APPORTS DE L'IMAGERIE DANS LA DÉPRESSION DU SUJET ÂGÉ

Recherches et compréhension des troubles psychiatriques de la Personne Âgée

SPLF, Limoges, Sept 2017

Société de Psychogériatrie de Langue Française

IMAGERIE ET CERVEAU
Unité Mixte de Recherche INSERM U930
Université François-Rabelais de Tours

Inserm
Institut national de la santé et de la recherche médicale

CONSULTATION INTERSECTORIELLE DE GÉRONTOPSYCHIATRIE

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AUCUN CONFLIT D'INTERÊT

DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS

FIFTH EDITION

DSM-5™

Major or Mild Neurocognitive Disorder Due to Alzheimer's Disease

Since amyloid beta-42 deposition in the brain occurs early in the pathophysiological cascade, amyloid-based diagnostic tests such as amyloid imaging on brain positron emission tomography (PET) scans and reduced levels of amyloid beta-42 in the cerebrospinal fluid (CSF) may have diagnostic value. Signs of neuronal injury, such as hippocampal and temporoparietal cortical atrophy on a magnetic resonance image scan, temporoparietal hypometabolism on a fluorodeoxyglucose PET scan, and evidence for elevated total tau and phospho-tau levels in CSF, provide evidence of neuronal damage but are less specific for Alzheimer's disease. At present, these biomarkers are not fully validated, and many are available only in tertiary care settings. However, some of them, along with novel biomarkers, will likely move into wider clinical practice in the coming years.

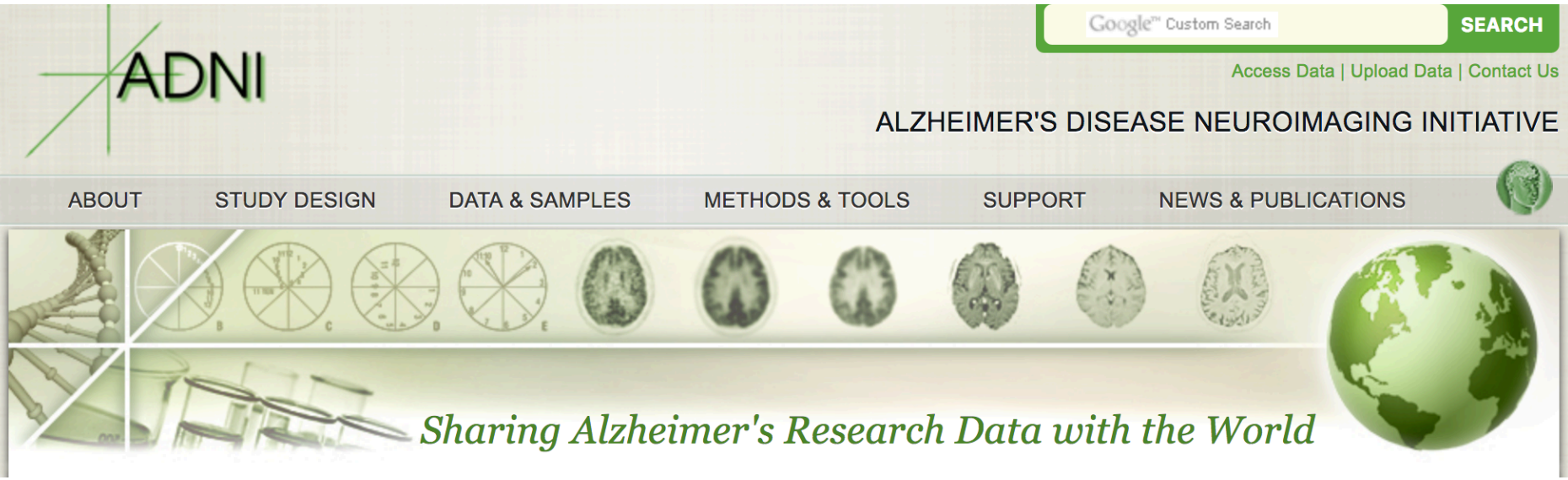
Strategic roadmap for an early diagnosis of Alzheimer's disease based on biomarkers

Lancet Neurol 2017; 16: 661–76

	Abnormality	Pathology
MRI		
Regional anatomy	Decreased volume of hippocampus and other temporal lobe structures	Tissue loss and neurodegeneration
PET		
^{18}F-fluorodeoxyglucose PET	Decreased uptake in posterior cingulate-precuneus and temporoparietal cortex	Glucose hypometabolism and neurodegeneration
^{11}C-PiB and fluorinated tracers for amyloid PET*	Increased cortical retention	Deposition of β-amyloid in the cortex
CSF measures		
Aβ42 or Aβ42:Aβ40	Decreased concentration or ratio	Abnormal metabolism of β-amyloid
Total tau and hyperphosphorylated tau	Increased concentration	Neuronal damage and accumulation of tau pathology; hyperphosphorylated tau is more specific for Alzheimer's disease neurodegeneration

Tau-PET is still under development and, therefore, is not included. PiB=Pittsburgh compound. Aβ=fibrillar β-amyloid.
*Using tracers such as florbetapir, flutemetamol, and florbetaben.

***Table 1*: Biomarkers for the diagnosis of Alzheimer's disease**



MEMENTO

FONDATION PLAN ALZHEIMER
FONDATION DE COOPÉRATION SCIENTIFIQUE POUR LA RECHERCHE SUR LA MALADIE D'ALZHEIMER & LES MALADIES APPARENTÉES

C·H·U Hôpitaux de Bordeaux

CIC-EC7 Centre d'investigation clinique Épidémiologie clinique Bordeaux

université de BORDEAUX

The Global ECT-MRI Research Collaboration (GEMRIC): Establishing a multi-site investigation of the neural mechanisms underlying response to electroconvulsive therapy

Leif Oltedal[a,b,c,d,*,1], Hauke Bartsch[b,c], Ole Johan Evjenth Sørhaug[a], Ute Kessler[a,e], Christopher Abbott[f], Annemieke Dols[g], Max L Stek[g], Lars Ersland[h], Louise Emsell[i], Philip van Eijndhoven[j], Miklos Argyelan[k], Indira Tendolkar[j], Pia Nordanskog[l], Paul Hamilton[l], Martin Balslev Jorgensen[m], Iris E Sommer[n], Sophie M Heringa[n], Bogdan Draganski[o,p], Ronny Redlich[q], Udo Dannlowski[q,r], Harald Kugel[s], Filip Bouckaert[t], Pascal Sienaert[t], Amit Anand[u], Randall Espinoza[v], Katherine L Narr[v,w], Dominic Holland[b,x], Anders M Dale[b,c,x], Ketil J Oedegaard[a,e,y]

