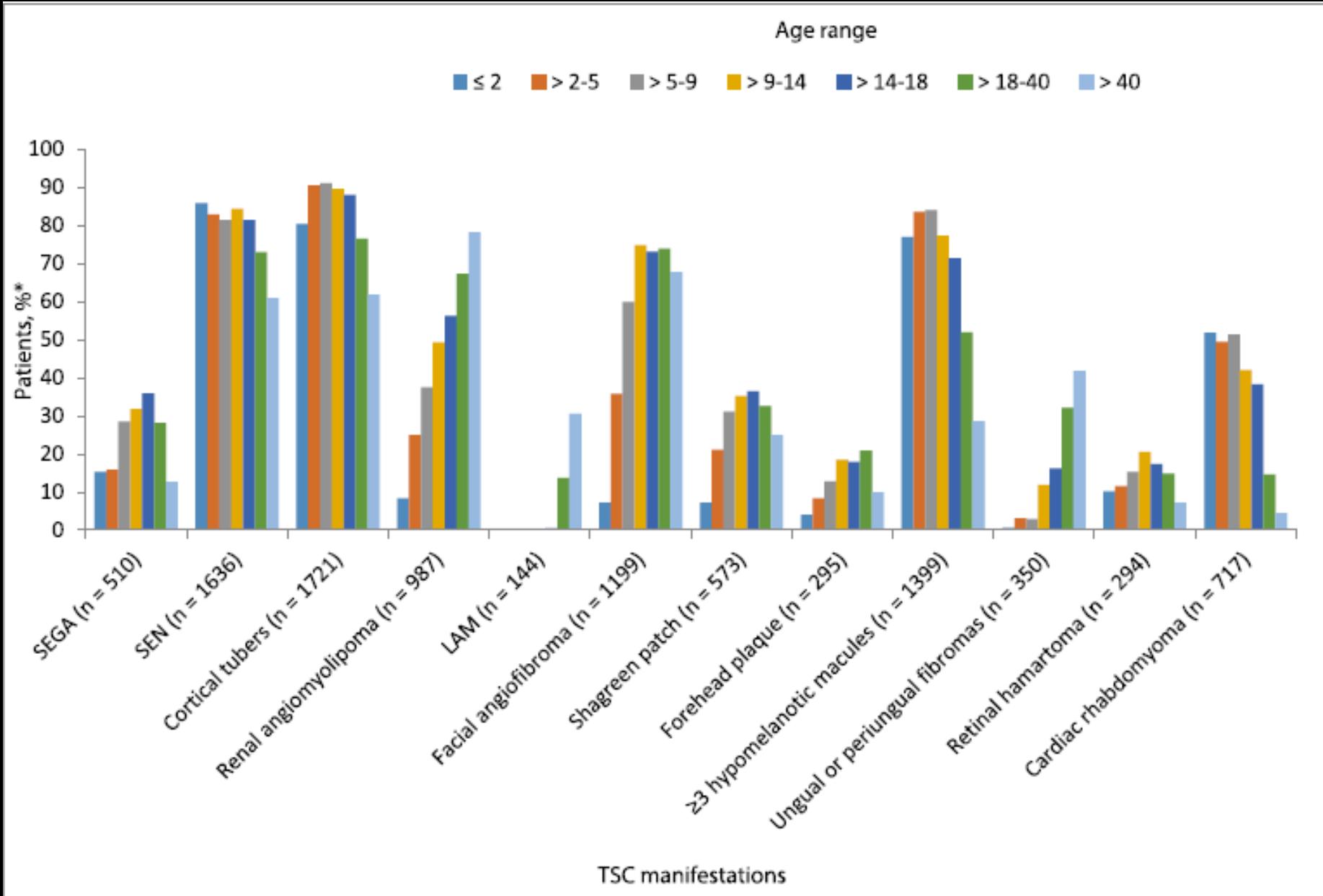
OUTLINE

- TUBEROUS SCLEROSIS COMPLEX (TSC)
- WHAT IS A BEHAVIORAL NEUROLOGIST?
- STUDY OF DEMENTIA
- TAND SYMPTOMS
- ONSET OF TAND THROUGHOUT ADULTHOOD

