AARHUS UNIVERSITY

# Press release

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**Basic information**

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Department of: Clinical Medicine

Main supervisor: Professor Nicola Pavese

Title of dissertation: Early markers of synucleinopathy disorders in patients with idiopathic rapid eye movement sleep behaviour disorder

Date for defence: 26th April 2018 at (time of day): 14:00 Place: Palle Juul Jensen Auditoriet, Aarhus Universitetshospital, Nørrebrogade 44, bygn.10

Press release (Danish)

## Tidlige markører for Parkinsons sygdom i patienter med REM søvn adfærd syndrom

Et nyt ph.d.-projekt fra Aarhus Universitet, Health, undersøger patofysiologiske mekanismer i patienter med idiopatisk REM søvn adfærdssyndrom ved at anvende in vivo positron-emissions tomografi. Projektet er udført af Morten Gersel Stokholm som forsvarer sin ph.d- afhandling d. 26. april 2018.

DANSK ABSTRACT (10-15 linjer)

Parkinsons sygdom er en hyppigt forekommende neurologisk lidelse der er karakteriseret ved langsomme bevægelser ofte med rysten samt muskelstivhed. Derudover er demens karakteristisk i tidlige eller sene sygdomsstadier. Sygdommen er kronisk og progredierende uden mulighed for kurativ behandling. Der findes god symptom dæmpende behandling, som er effektiv i en længere årrække. Ved diagnosetidspunktet er en betydelig mængde af de dopamin producerende neuroner i hjernen allerede gået til grunde. Hvis lægemidler med evne til at beskytte disse neuroner, såkaldt neuroprotektiv behandling bliver udviklet skal de derfor gives tidligt i sygdomsforløbet for at opnå den bedst mulige effekt. For at udvikle disse lægemidler, samt identificere markører der kan måle effekten af disse lægemidler, er det vigtigt at opnå viden omkring patologiske mekanismer i den tidlige sygdomsfase. Studierne inkluderet i denne afhandling bruger molekylære billeddannende teknikker til at undersøge patologiske mekanismer i hjernen hos personer med søvnforstyrrelsen, REM søvn adfærdssyndrom (adfærdsforstyrrelser i drømmesøvnen, engelsk forkortelse iRBD). Dette er en søvnforstyrrelse der er kendetegnet ved, at man udlever sine drømme med bevægelse af arme og ben og verbale udbrud i REM søvnfasen. Raske personer ligger normalt stille i REM søvnfasen. Opfølgningsstudier af iRBD patienter har vist at de med stor sandsynlighed er i prodromal stadiet af Parkinsons sygdom. Resultaterne af de udførte studier, viser at mange patienter med iRBD allerede har et dysfunktionelt dopamin system i hjernen, samt en øget aktivering af mikroglia celler i substantia nigra. Derudover har de et dysfunktionelt monoamin neurotransmitter system i thalamus, samt øget aktivering af mikroglia celler i occipitallappen. Yderligere har disse patienter en cholinerg denervering af kortikale områder. Disse fund indikerer betydelige forandringer i hjernen hos mange iRBD patienter, som sandsynligvis befinder sig i den prodromale fase af Parkinsons sygdom. Fremtidige opfølgningsstudier af disse iRBD patienter vil belyse, om den øgede aktivering af mikroglia celler udgør et terapeutisk mål for lægemidler rettet imod at sænke eller stoppe sygdomsudviklingen, derudover vil den mulige kliniske betydning af de observerede ændringer i det dopaminerge, monoaminerge og cholinerge neurotransmitter system blive belyst.

Forsvaret af ph.d.-projektet er offentligt. Det holdes på engelsk og finder sted den 26/4 kl. 14.00 i Palle Juul Jensen Auditoriet, Aarhus Universitetshospital, Nørrebrogade 44, bygn.10, Aarhus C. Titlen på projektet er "Early markers of synucleinopathy disorders in patients with idiopathic rapid eye movement sleep behaviour disorder" .

Yderligere oplysninger: Ph.d.-studerende Morten Stokholm, Nuklearmedicinsk Afdeling & PET-Center, e-mail: mortenstokholm@clin.au.dk, tlf. 78461610, eller hovedvejleder, professor Nicola Pavese, e-mail: npavese@clin.au.dk.

Bedømmelsesudvalg:
Formand: Professor Leif Østergaard, CFIN, Aarhus Universitet
Bedømmere: Professor Antonio Strafella, University of Toronto, Canada
Professor Espen Dietrichs, Oslo University, Norway

Press release (English)

## Early markers of synucleinopathy disorders in patients with idiopathic rapid eye movement sleep behaviour disorder

A new project from Aarhus University investigates pathophysiological changes in patients with idiopathic rapid eye movement sleep behaviour disorder (iRBD) by the use of in vivo molecular imaging. The project was carried out by Morten Stokholm who is defending his dissertation on 26th April 2018.

Parkinson's disease is a progressive neurodegenerative disorder characterised by bradykinesia, resting tremor, postural instability, and muscular rigidity. Additionally, patients may suffer from dementia in early or late disease stages. At present, no curative treatment exists for Parkinson's disease; however, patients may benefit from symptomatic treatment. At the time of diagnosis, a substantial degeneration of dopamine producing neurons in the brain has occurred. Therefore, if disease-modifying therapies are developed, they should preferably be administered in the early disease phase. To develop neuroprotective therapies and identify biomarkers that could serve to measure the efficacy of these therapies, it is important to elucidate the underlying pathophysiology occurring in the early disease phases. The included studies apply in vivo molecular imaging to examine pathophysiological changes in patients with idiopathic rapid eye movement sleep behaviour disorder (iRBD). iRBD is a parasomnia characterised by dream-enactment behaviour with an absence of muscle atonia during REM sleep, and often with nightmares. Longitudinal follow-up studies show that iRBD patients are likely to be in a prodromal phase of Parkinson's disease with or without concurrent dementia.
The findings of the current examinations show that iRBD patients already have a dysfunctional nigrostriatal dopaminergic system, with raised microglial activation in the substantia nigra. Additionally, impairment of the monoaminergic system in the thalamus was observed along with increased levels of microglial activation bilaterally in the occipital lobe.
Moreover, neocortical denervation also occurred in the cholinergic neurotransmitter system of these iRBD patients. Results indicate that substantial changes are occurring already in the prodromal phase of Parkinson's disease. Longitudinal follow-up studies will elucidate whether raised microglial activation represents a therapeutic target with possible disease-modifying capabilities, and in addition, the clinical importance of the observed alterations in dopaminergic, monoaminergic, and cholinergic neurotransmitter systems will be elucidated.

The defence is public and takes place on 26th April 2018 at14:00 in Palle Juul Jensen Auditorium, Aarhus University Hospital, Nørrebrogade 44, bldg. 10, Aarhus.
The title of the project is "Early markers of synucleinopathy disorders in patients with idiopathic rapid eye movement sleep behaviour disorder".

For more information, please contact PhD student Morten Stokholm, Dept. of Nuclear Medicine & PET Centre, email: mortenstokholm@clin.au.dk, Phone +45 78461610 or main supervisor Professor Nicola Pavese, e-mail: npavese@clin.au.dk

Assessment committee:
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Examiners: Professor Antonio Strafella, University of Toronto, Canada
Professor Espen Dietrichs, Oslo University, Norway

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