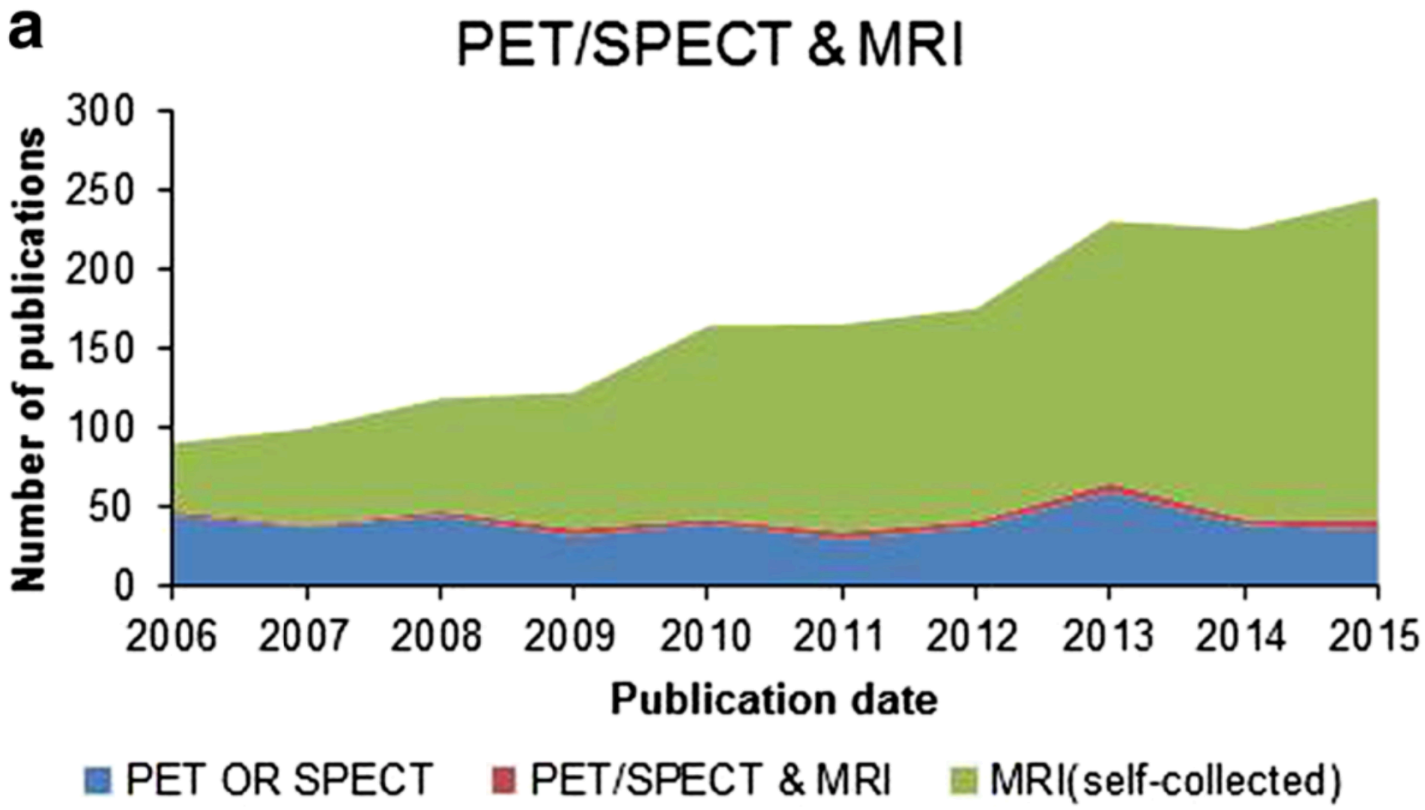
NeuroImage: Clinical 14 (2017) 422–432

GEMRIC
The Global ECT-MRI Research Collaboration

European Sites (10)
Norway: University of Bergen (coordinator), Belgium: KU Leuven,
Denmark: Copenhagen University, Sweden: Linköping and Lund University,
The Netherlands: VUmc Amsterdam, Radboudumc Nijmegen, UMC Utrecht,
Germany: University of Müenster, Switzerland: University of Lausanne

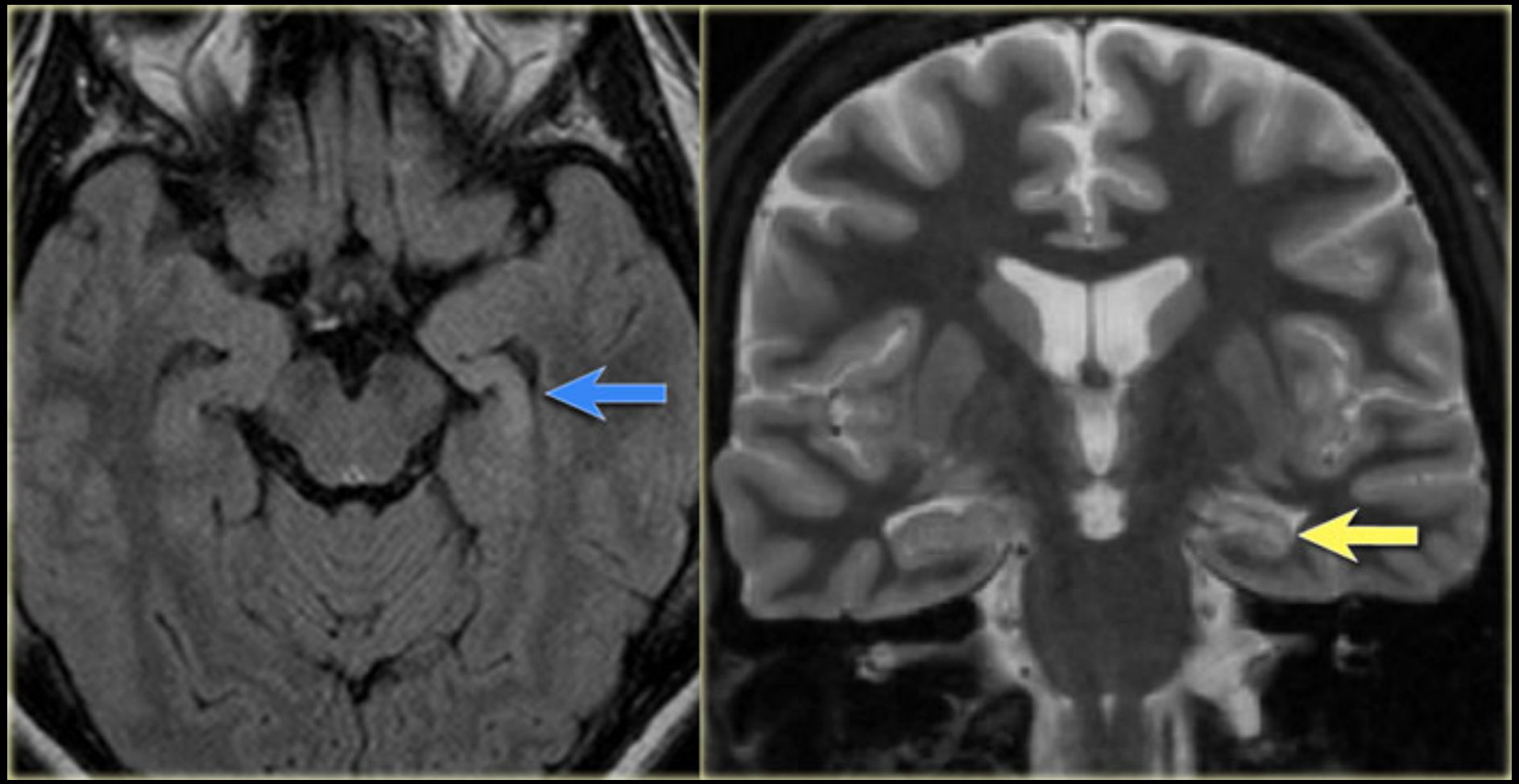
North American Sites (5)
Cleveland Clinic, UCLA Los Angeles, University of New Mexico,
The Feinstein Institute for Medical Research New York,
UC San Diego (Imaging Core)


SIEMENS


a
PET/SPECT & MRI
Number of publications
300
250
200
150
100
50
0
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
Publication date
PET OR SPECT
PET/SPECT & MRI
MRI(self-collected)

L’IRM

Atrophie, lésions cérébrovasculaires, intégrité des fibres blanches, IRM fonctionnelle



Brain grey matter volume alterations in late-life depression

Mingying Du, MD*; Jia Liu, MD*; Ziqi Chen, MD; Xiaoqi Huang, MD, PhD; Jing Li, MD; Weihong Kuang, MD; Yanchun Yang, MD; Wei Zhang, MD; Dong Zhou, MD; Feng Bi, MD; Keith Maurice Kendrick, PhD; Qiyong Gong, MD, PhD