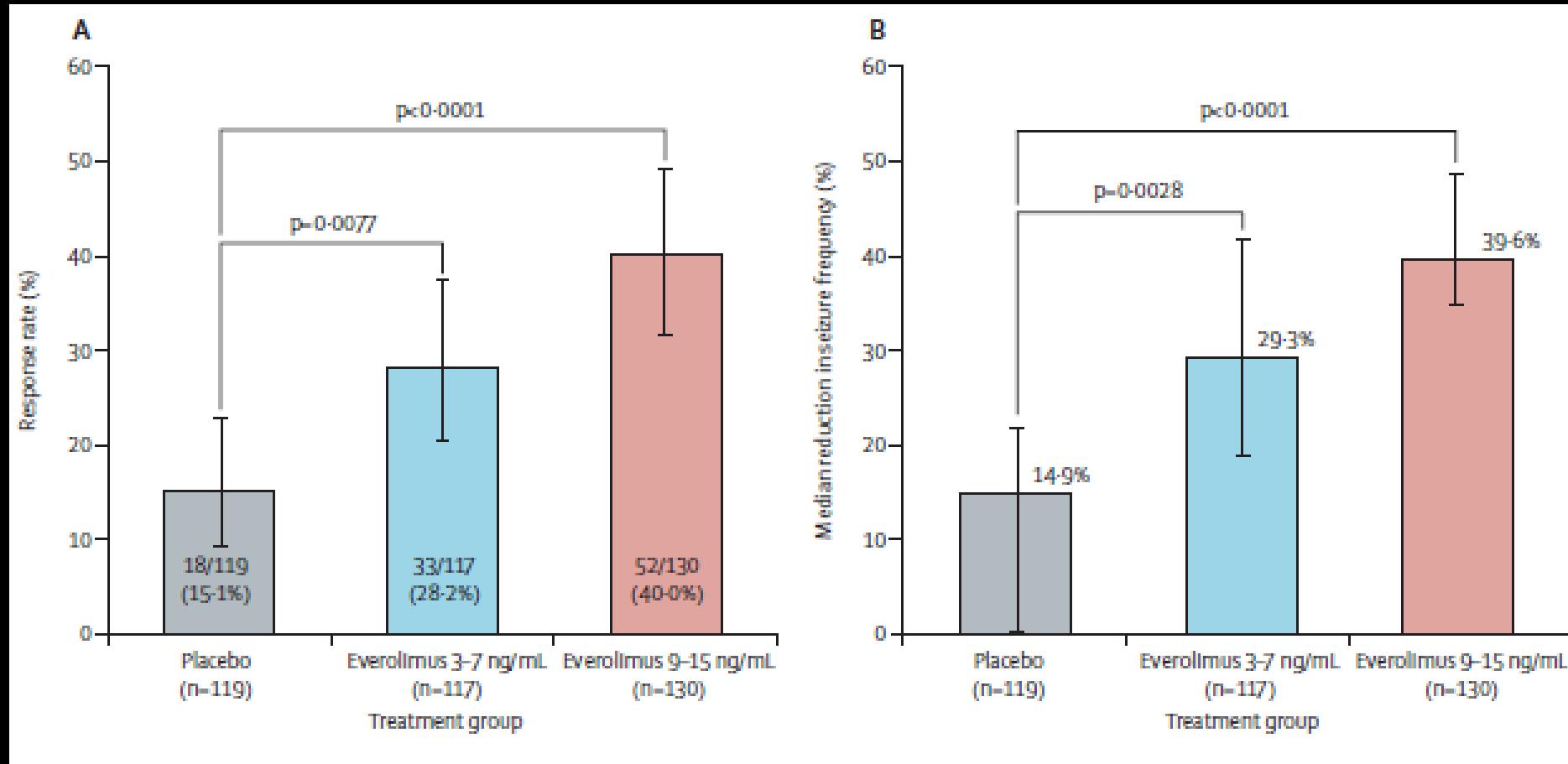
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PHYSICAL TRAITS OF TSC THROUGHOUT LIFE



