ALLFTD Winter 2023 Newsletter:
Simplified Science Shorts

Learn more about what we're learning in ALLFTD and how it impacts you by reading these brief summaries of some of our recent publications:

Temporal order of clinical and biomarker changes in familial frontotemporal dementia

Even with research studies like ALLFTD, we still don't know enough about familial FTD (f-FTD) to predict when someone might start showing FTD symptoms. This is challenging for families impacted by FTD, and it creates an extra challenge for clinical trials that are hoping to have people enroll right before they start showing symptoms. Using data collected in ALLFTD and the GENFI (the European equivalent of ALLFTD) studies, we developed models for f-FTD disease progression. With these models we were able to learn more about which symptoms might be present initially across the three main genetic groups (*GRN, MAPT,* and *C9orf72*) and we were able to estimate the number of people that would need to participate in a clinical trial so scientists can tell if the drug is working or not. The models considered clinical information (like diagnosis and measures of disease severity), memory and thinking test scores, MRI information, and plasma neurofilament light chain concentration. Excitingly, there were strong similarities between these models when comparing the ALLFTD and GENFI cohorts – the two different studies have different methods, but similar results. Even with these helpful models, having enough people to enroll in clinical trials will be a challenge.

- PubMed – National Library of Medicine
- Nature Medicine – Journal of the Nature Portfolio

Association of Physical Activity With Neurofilament Light Chain Trajectories in Autosomal Dominant Frontotemporal Lobar Degeneration Variant Carriers

Lifestyle factors implicated in brain health are thought to account for more than 40% of dementia risk. In this study, we evaluated 160 participants that were known to carry a mutation in one of the 3 most common FTD-associated genes (*GRN, MAPT,* and *C9orf72*). Around 2/3 of those included in this study didn't have any symptoms or had very mild symptoms. Most participants included had had at least 2 research visits. This study compared blood plasma neurofilament light (NfL) concentration to a self-reported measure of physical activity (Physical Activity Scale for the Elderly: PASE). The PASE questionnaire is 11 items, and this study used a total score across all items to represent overall physical activity for each participant. We know from previous studies that blood plasma NfL concentration increases with disease progression (review the NfL study we reported in the Summer Newsletter for more information). This study found that people who reported more physical activity at their first visit had lower levels of plasma NfL and slower increases of NfL levels between visits than people who reported less physical activity at their first visit. This study suggests that lifestyle interventions, especially those related to physical activity, may have a beneficial outcome in FTD disease progression.

- PubMed – National Library of Medicine
- JAMA Neurology – American Medical Association Publication

Differences in Motor Features of *C9orf72, MAPT,* or *GRN* Variant Carriers With Familial Frontotemporal Lobar Degeneration

FTLD is widely accepted to be a diverse spectrum of neurodegenerative disorders. This study looked at whether there were specific clinical features that corresponded with different genes and included 184 participants who were symptomatic and carried one of the FTD genetic variants. Motor symptoms onset occurred earliest in those with a *MAPT* variant, and those with a *GRN* variant had motor symptoms occur latest. Individuals with a *C9orf72* expansion are more likely to have muscle atrophy and weakness. This study, and other like it, are important because they help clinicians have a more comprehensive understanding of the differences in FTLD related to different gene variants and may help with earlier diagnoses.

- PubMed – National Library of Medicine
- Neurology – American Academy of Neurology

Do you enjoy reading scientific publications? Use this link to review all publications related to ALLFTD. None of these important scientific works would be possible without your contributions. Thanks for participating in ALLFTD and all FTD-related research studies!