

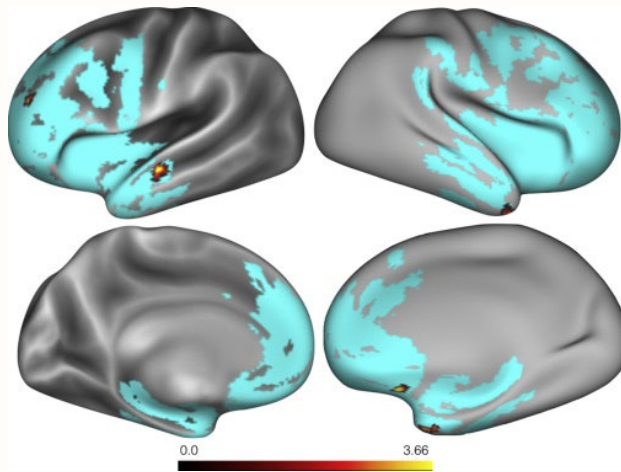
Image credit: Niikura, et. al. 2014 under CC BY license

UNC13A: Subgrouping ALS by Genotype?

November 9, 2018 News in Brief [Michelle Pflumm](#)

A key challenge in developing therapies for ALS is the heterogeneity of the disease. To overcome this obstacle, some scientists are scouring the genomes of people with ALS to spot variants that could indicate whether they might benefit from these treatment strategies (see [van Eijk et al., 2017](#)).

Now, a research team led by Corey McMillan at the University of Pennsylvania in Philadelphia reports that a key change in the gene UNC13A may help determine whether people with ALS also develop frontotemporal disease. The retrospective analysis found that people with sporadic ALS harboring this variant exhibited signs of atrophy in the prefrontal and temporal lobes of the brain –the same regions of the brain targeted by FTD. A total of 109 people with sporadic ALS and 113 healthy volunteers participated in the study.



Subgrouping by genotype? Increased atrophy could be detected in the frontal and temporal lobes of the brain of people with sporadic ALS harboring a key change in synaptic protein UNC13A. [Courtesy of [Placek et al., 2018](#), *Neurobiology of Aging*.]

The findings build on previous work, which found that this variant of UNC13A is associated with increased risk of developing ALS and FTD (see [March 2018](#), [April 2018](#) news; [van Es et al., 2009](#); [Karch et al., 2018](#)).

Enter search term, click "enter".

Sort by:

Date: Relevance:

Filter articles published since 2015 by topic, disease, or article type.

[Guidelines for filtering](#)

Topic:

- Biomarkers
- Clinical Research
- Drug Development
- Genetics
- Laboratory Research
- New Methods
- Policy
- Research Models
- Risk Factors

Disease:

- Alzheimer's disease
- Amyotrophic lateral sclerosis
- Autism
- Cancer
- Crohn's disease
- FAP
- Frontotemporal dementia
- Hereditary neuropathies
- Huntington's disease

About 16% of people with sporadic ALS harbor this minor allele of the UNC13A gene (see [van Eijk et al., 2017](#)).

The synaptic protein UNC13A is thought to help ensure that signals are transmitted quickly and efficiently between neurons in the brain ([Böhme et al., 2016](#); [Reddy-Alla et al., 2017](#)).

The study [appeared](#) in the January 2019 issue of *Neurobiology of Aging*.

Featured Paper

Placek K, Baer GM, Elman L, McCluskey L, Hennessy L, Ferraro PM, Lee EB, Lee VMY, Trojanowski JQ, Van Deerlin VM, Grossman M, Irwin DJ, McMillan CT. UNC13A polymorphism contributes to frontotemporal disease in sporadic amyotrophic lateral sclerosis. *Neurobiol Aging*. 2018 Sep 27;73:190-199. [[PubMed](#)].

References

van Eijk RPA, Jones AR, Sproviero W, Shatunov A, Shaw PJ, Leigh PN, Young CA, Shaw CE, Mora G, Mandrioli J, Borghero G, Volanti P, Diekstra FP, van Rheenen W, Verstraete E, Eijkemans MJC, Veldink JH, Chio A, Al-Chalabi A, van den Berg LH, van Es MA; For UKMND-LiCALS and LITALS Study Group. Meta-analysis of pharmacogenetic interactions in amyotrophic lateral sclerosis clinical trials. *Neurology*. 2017 Oct 31;89(18):1915-1922. [[PubMed](#)].