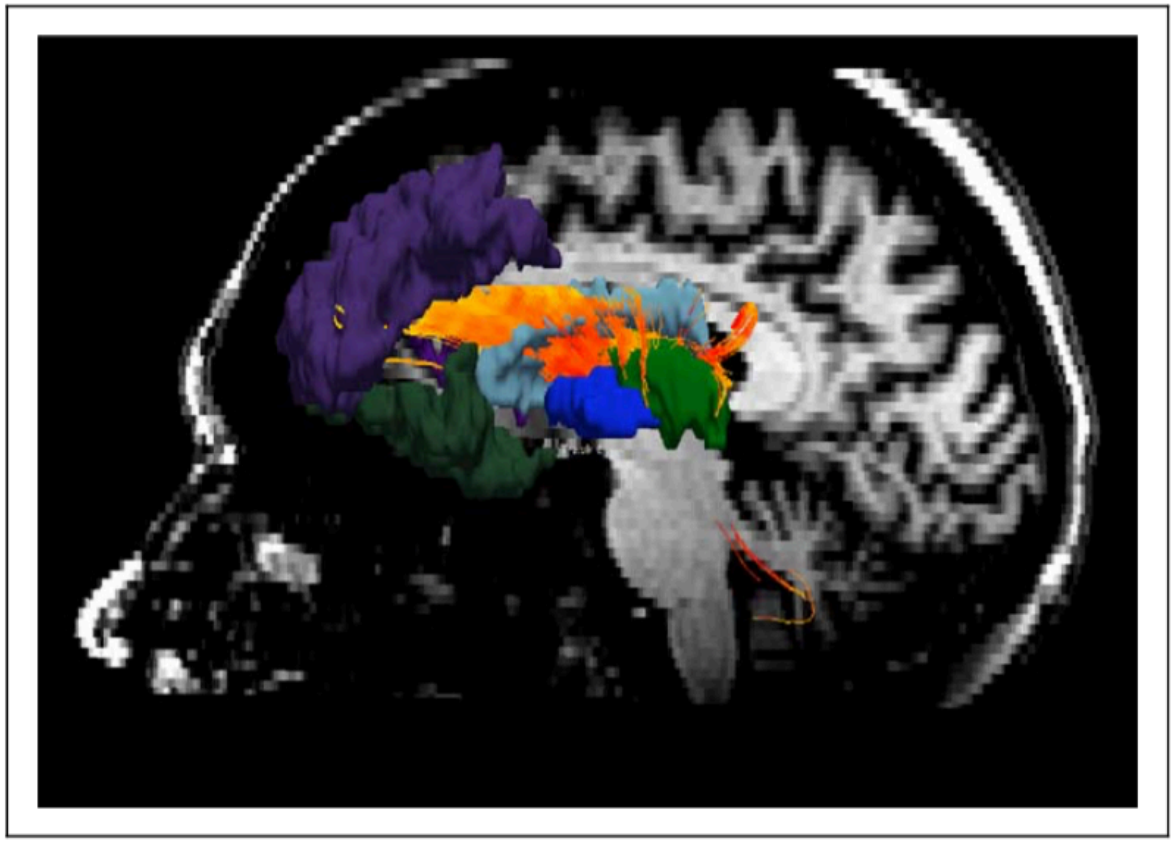
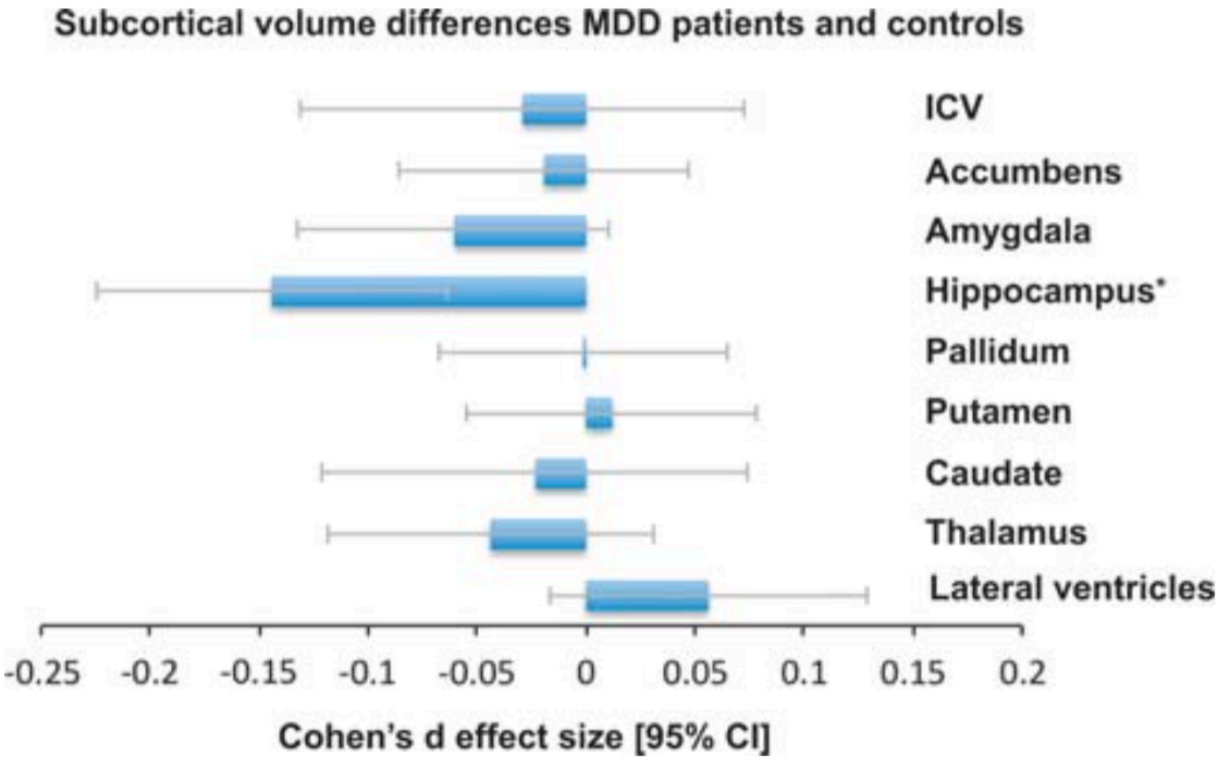


Figure 4. Corticostriatal circuits. There are 3 major corticostriatal

Subcortical brain alterations in major depressive disorder: findings from the ENIGMA Major Depressive Disorder working group

L Schmaal[1], DJ Veltman[1], TGM van Erp[2], PG Sämann[3], T Frodl[4,5], N Jahanshad[6], E Loehrer[7], H Tiemeier[7,8], A Hofman[7], WJ Niessen[9,10], MW Vernooij[7,9], MA Ikram[7,9,11], K Wittfeld[12], HJ Grabe[12,13,14], A Block[13], K Hegenscheid[15], H Völzke[16], D Hoehn[3], M Czisch[3], J Lagopoulos[17], SN Hatton[17], IB Hickie[17], R Goya-Maldonado[18], B Krämer[18], O Gruber[18], B Couvy-Duchesne[19,20,21], ME Rentería[22], LT Strike[19,20,21], NT Mills[22,23], GI de Zubicaray[20], KL McMahon[21], SE Medland[24], NG Martin[22], NA Gillespie[25], MJ Wright[19], GB Hall[26], GM MacQueen[27], EM Frey[4], A Carballedo[28], LS van Velzen[1], MJ van Tol[29], NJ van der Wee[30,31], IM Veer[32], H Walter[32], K Schnell[33], E Schramm[34], C Normann[34], D Schoepf[35], C Konrad[36], B Zurowski[37], T Nickson[38], AM McIntosh[38,39], M Papmeyer[38], HC Whalley[38], JE Sussmann[38], BR Godlewska[40], PJ Cowen[40], FH Fischer[41,42], M Rose[41,43], BWJH Penninx[1], PM Thompson[6] and DP Hibar[6] for the ENIGMA-Major Depressive Disorder Working Group[44]

Molecular Psychiatry (2016) 21, 806–812



Hippocampus atrophy and the longitudinal course of late-life depression

Warren D. Taylor, MD, MHSc[a], **Douglas R. McQuoid, MS**[b], **Martha E. Payne, PhD, MPH, RD**[b], **Anthony S. Zannas, MD**[b], **James R. MacFall, PhD**[c], and **David C. Steffens, MD, MHSc**[d]

