Imaging of Brain Prion Protein Amyloid in Patients with Gertstmann-Sträussler-Scheinker Disease

Slikanje prionskega proteina možganov beta-amiloida pri bolnikih z Gerstmann-Sträussler-Scheinkerjevim sindromom

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Gerstmann–Sträussler– Scheinker (GSS) disease is a transmissible spongiform encephalopathy, which is a rare but fatal neurodegenerative disease, characterized by accumulation of an abnormal, protease-resistant form of the prion protein (PrP) in the brain.[1] Although it typically affects patients from age of 35 to 55, the disease onset could occur in persons as young as 25 years of age.[2] While the definitive diagnosis can be made at neuropathological examination of post-mortem tissue, clinical progression is accompanied with changes in the brain that can be followed by either immunoassays for a number of different wet biomarkers or by imaging techniques based on CT and MRI scanning or [18F]-FDG PET.[3] However, these imaging methods provide low sensitivity and specificity, indecisive in diagnosing prion diseases or giving sensitive readouts of disease progression.

PET imaging using the radiofluorinated 2-(1-{6-[(2-[F-18]fluoroethyl)(methyl) amino]-2-naphthyl}ethylidene)malononitrile, [18F]-FDDNP has been evaluated in a number of diseases, targeted Amyloid-beta peptide and tangles tau protein in Alzheimer's disease (AD),[4,5] depression and anxiety.[6]

The potential use of FDDNP for detecting the target prion amyloid in GSS [18F]-FDDNP had previously been shown to be feasible in at least *in vitro* tissue specimens.[7,8] However, its application for *in vivo* PET imaging had not been investigated in humans. Kepe and coworkers took this approach forward and were the first to demonstrate the feasibility of detecting prion accumulation in living patients with GSS using ([18F]-FDDNP PET and published their exciting results recently in *Brain Pathology*.[9]

Kepe et al performed [18F]-FDDNP PET imaging in 6 GSS subjects with known point mutations of the prion protein (PRNP) gene. These data were later compared with [18F]-FDG PET as well as with structural MRI brain scans. The results showed an increased [18F]-FDDNP binding in the cerebellum, neocortex and subcortical areas of all symptomatic gene carriers, which are in agreement with the clinical symptoms while the two asymptomatic gene carriers showed no cortical [18F]-FDDNP binding. The authors examined further the distribution of [18F]-FDDNP in these patients by comparing it with the *in vitro* results from brain tissue specimens from deceased GSS subjects. The in vivo accumulation of [18F]-FDDNP was very closely related to the distribution of prion protein pathology. Another strength in this study is the follow-up examinations in 2 patients after 12–28 months, where the

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progression of the disease was in agreement with the clinical symptoms. Also, the parallel [18F]-FDG scans showed reduced glucose metabolism in the neocortex and thalamus, confirming neuronal dysfunction.

It would be desirable to further examine the diagnostic sensitivity and specificity of [18F]-FDDNP for GSS versus AD and other prion-based disorders. The result of these initial studies by Kepe and colleagues are very interesting and have potential for clinical use in the future, providing an additional tool in identifying patients early, at the onset of the disease. Such studies could eventually lead to better tools to quantify the changes in brain amyloid and help to develop better treatments that can promise disease modification.

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