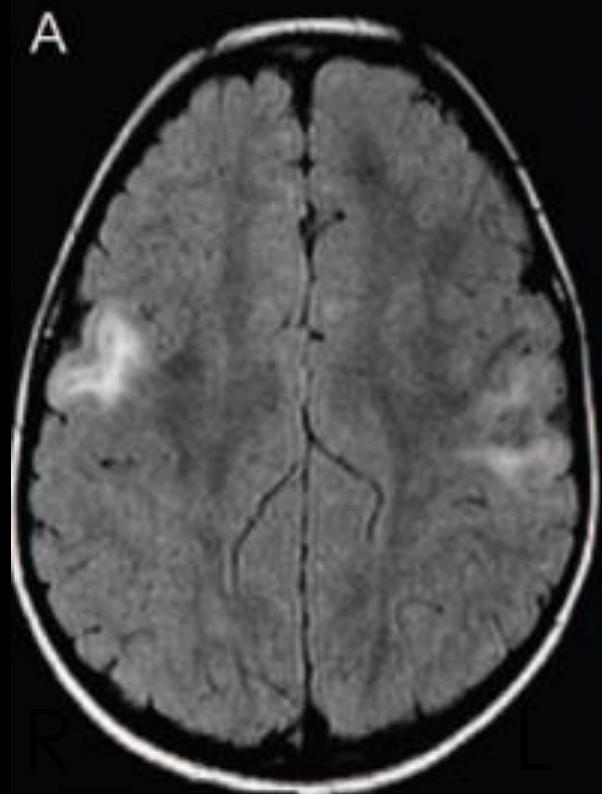
MEDICAL ADVANCEMENT: EXIST-3 TRIAL



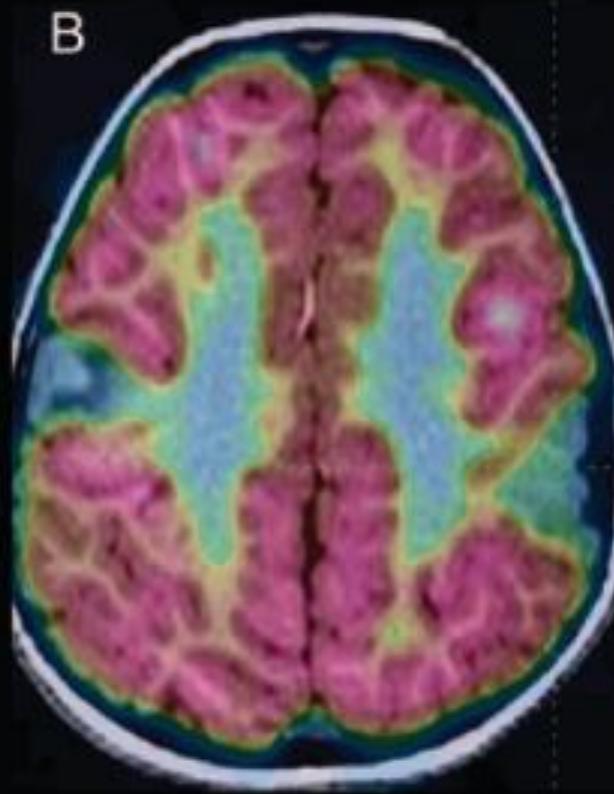
French et al. 2016

MEDICAL AND SURGICAL ADVANCEMENT

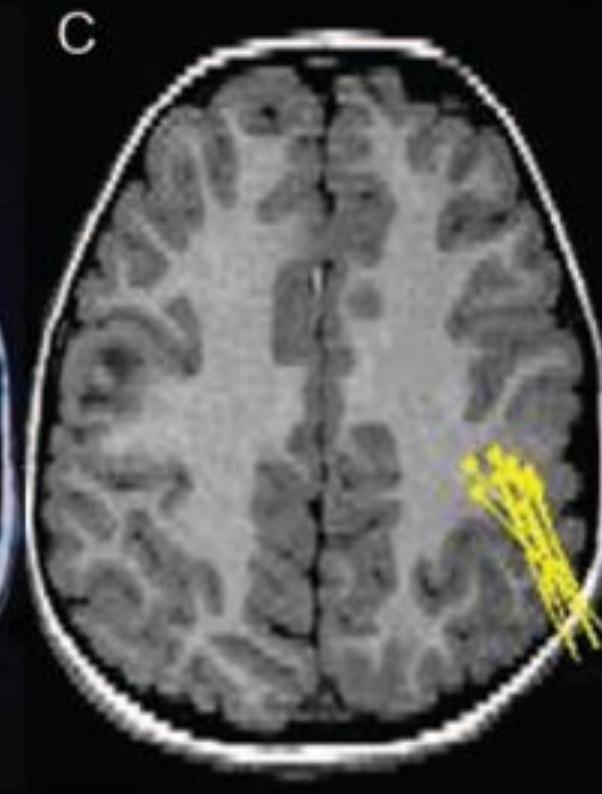
Magnetic Resonance
Imaging (MRI) FLAIR



Positron Emission
Tomography (PET)