Karch CM, Wen N, Fan CC, Yokoyama JS, Kouri N, Ross OA, Höglinger G, Müller U, Ferrari R, Hardy J, Schellenberg GD, Sleiman PM, Momeni P, Hess CP, Miller BL, Sharma M, Van Deerlin V, Smeland OB, Andreassen OA, Dale AM, Desikan RS; International Frontotemporal Dementia (FTD)–Genomics Consortium, International Collaboration for Frontotemporal Dementia, Progressive Supranuclear Palsy (PSP) Genetics Consortium, and International Parkinson’s Disease Genomics Consortium. Selective Genetic Overlap Between Amyotrophic Lateral Sclerosis and Diseases of the Frontotemporal Dementia Spectrum. *JAMA Neurol*. 2018 Jul 1;75(7):860-875. [[PubMed](#)].

van Es MA, Veldink JH, Saris CG, Blauw HM, van Vught PW, Birve A, Lemmens R, Schelhaas HJ, Groen EJ, Huisman MH, van der Kooij AJ, de Visser M, Dahlberg C, Estrada K, Rivadeneira F, Hofman A, Zwarts MJ, van Doormaal PT, Rujescu D, Strengman E, Giegling I, Muglia P, Tomik B, Slowik A, Uitterlinden AG, Hendrich C, Waibel S, Meyer T, Ludolph AC, Glass JD, Purcell S, Cichon S, Nöthen MM, Wichmann HE, Schreiber S, Vermeulen SH, Kiemeny LA, Wokke JH, Cronin S, McLaughlin RL, Hardiman O, Fumoto K, Pasterkamp RJ, Meininger V, Melki J, Leigh PN, Shaw CE, Landers JE, Al-Chalabi A, Brown RH Jr, Robberecht W, Andersen PM, Ophoff RA, van den Berg LH. Genome-wide association study identifies 19p13.3 (UNC13A) and 9p21.2 as susceptibility loci for sporadic amyotrophic lateral sclerosis. *Nat Genet*. 2009 Oct;41(10):1083-7. [[PubMed](#)].

Reddy-Alla S, Böhme MA, Reynolds E, Beis C, Grasskamp AT, Mampell MM, Maglione M, Jusyte M, Rey U, Babikir H, McCarthy AW, Quentin C, Matkovic T, Bergeron DD, Mushtaq Z, Göttfert F, Oswald D, Mielke T, Hell SW, Sigrist SJ, Walter AM. Stable Positioning of Unc13 Restricts Synaptic Vesicle Fusion to Defined Release Sites to Promote Synchronous Neurotransmission. *Neuron*. 2017 Sep 13;95(6):1350-1364.e12. [[PubMed](#)].

Multiple sclerosis
Myotonic dystrophy
OCD
Parkinson's disease
Schizophrenia
Spinal cord or traumatic brain injury
Spinal muscular atrophy
Spinocerebellar ataxia

Article type:

News Analysis
News in Brief

9p21.2 as susceptibility loci for sporadic amyotrophic lateral sclerosis. *Nat Genet.* 2009 Oct;41(10):1083-7. [[PubMed](#)].

Reddy-Alla S, Böhme MA, Reynolds E, Beis C, Grasskamp AT, Mampell MM, Maglione M, Jusyte M, Rey U, Babikir H, McCarthy AW, Quentin C, Matkovic T, Bergeron DD, Mushtaq Z, Göttfert F, Oswald D, Mielke T, Hell SW, Sigrist SJ, Walter AM. Stable Positioning of Unc13 Restricts Synaptic Vesicle Fusion to Defined Release Sites to Promote Synchronous Neurotransmission. *Neuron.* 2017 Sep 13;95(6):1350-1364.e12. [[PubMed](#)].

Böhme MA, Beis C, Reddy-Alla S, Reynolds E, Mampell MM, Grasskamp AT, Lützkendorf J, Bergeron DD, Driller JH, Babikir H, Göttfert F, Robinson IM, O'Kane CJ, Hell SW, Wahl MC, Stelzl U, Loll B, Walter AM, Sigrist SJ. Active zone scaffolds differentially accumulate Unc13 isoforms to tune Ca(2+) channel-vesicle coupling. *Nat Neurosci.* 2016 Oct;19(10):1311-20. [[PubMed](#)].

Further Reading

Diekstra FP, van Vught PW, van Rheeën W, Koppers M, Pasterkamp RJ, van Es MA, Schelhaas HJ, de Visser M, Robberecht W, Van Damme P, Andersen PM, van den Berg LH, Veldink JH. UNC13A is a modifier of survival in amyotrophic lateral sclerosis. *Neurobiol Aging.* 2012 Mar;33(3):630.e3-8. [[PubMed](#)].

Lipstein N, Verhoeven-Duif NM, Michelassi FE, Calloway N, van Hasselt PM, Pienkowska K, van Haaften G, van Haelst MM, van Empelen R, Cuppen I, van Teeseling HC, Evelein AM, Vorstman JA, Thoms S, Jahn O, Duran KJ, Monroe GR, Ryan TA, Taschenberger H, Dittman JS, Rhee JS, Visser G, Jans JJ, Brose N. Synaptic UNC13A protein variant causes increased neurotransmission and dyskinetic movement disorder. *J Clin Invest.* 2017 Mar 1;127(3):1005-1018. [[PubMed](#)].

Share this:



[Privacy](#)

[Terms of Use](#)

[How to Cite](#)

[Support Us](#)

[Feedback](#)

[Image Credits](#)

alsresearchforum@prize4life.org