

FUNCTIONAL AND PERFUSION MRI IN DEMENTIA

Maja Anna Agatha Binnewijzend

Cover image: Joel Amat Güell (www.joelamatguell.com)
Cover design: Mario García de León Recio
Layout and printing: Proefschriftmaken.nl || Uitgeverij BOXPress
Published by: Uitgeverij BOXPress, 's-Hertogenbosch

Copyright © 2014 Maja Binnewijzend, Amsterdam.
All rights reserved. No part of this thesis may be reproduced or transmitted in any form or by any means without prior written permission of the author.

ISBN 978-90-8891-821-6

The studies described in this thesis were carried out at the Department of Radiology and Nuclear Medicine and the Alzheimercenter of the VU University Medical Center, Amsterdam, The Netherlands. The VUmc Alzheimercenter is supported by Innovatiefonds Ziekteverzekerders and by unrestricted grants to the Stichting VUmc Fonds from: AEGON Nederland NV, Heer en Mw Capitain, Heineken Nederland NV, Gebroeders Boeschen, Genootschap tot Steun VUmc Alzheimercentrum, Kroonenberg Groep, KPMG, Marcel Boekhoorn, Onvergetelijke vrienden VUmc Alzheimercentrum, RABO Bank Amsterdam, Stichting ZABAWAS, Stichting Alzheimer Nederland, 2BikeforAlzheimer, AlzheimerRally, Stichting Dioraphte, Stichting Buytentwist, Purplefield Investments, Stichting Mooiste Contact Fonds (initiatief van KPN), Stichting Noaber Foundation, Twentse Kabel Groep Holding NV, Van Leeuwen-Rietberg Stichting, Willem Meindert de Hoop Stichting, and many individual donors.

Printing of this thesis was kindly supported by: Alzheimer Nederland and Internationale Stichting Alzheimer Onderzoek.



VRIJE UNIVERSITEIT

FUNCTIONAL AND PERFUSION MRI IN DEMENTIA

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad Doctor aan
de Vrije Universiteit Amsterdam,
op gezag van de rector magnificus
prof.dr. F.A. van der Duyn Schouten,
in het openbaar te verdedigen
ten overstaan van de promotiecommissie
van de Faculteit der Geneeskunde
op vrijdag 21 maart 2014 om 11.45 uur
in de aula van de universiteit,
De Boelelaan 1105

door

Maja Anna Agatha Binnewijzend

geboren te Alkmaar

promotoren: prof.dr. F. Barkhof
prof.dr. Ph. Scheltens

copromotor: dr. J.P.A. Kuijer

'In a way, it's up to history to decide what's right
and what's wrong. The reasonable is that which is viable.'

'Whatever survives is right.'

'Or vice versa: that which is right survives.'

- Jostein Gaarder, *Sofie's World*

CONTENTS

Chapter 1	General introduction	
	Introduction	10
	Thesis outline	13
Chapter 2	Functional connectivity: resting-state BOLD fMRI	
	2.1 Resting-state fMRI changes in AD and MCI	19
	2.2 Widespread disruption of functional brain organization in early-onset AD	41
	2.3 Brain network alterations in AD measured by Eigenvector centrality in fMRI are related to cognition and CSF biomarkers ..	61
Chapter 3	Cerebral perfusion: arterial spin-labeling MRI	
	3.1 Cerebral blood flow measured with 3D-PCASL MRI in AD and MCI: a marker for disease severity	83
	3.2 Distinct perfusion patterns in AD, FTD and DLB	103
	3.3 Cerebral perfusion in the prodementia stages of AD.....	119
	3.4 Normalized brain volume and white matter hyperintensities as determinants of cerebral blood flow in AD	137
Chapter 4	Summary and general discussion	
	Summary	152
	Discussion	154
Chapter 5	Nederlandse samenvatting	165
	Appendices	
	Dankwoord	174
	Theses VUmc Alzheimercenter	177
	List of publications	179
	Curriculum Vitae	180