Am J Geriatr Psychiatry. 2014 December ; 22(12): 1504–1512

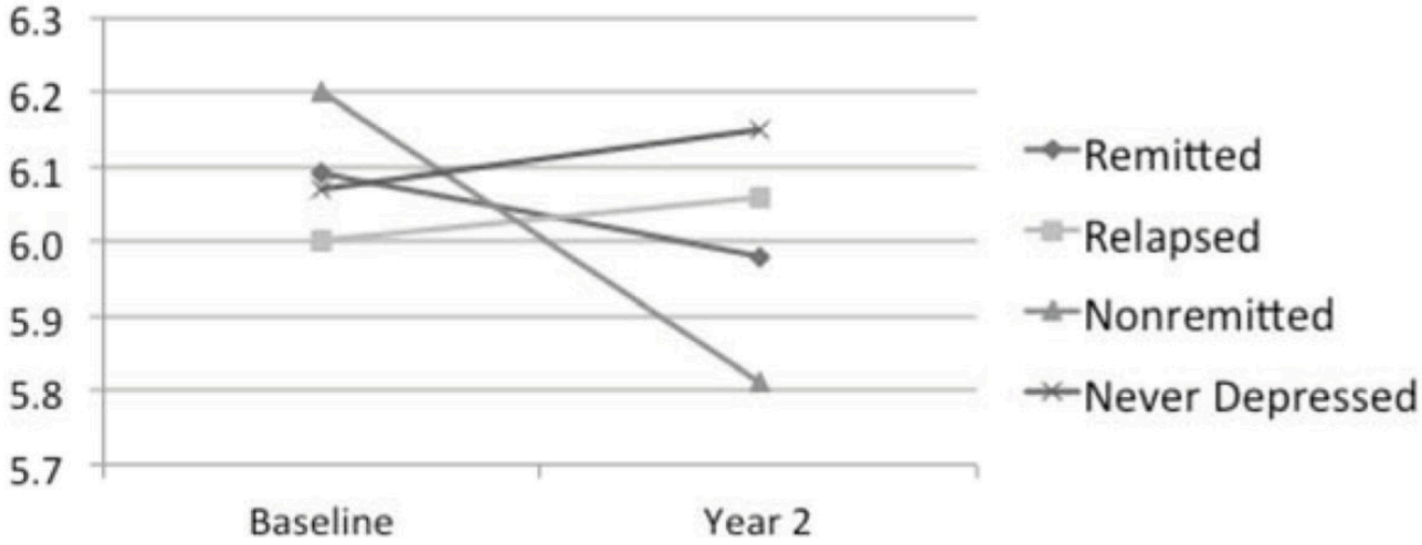
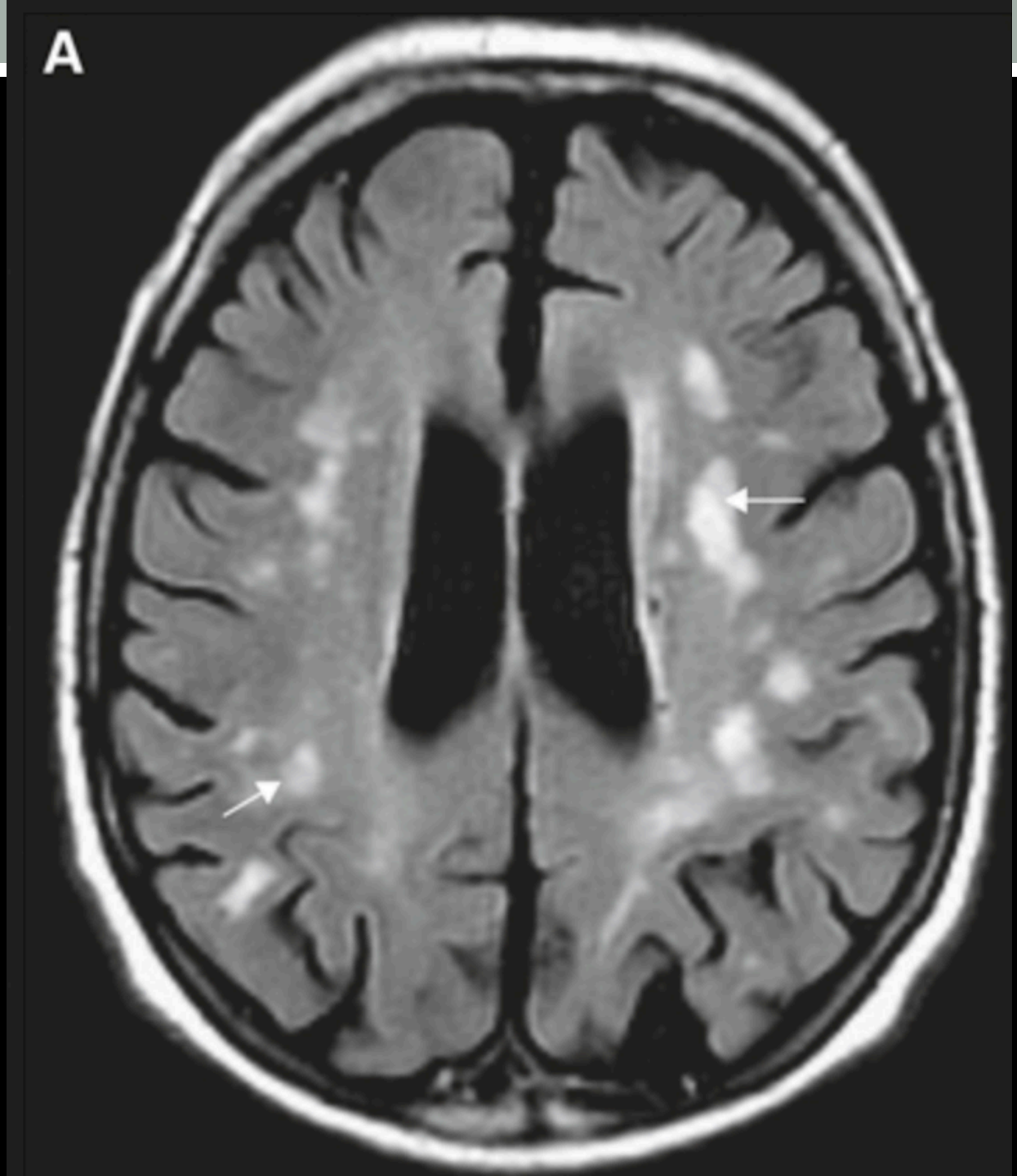


Figure 1.

Two-year change in proportional hippocampus volumes

Total hippocampal volumes at baseline and year two. Presented are adjusted means for each


A

White matter hyperintensities in late life depression: a systematic review

L L Herrmann, M Le Masurier, K P Ebmeier

J Neurol Neurosurg Psychiatry 2008;**79**:619–624

Table 2 Presence and severity of white matter hyperintensities

Presence and absence of WMH (grouped as absent or minimal vs moderate or large)				Severity of WMH		
Location	**n**	**Odds ratio (95% CI)**	**Qχ^2**	**n**	**Cohen's d (95% CI)**	**Qd**
Periventricular WM						
LLD/controls	11 (472/510)	2.15 (1.5–3.1)***	13.3	13 (535/364)	0.60 (0.3–0.9)	40.3***
LOD/controls	5 (183/296)	2.57 (1.6–4.2)***	4.0	5 (198/143)	0.90 (0.3–1.5)	26.1***
LOD/EOD	5 (133/87)	4.51 (2.2–9.2)***	4.5	6 (158/126)	0.73 (0.5–1.0)	5.8
Deep WM						
LLD/controls	11 (514/527)	1.92 (1.2–3.0)**	21.7*	13 (559/370)	0.39 (0.2–0.6)	26.1*
LOD/controls	7 (212/338)	2.64 (1.3–5.5)*	14.0*	5 (198/143)	0.46 (0.2–0.7)	2.5
LOD/EOD	9 (362/160)	4.33 (2.7–6.9)***	8.3	7 (165/134)	0.87 (0.6–1.1)	7.0
Combined WM						
LLD/controls				12 (598/490)	0.36 (0.2–0.5)	19.9*
LOD/controls				6 (258/308)	0.44 (0.3–0.6)	5.1
LOD/EOD				8 (262/183)	0.73 (0.5–0.9)	5.8

*$p<0.05$; **$p<0.01$; ***$p<0.001$.

EOD, early onset depression; LLD, late life depression; LOD, late onset depression; n, number of studies, Qχ^2, Cochrane Q for non-combinability of odds ratios; Qd, "non-combinability" for d+ test; WM, white matter; WMH, white matter hyperintensities.

MRI signal hyperintensities and failure to remit following antidepressant treatment

Joel R. Sneed [a,b,g,h,*], Michelle E. Culang-Reinlieb [b], Adam M. Brickman [c,d], Faith M. Gunning-Dixon [e], Lauren Johnert [b], Ernst Garcon [f], Steven P. Roose [g,h]

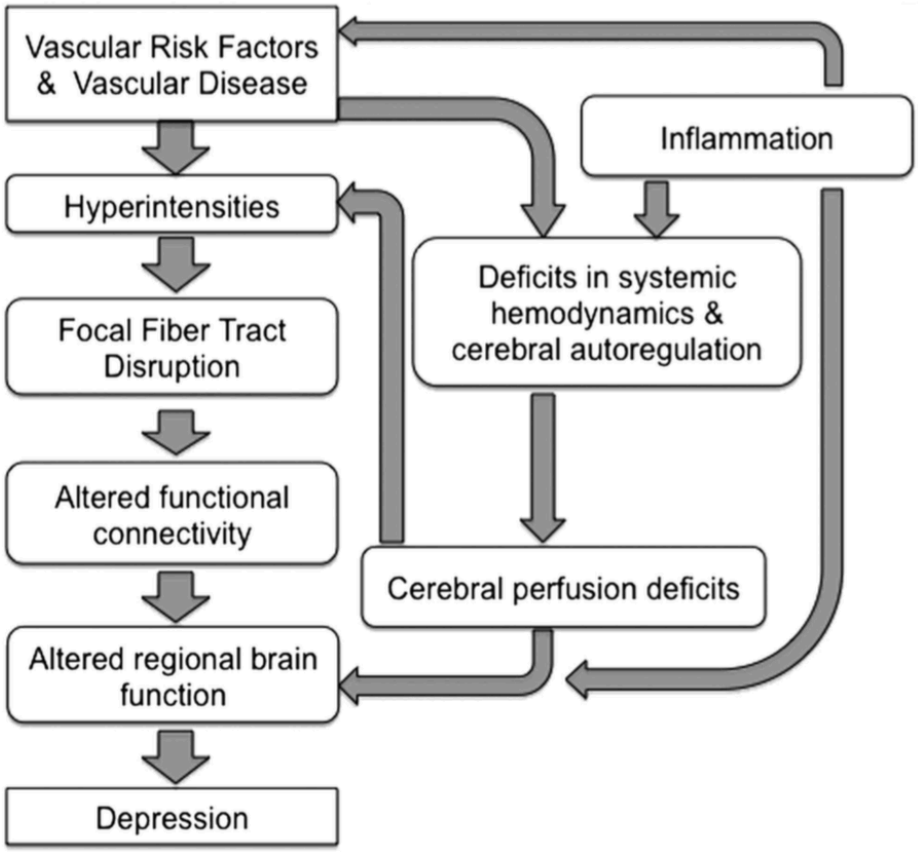
Journal of Affective Disorders 135 (2011) 315–320

