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BIOMARKERS

POSTER PRESENTATION

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NEUROIMAGING

Clinical value of ^{18}F-PI2620-PET in the diagnostic workup of patients with suspected Progressive Supranuclear Palsy

Carla Palleis[1,2,3] | Nicolai Franzmeier[4,5,6,7] | Johannes Gnörich[2] | Alexander Jäck[8,9] | Alexander M Bernhardt[8,9] | Sabrina Katzdobler[6,8,9] | Urban M Fietzek[8,10] | Endy Weidinger[8,9] | Lukas Frontzkowski[5,8] | Sebastian Roemer-Cassiano[5,11,12] | Andreas Zwergal[8] | Henryk Barthel[13,14] | Osama Sabri[13] | Johannes Levin[8,9,15] | Günter U Höglinger[1,2,6] | Matthias Brendel[1,6,16]

[1]German Center for Neurodegenerative Diseases (DZNE), Munich, Germany

[2]University Hospital, LMU Munich, Munich, Germany

[3]Munich Cluster for Systems Neurology (SyNergy), Munich, Germany

[4]University of Gothenburg, The Sahlgrenska Academy, Institute of Neuroscience and Physiology, Psychiatry and Neurochemistry, Gothenburg, Sweden

[5]Institute for Stroke and Dementia Research (ISD), University Hospital, LMU Munich, Munich, Bavaria, Germany

[6]Munich Cluster for Systems Neurology (SyNergy), Munich, Bavaria, Germany

[7]Institute for Stroke and Dementia Research (ISD), LMU University Hospital, LMU, Munich, Bavaria, Germany

[8]University Hospital, LMU Munich, Munich, Bavaria, Germany

[9]German Center for Neurodegenerative Diseases (DZNE), Munich, Bavaria, Germany

[10]Schön Klinik Schwabing, Munich, Bavaria, Germany

[11]Department of Neurology, University Hospital, LMU Munich, Munich, Bavaria, Germany

[12]Max Planck School of Cognition, Leipzig, Sachsen, Germany

[13]Department of Nuclear Medicine, University of Leipzig, Leipzig, Germany

[14]Leipzig University Medical Center, Leipzig, Germany

Abstract

Background: Progressive Supranuclear Palsy (PSP) is a rapidly progressing 4-repeat tauopathy, presenting with clinically heterogeneous phenotypes. Currently, diagnoses are based solely on clinical criteria but reliable diagnostic classification remains particularly challenging at early stages. ^{18}F-PI-2620 tau-PET is an evolving neuroimaging biomarker to capture 4-repeat tau (4RT) deposits in vivo with clear diagnostic potential in research settings. To determine the added clinical value of ^{18}F-PI-2620 tau-PET in the diagnostic workup of PSP, we evaluated whether ^{18}F-PI-2620-assessed 4RT positivity (i.e. using the basal ganglia as a target readout) predicts subsequent increases of diagnostic certainty for PSP, indicative of 4RT pathology driving clinical progression.

Method: We collected monocentric longitudinal data at the LMU Hospital in Munich, from a non-randomized prospective cohort study between October 2018 and December 2024. Data collection included pre-PET visits with routine clinical classification following the MDS criteria. In addition, we performed ^{18}F-PI-2620 tau-PET with dichotomous visual read assessments of 4RT pathology by an expert reader and collected clinical follow-up data or autopsy information.