MRIT1



Wu et al 2010

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BEHAVIORAL NEUROLOGIST

- COGNITIVE
- BEHAVIORAL
- PSYCHIATRIC

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DEMENTIAS

- ALZHEIMER'S DISEASE
- DEMENTIA WITH LEWY BODIES
- FRONTOTEMPORAL DEMENTIAS

ALZHEIMER'S DISEASE (AD)

- AMNESTIC VARIANT
- VISUOSPATIAL VARIANT
- LANGUAGE VARIANT
- BEHAVIORAL/DYSEXECUTIVE VARIANT

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TAND SYMPTOMS

Cognitive	Behavioral	Psychiatric
Memory	Aggressive outbursts	Depressed mood
Visuospatial function	Apathy	Anxiety
Attention	Self-injury	Mood swings
Multi-tasking	Repeating words	Compulsive behaviors
Planning	Disinhibition	Psychotic disorder
Organizing	Perseverative	
Language difficulties	Hyperactive	

OVERLAP BETWEEN TAND SYMPTOMS AND ALZHEIMER'S DISEASE

Cognitive	Behavioral	Psychiatric
Memory	Aggressive outbursts	Depressed mood
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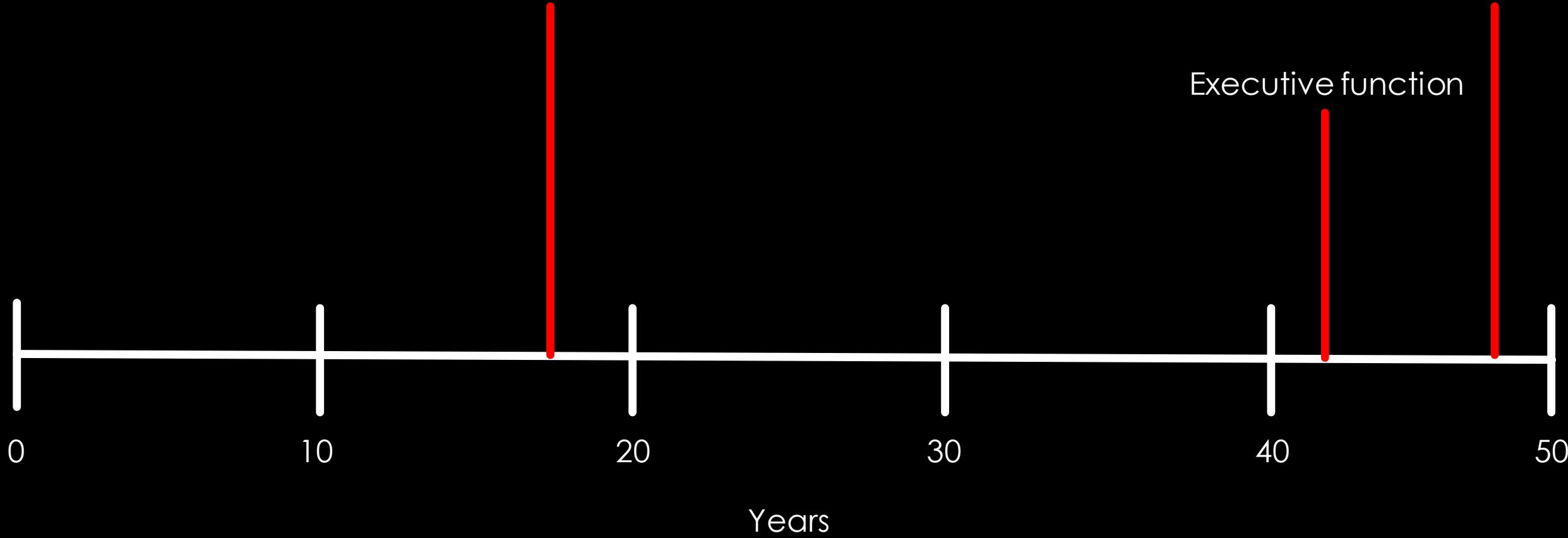
TAND AGE OF ONSET