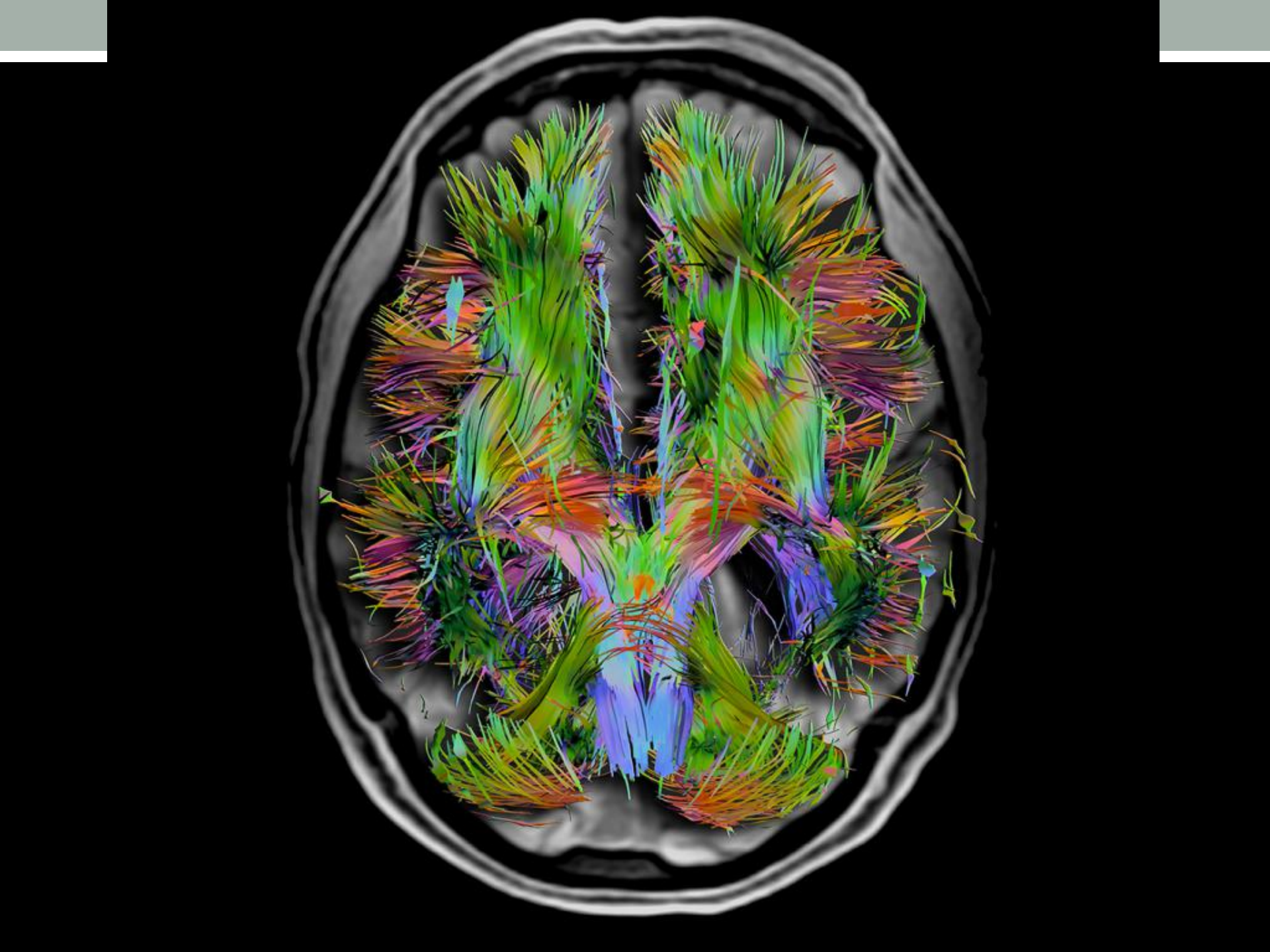
Results: Patients classified as having high DWMH were 7.14 times more likely not to remit following antidepressant treatment compared to patients classified as having low DWMH ($p = 0.02$). Similar odds ratios were obtained for PVH ($OR = 4.17$, $p = 0.16$) and total volumes ($OR = 5.00$, $p = 0.05$). Importantly, adjusting for age did not change the magnitude of these effects.

Vascular depression consensus report – a critical update

Howard J. Aizenstein[1], Andrius Baskys[2], Maura Boldrini[3,4], Meryl A. Butters[5], Breno S. Diniz[6], Manoj Kumar Jaiswal[3,7], Kurt A. Jellinger[8*], Lev S. Kruglov[9], Ivan A. Meshandin[10], Milija D. Mijajlovic[11], Guenter Niklewski[12], Sarah Pospos[2], Keerthy Raju[13], Kneginja Richter[12,14], David C. Steffens[15], Warren D. Taylor[16,17] and Oren Tene[18,19]

Aizenstein *et al. BMC Medicine* (2016) 14:161





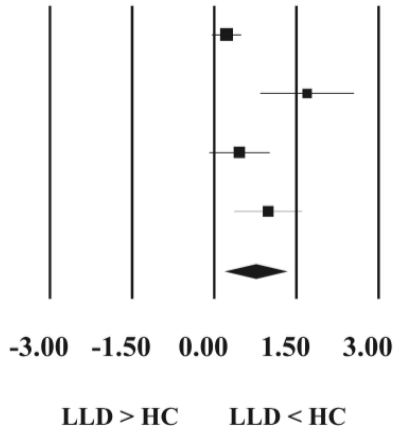
Diffusion tensor imaging studies in late-life depression: systematic review and meta-analysis

Ming-Ching Wen[1], David C. Steffens[2], Mei-Kuang Chen[3] and Nur Hani Zainal[1]

Int J Geriatr Psychiatry 2014

Conclusion: Diffusion tensor imaging studies of LLD consistently showed reduced anisotropy in the DLPFC and UF of patients with LLD. These damaged regions are located with the frontostriatal and limbic networks. Thus, our findings showed that the disruption of frontal and frontal-to-limbic white matter tracts contributes to the pathogenesis of LLD.

Study name	Hedges's g	Lower limit	Upper limit	p-Value
Bae et al. (2006)	0.22	-0.06	0.51	0.12
Nobuhara et al. (2006)	1.70	0.82	2.57	0.00
Taylor et al. (2011)	0.46	-0.11	1.03	0.11
Yang et al. (2007)	0.99	0.35	1.62	0.00
Mean	0.75	0.18	1.32	0.01