Results: 342 patients with a pre-PET differential diagnosis of PSP were referred to ^{18}F-PI-2620 tau-PET in clinical routine. Of those, 200 patients (61.5% male, mean±sd age 69.2±8.3 years) had a post-PET clinical follow-up between 12-24 months (mean±sd 17.1±4.2 months). 137 patients (68.5%) were rated 4RT-positive at baseline (Figure 1). The distribution of certainty of PSP diagnosis at baseline and at follow-up is displayed in Figure 2 (**A&B**: all PSP phenotypes; **C&D**: PSP-Richardson Syndrome [RS]; **E&F**:

[15]Munich Cluster for Systems Neurology (SyNergy), Munich, Munich, Germany

[16]LMU University Hospital, Munich, Germany

Correspondence
Carla Palleis, German Center for Neurodegenerative Diseases (DZNE), Munich, Germany.
Email: Carla.Palleis@med.uni-muenchen.de

variant PSP subtypes). Change to a non-PSP diagnosis at follow-up occurred in 23.5%, identified by a negative baseline tau-PET in 95.5%. In contrast, 79% of tau-PET-positive patients with suggestive PSP progressed to a higher diagnostic certainty, 3% had histopathological confirmation of PSP diagnosis, 13% remained suggestive PSP, and 5% received a non-PSP diagnosis at follow-up.

Conclusion: ^{18}F-PI-2620 tau-PET can successfully identify patients that progress along expected 4RT clinical spectra. This supports ^{18}F-PI-2620 tau-PET as a 4RT biomarker, with the potential to facilitate early biomarker-based diagnosis when clinical criteria may still lack sensitivity and specificity. This development can be transformative for clinical decision making, pre-symptomatic identification of PSP and stratifying patients for disease modifying clinical trials.

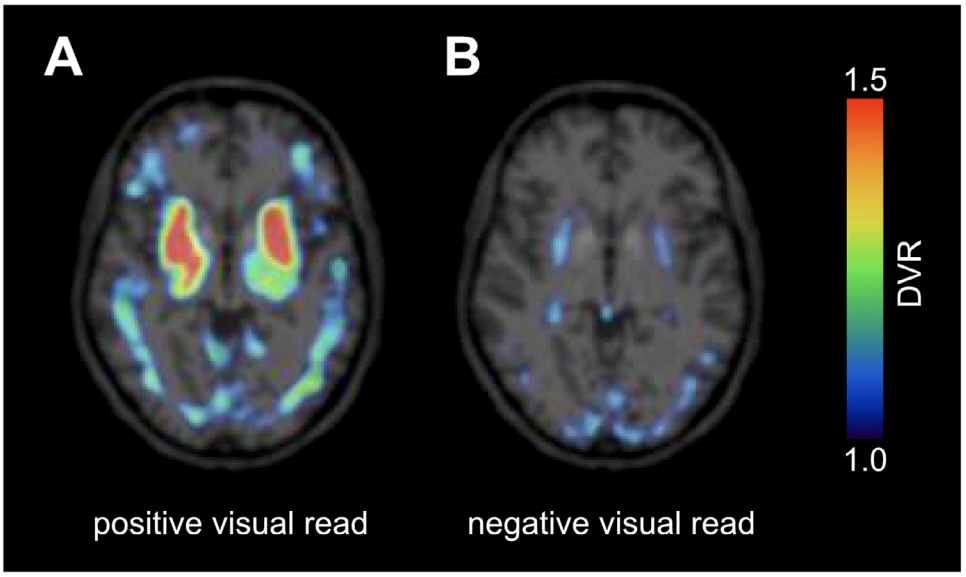

Figure 1 *Exemplary subcortical ^{18}F-PI-2620 binding (distribution volume ratio, DVR) in a patient with positive visual read (A) and in a patient with negative visual read (B).*

