Multi-center, multi-tracer PET studies harmonized to detect neuroinflammation in ALS

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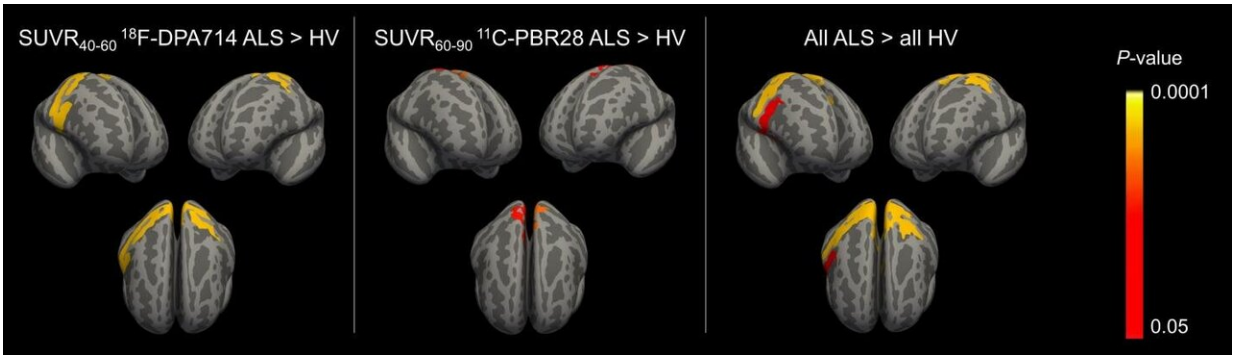

Surface-based analysis between participants with ALS and HVs for 18F-DPA714 SUVR40-60, 11C-PBR28 SUVR60-90, and both tracers (18F-DPA714 SUVR40-60 combined with 11C-PBR28 SUVR60-90) using WB without ventricles as pseudo reference region. Credit: Van Weehaeghe et al. JNM. 2020.

A novel ALS (amyotrophic lateral sclerosis) study has pooled data from multiple sites to effectively visualize neuroinflammation, which is key to developing drugs to treat the disease. Pooling data acquired from different scanners, different neuroinflammation positron emission tomography (PET) markers and different sites enhanced researchers' ability to detect neuroinflammation in ALS patients. This research was published in the November issue of The *Journal of Nuclear Medicine*.

ALS is a rare and fatal neurodegenerative disease that causes progressive weakness, respiratory failure and eventual death. Developing drugs to treat the disease is uniquely challenging because it is so rare. "In rare diseases such as ALS, only a limited pool of participants is available to participate in imaging studies," noted Donatienne Van Weehaeghe, MD, Ph.D., researcher in the department of imaging and pathology at University Hospital Leuven in Leuven, Belgium. "Therefore, conducting collaborative research across various sites and bringing in data to a common analysis pool is valuable to accelerate imaging biomarker development."

The study investigated two second-generation translator protein (TSPO) tracers, 18F-DPA714 and 11C-PBR28, that are currently being developed in the United States and Europe as promising ALS biomarkers. Researchers first sought to validate the established 11C-PBR28 PET pseudo reference analysis technique (which is used as a substitute for full dynamic modeling) for 18F-DPA714; they then evaluated whether multicenter data pooling of 18F-DPA714 and 11C-PBR28 data was feasible.

ALS patients and healthy volunteers from the United States and Belgium were recruited for the study and underwent dynamic 18F-DPA714 or 11C-PBR28 PET/MRI (magnetic resonance imaging). Data from the 18F-DPA714 or 11C-PBR28 images were analyzed, and results were compared.

The pseudo reference analysis technique was found to produce results comparable to those of gold standard PET analyses obtained by full dynamic modeling. The most sensitive pseudo reference region was whole brain without ventricles. Analysis of the 18F-DPA714 and 11C-PBR28 data from multiple sites showed a much greater power to detect inflammation compared to individual site data alone.

"In this exciting study, we have shown the ability to pool together and analyze brain neuroinflammation PET imaging data acquired at multiple institutions with varying scanner capabilities, using state-of-the-art analytical tools. This is the essential first step for bringing cutting-edge research closer to ALS patients globally and for accelerating the pace of biomarker readouts for future ALS clinical trials," said Suma Babu, MBBS, MPH, assistant professor of neurology at Harvard Medical School and physician investigator at Massachusetts General Hospital in Boston, Massachusetts. "This approach could reduce time and travel burden for patients, allowing them to participate in novel biomarker research while remaining close to home. From a scientific study conduct standpoint, this approach retains scientific rigor, increases statistical power, reduces trial durations and reduces risks of attrition."

"Developing mechanistic central nervous system biomarkers that can be acquired across multiple study sites would greatly accelerate the pace of finding effective treatments for neurodegenerative diseases, including ALS," said Nazem Atassi, MD, MMSc, associate professor of neurology at Harvard Medical School and head of early neuro-development at Sanofi-Genzyme.

PET imaging of neuroinflammation is relevant to multiple neurological conditions, not just ALS. "The ability to combine data across different radiotracers allows researchers to build on the foundation laid by prior research without the need to start from scratch every time with a new radioligand. If ongoing and future collaborative research in this field is successful, it could directly impact the use of PET imaging markers in future clinical trials testing anti-neuroinflammatory medications in ALS and other neurological conditions," remarked Van Weehaeghe.

More information: Donatienne Van Weehaeghe et al, Moving Toward Multicenter Therapeutic Trials in Amyotrophic Lateral Sclerosis: Feasibility of Data Pooling Using Different Translocator Protein PET

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