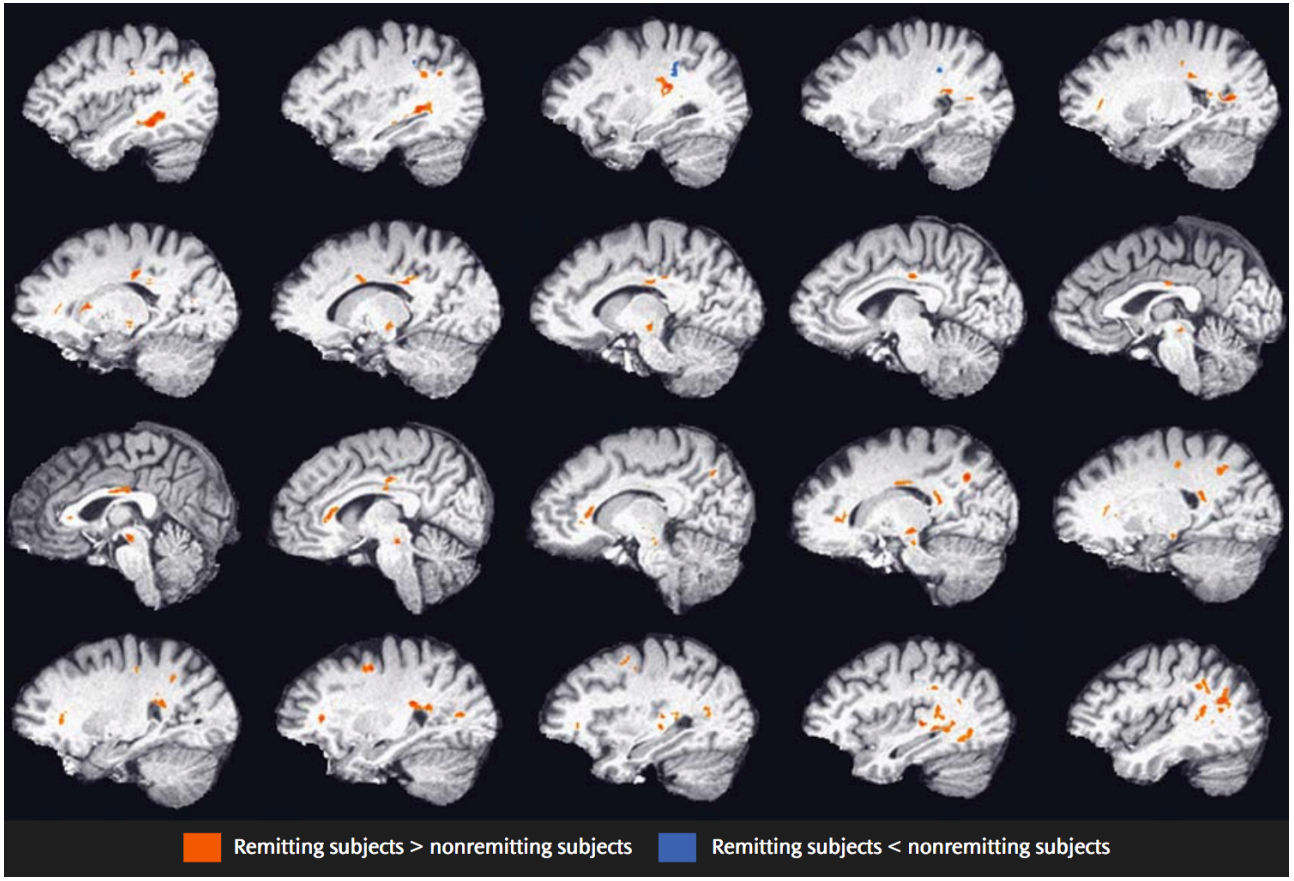
Note: CI= Confidence interval; LLD= Late-life depression; HC= Healthy control; Q= 12.86; $p < .01$; I^2= 76.68%

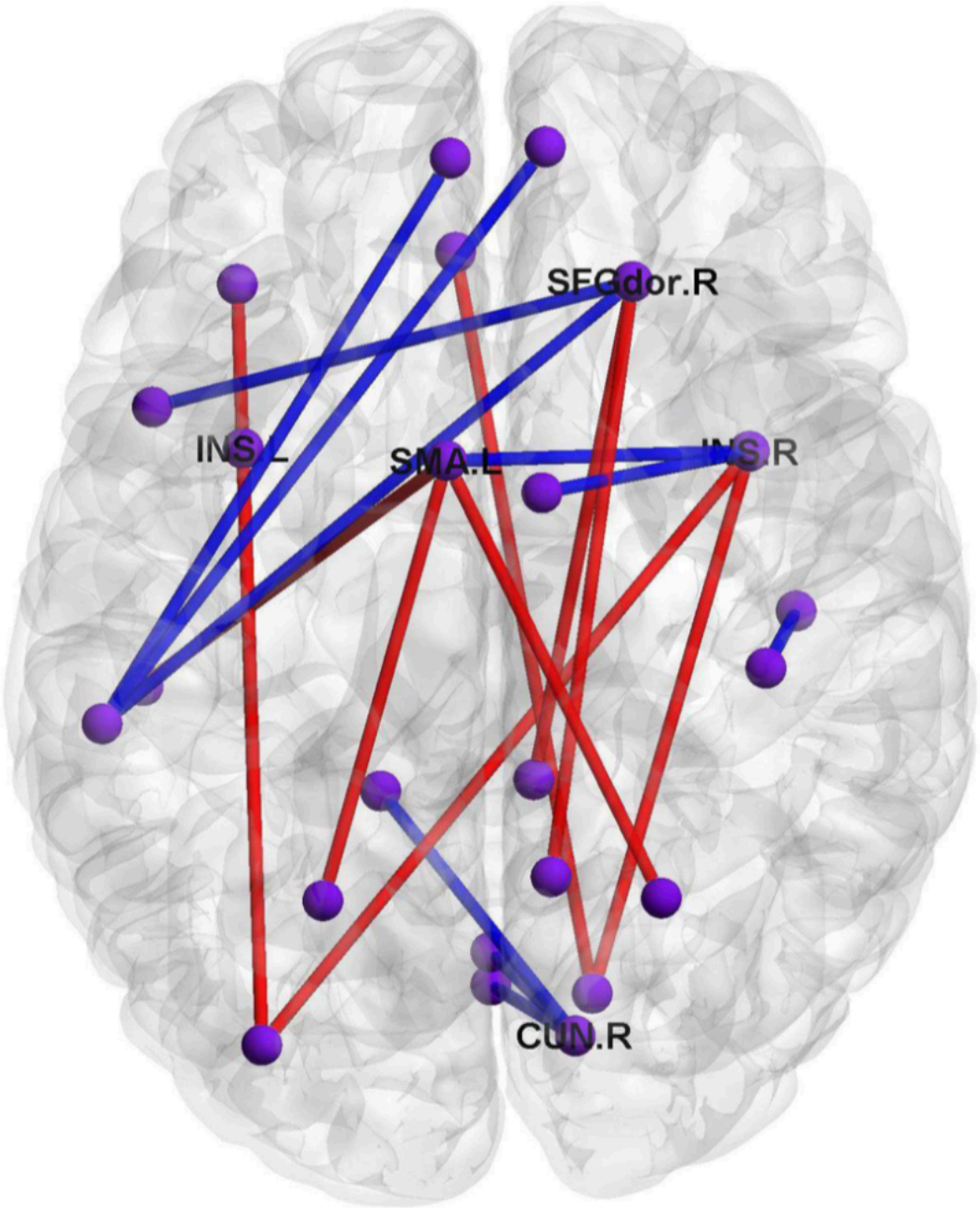
Forest plot for the fractional anisotropy of the dorsolateral prefrontal cortex in LLDs versus HCs for the region of interest studies.

Microstructural White Matter Abnormalities and Remission of Geriatric Depression

(Am J Psychiatry 2008; 165:238–244)

Results: Subjects who failed to achieve remission (N=23) had lower fractional anisotropy in multiple frontal limbic brain

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INS.L
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CUN.R