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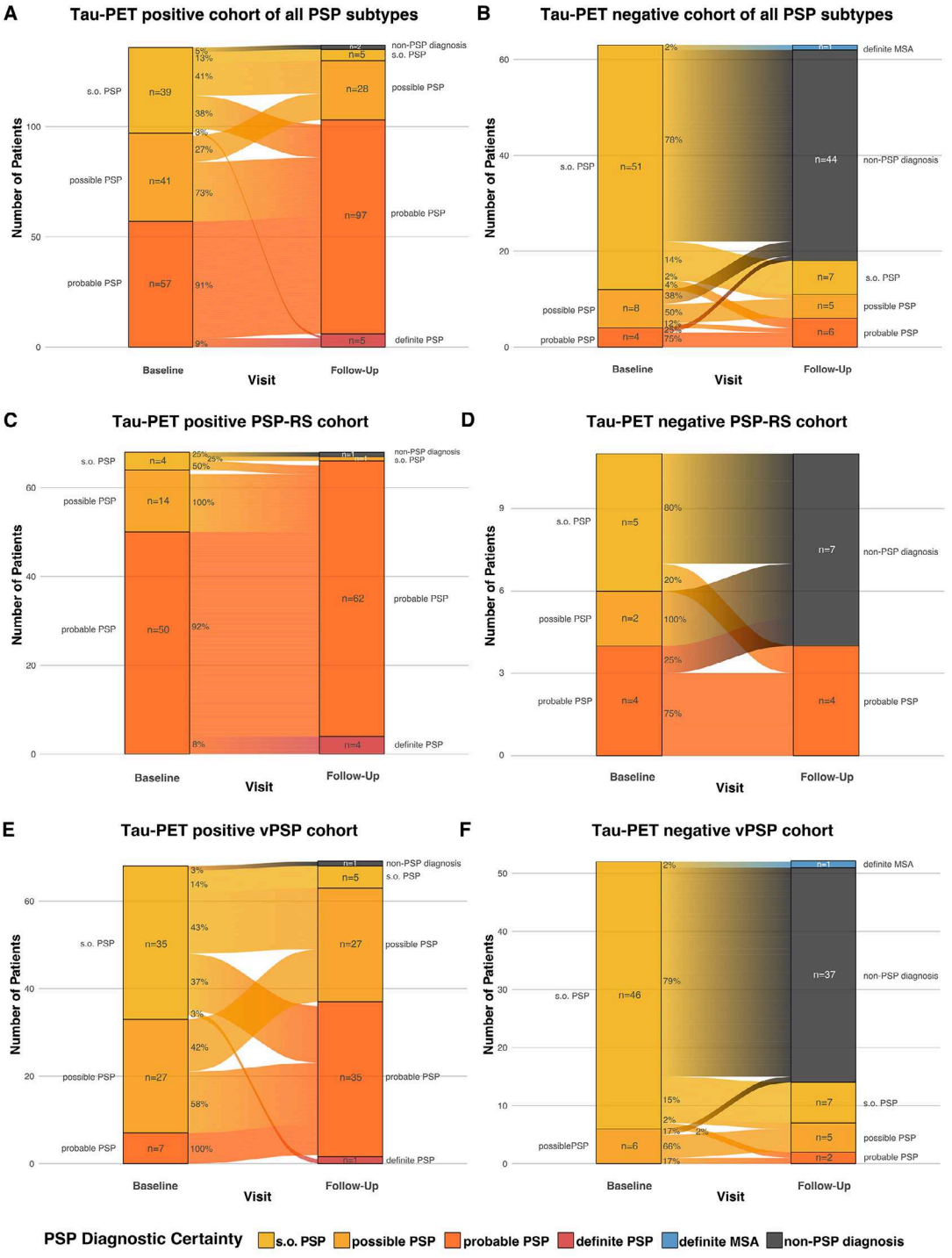

Figure 2

Alluvial charts showing the distribution of certainty of Progressive Supranuclear Palsy (PSP) diagnosis at baseline and at follow-up for positive (left) and negative (right) ^{18}F-PI-2620 tau-PET read at baseline, respectively. PSP diagnostic certainty levels are graded as "suggestive of" (s.o.), "possible", "probable", and "definite", according to the current MDS-PSP criteria. All clinical diagnoses other than PSP at follow-up are defined as "non-PSP". One patient had a histopathological diagnosis of "definite" Multiple System Atrophy (MSA). ***A&B:*** *all PSP phenotypes;* ***C&D****: PSP-Richardson Syndrome (RS);* ***E&F:*** *variant (v) PSP subtypes.*