Behavioral symptoms

Anxiety and depression

Memory

Executive function



THANK YOU

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[HTTPS://WWW.DUKEHEALTH.ORG/FIND-DOCTORS-PHYSICIANS/ANDY-LIU-MD-MS](https://www.dukehealth.org/find-doctors-physicians/andy-liu-md-ms)

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- NICK OLNEY, MD

REFERENCES

- FRENCH, J. A., LAWSON, J. A., YAPICI, Z., IKEDA, H., POLSTER, T., NABBOUT, R., ... FRANZ, D. N. (2016). ADJUNCTIVE EVEROLIMUS THERAPY FOR TREATMENT-RESISTANT FOCAL-ONSET SEIZURES ASSOCIATED WITH TUBEROUS SCLEROSIS (EXIST-3): A PHASE 3, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY. *THE LANCET*, 388(10056), 2153–2163. [HTTPS://DOI.ORG/10.1016/S0140-6736\(16\)31419-2](https://doi.org/10.1016/S0140-6736(16)31419-2)
- KINGSWOOD, J. C., D'AUGÈRES, G. B., BELOUSOVA, E., FERREIRA, J. C., CARTER, T., CASTELLANA, R., ... JANSEN, A. C. (2017). TUBEROUS SCLEROSIS REGISTRY TO INCREASE DISEASE AWARENESS (TOSCA) - BASELINE DATA ON 2093 PATIENTS. *ORPHANET JOURNAL OF RARE DISEASES*, 12(1). [HTTPS://DOI.ORG/10.1186/s13023-016-0553-5](https://doi.org/10.1186/s13023-016-0553-5)
- Wu, J. Y., SALAMON, N., KIRSCH, H. E., MANTLE, M. M., NAGARAJAN, S. S., KURELOWECH, L., ... MATHERN, G. W. (2010). NONINVASIVE TESTING, EARLY SURGERY, AND SEIZURE FREEDOM IN TUBEROUS SCLEROSIS COMPLEX. *NEUROLOGY*, 74(5), 392–398. [HTTPS://DOI.ORG/10.1212/WNL.0b013e3181ce5d9e](https://doi.org/10.1212/WNL.0b013e3181ce5d9e)
- DE VRIES PJ, WHITTEMORE VH, LECLEZIO L, ET AL. TUBEROUS SCLEROSIS ASSOCIATED NEUROPSYCHIATRIC DISORDERS (TAND) AND THE TAND CHECKLIST. *PEDIATRIC NEUROLOGY*. 2015;52(1):25-35. [HTTP://WWW.NCBI.NLM.NIH.GOV/PUBMED/25532776](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4380776/). DOI: 10.1016/j.pediatrneurol.2014.10.004.
- OLNEY N, SPINA S, MILLER B. FRONTOTEMPORAL DEMENTIA. *NEUROLOGIC CLINICS*. 2017;180(2):140-143. [HTTP://BJP.RCPSCYCH.ORG/CGI/CONTENT/ABSTRACT/180/2/140](http://bjp.rcpsych.org/cgi/content/abstract/180/2/140). DOI: 10.1192/bj.180.2.140.
- OLNEY N, ALQUEZAR C, RAMOS E, ET AL. LINKING TUBEROUS SCLEROSIS COMPLEX, EXCESSIVE mTOR SIGNALING, AND AGE-RELATED NEURODEGENERATION: A NEW ASSOCIATION BETWEEN TSC1 MUTATION AND FRONTOTEMPORAL DEMENTIA. *ACTA NEUROPATHOL*. 2017;134(5):813-816. [HTTPS://SEARCH.PROQUEST.COM/DOCVIEW/1951870885](https://search.proquest.com/docview/1951870885). DOI: 10.1007/s00401-017-1764-0.
- LIU, A.J., STAFFARONI A.M., ROJAS, J.C., OLNEY, N.T., ALQUEZAR-BURILLO, C., LJUBENKOV, P.A., LA JOIE, R., FONG, JC., TAYLOR, J., KARYDAS, B.A., RAMOS, E.M., COPPOLA, G., BOXER, A.L., RABINOVICI, G.D., MILLER, B.L., KAO, A.W. OVERLAP IN COGNITIVE AND BEHAVIORAL FEATURES BETWEEN ADULTS WITH TUBEROUS SCLEROSIS AND FRONTOTEMPORAL DEMENTIA. *JAMA NEUROLOGY*. ACCEPTED DECEMBER 2019.