Brain Network Dysfunction in Late-Life Depression: A Literature Review

Journal of Geriatric Psychiatry and Neurology
2014, Vol. 27(1) 5-12

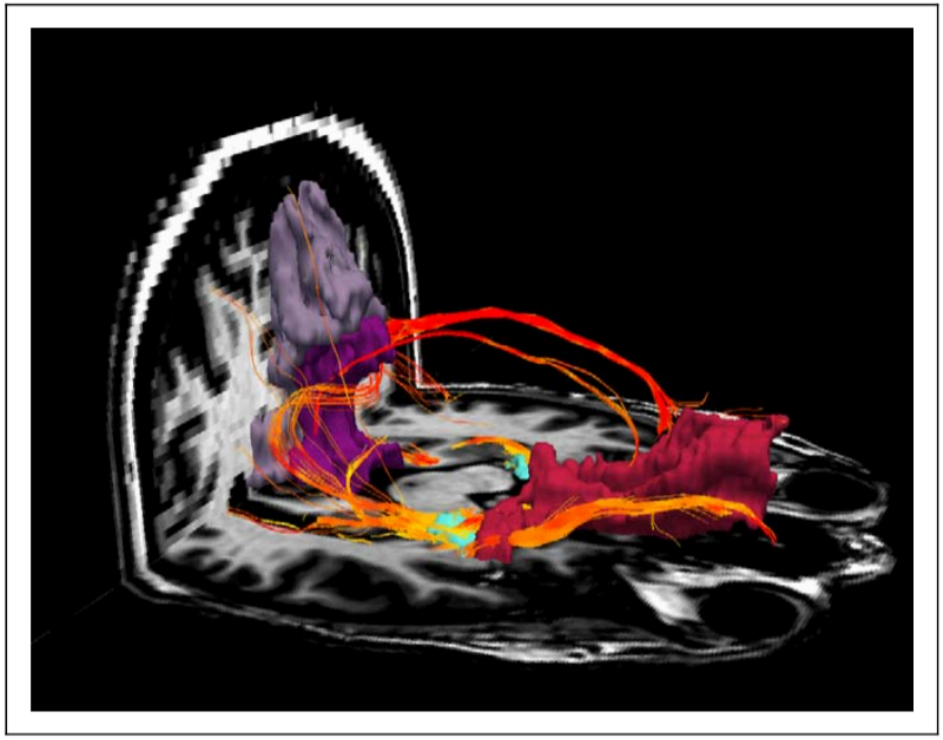

Figure 1. Default mode network. This side view of the default mode

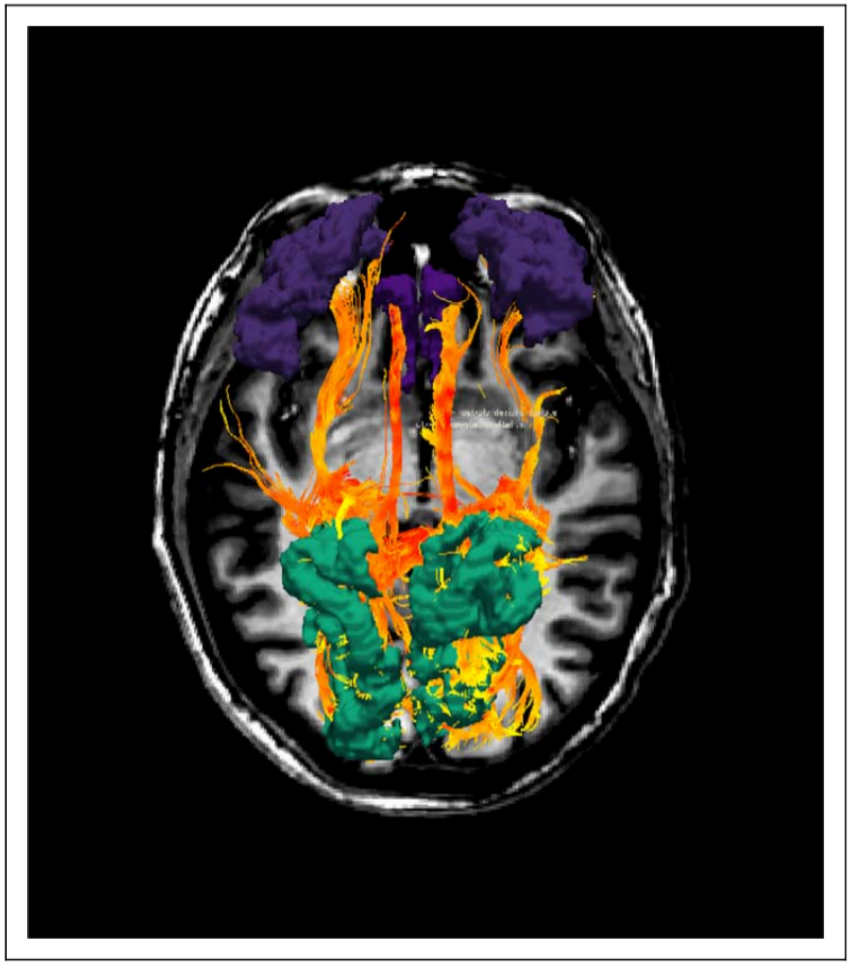

Figure 2. Cognitive control network. This is a superior view of the

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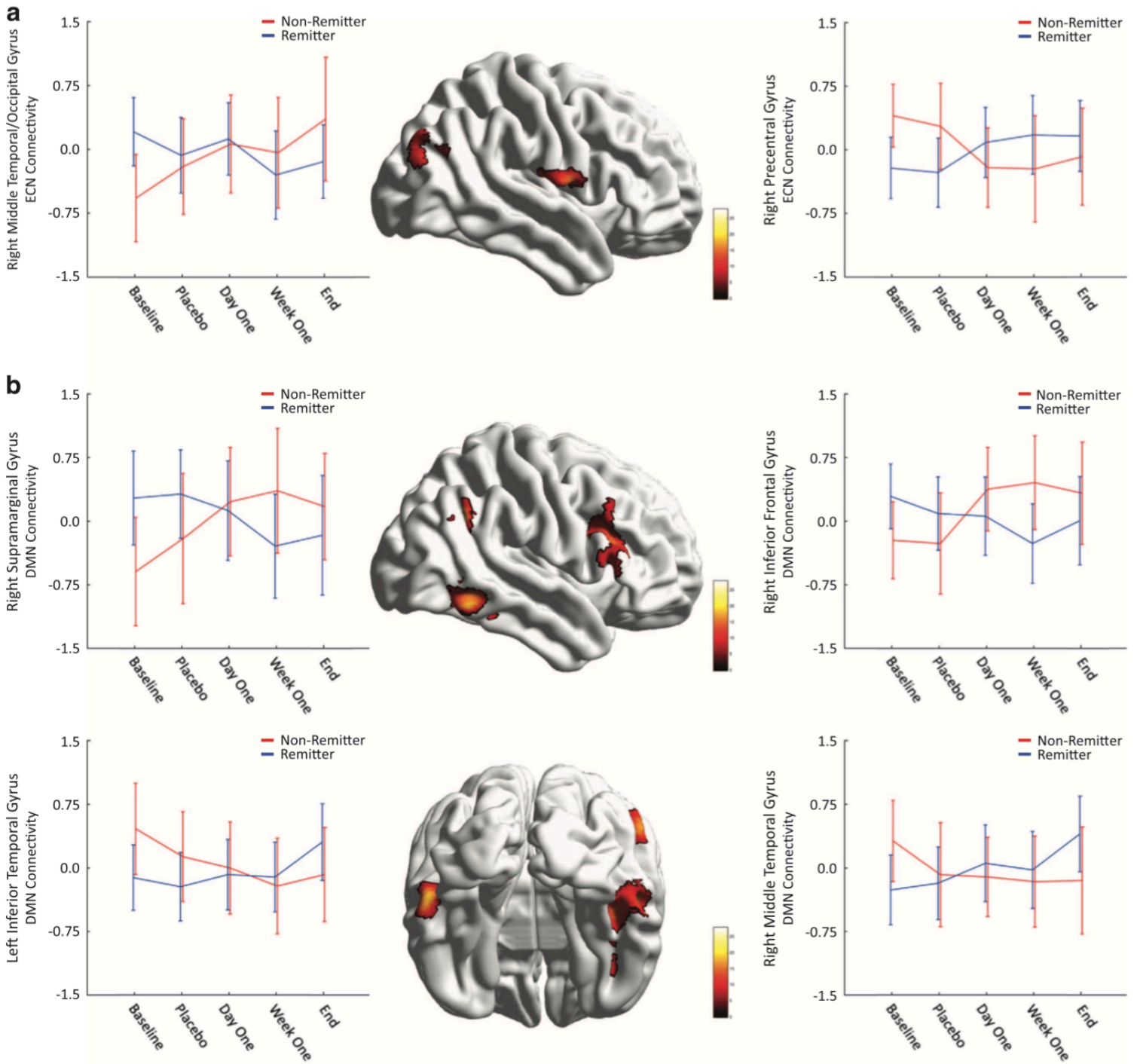
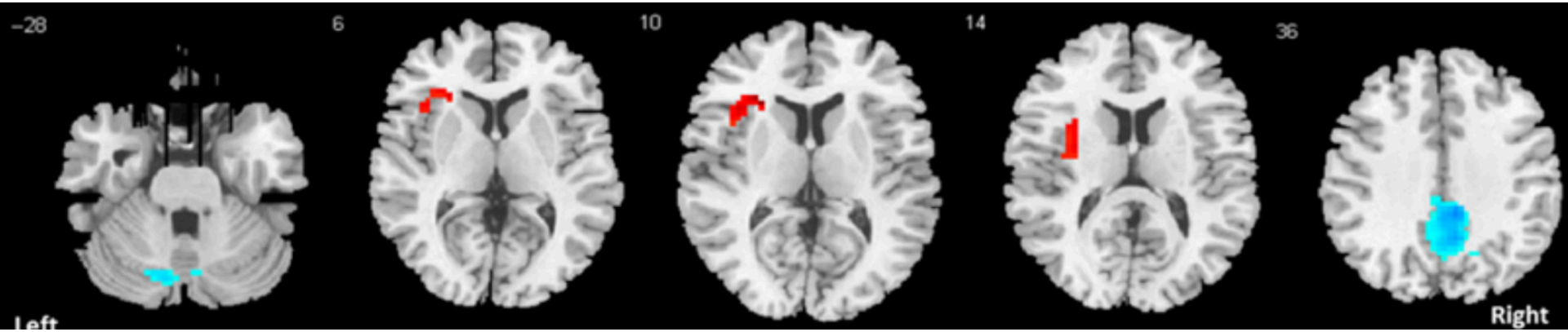


Clinical utility of a short resting-state MRI scan in differentiating bipolar from unipolar depression

Acta Psychiatr Scand 2017: 136: 288–299

Significant outcomes

- An 8-min resting scan approach can successfully discriminate bipolar depression from unipolar depression with high degree of accuracy (86%).
- Bipolar depression and unipolar depression have 70% dissimilarity of illness-specific connectivity profile and only 30% similarity of transdiagnostic dysconnectivity.
- A reduction in the centrality of insula along with an increase in centrality of precuneus uniquely relates to the pathophysiology of bipolar depression.



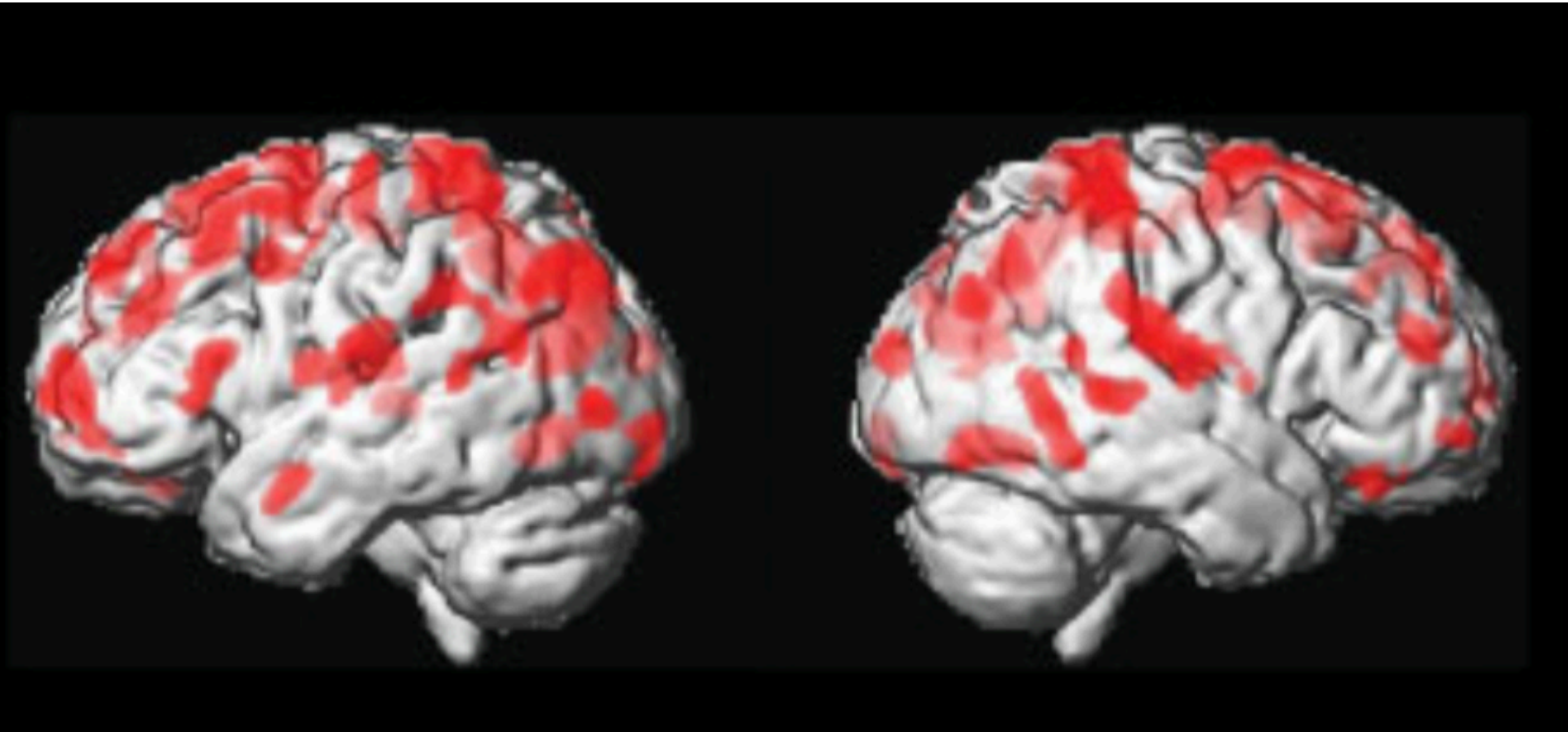
TOMOGRAPHIE PAR EMISSION DE POSITONS

TEP-FDG, TEP Amyloide, …

The functional neuroanatomy of geriatric depression

Gwenn S. Smith[1,3]*, Elisse Kramer[2], Yilong Ma[3], Peter Kingsley[4], Vijay Dhawan[3], Thomas Chaly[3] and David Eidelberg[3]

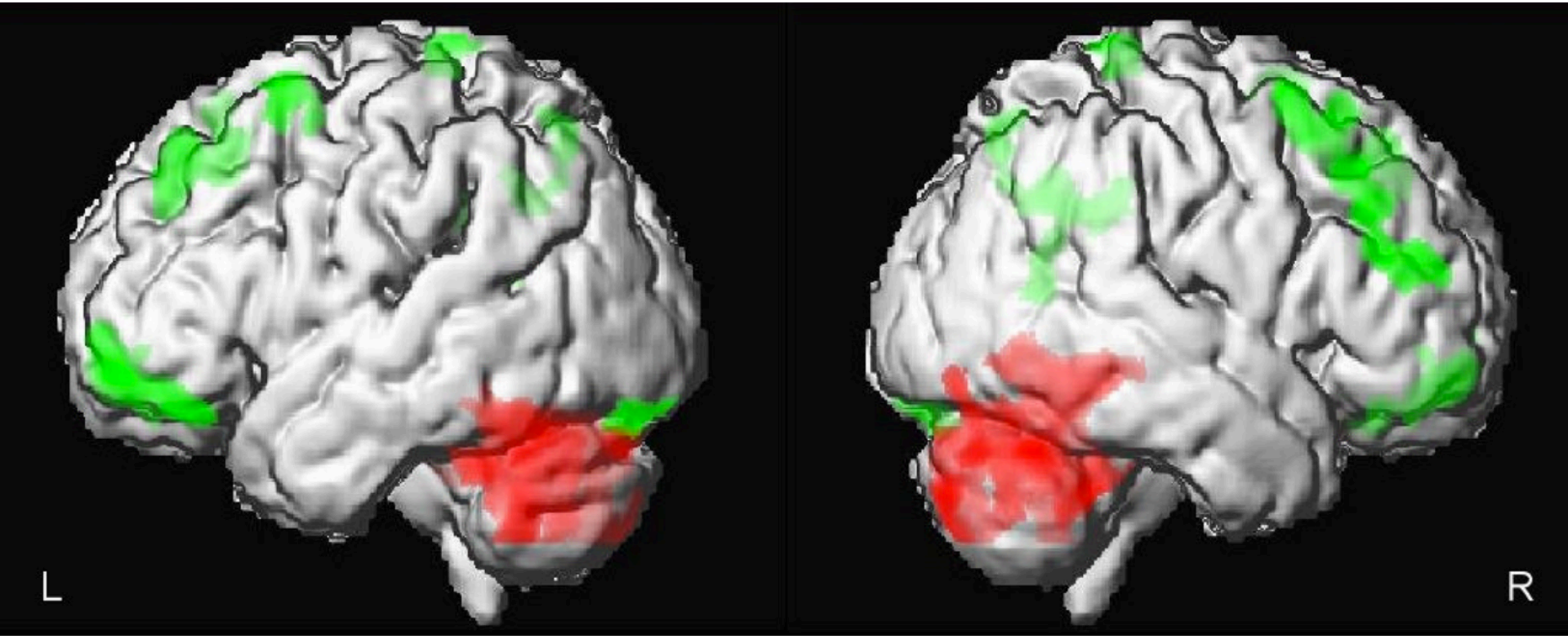
Int J Geriatr Psychiatry 2009; **24**: 798–808.



Serotonin Modulation of Cerebral Glucose Metabolism in Depressed Older Adults

Gwenn S. Smith, Ph.D.[1,3], **Elisse Kramer, Ph.D.**[2], **Carol. Hermann, M.D.**[2], **Yilong Ma, Ph.D.**[3], **Vijay Dhawan, Ph.D.**[3], **Thomas Chaly, Ph.D.**[3], and **David Eidelberg, M. D**[3]

Biol Psychiatry. 2009 August 1; 66(3): 259–266.



AGING & MENTAL HEALTH, 2017
VOL. 21, NO. 9, 889–894
http://dx.doi.org/10.1080/13607863.2016.1247413

Routledge
Taylor & Francis Group

Is ^{18}F-FDG-PET suitable to predict clinical response to the treatment of geriatric depression? A systematic review of PET studies

Franco De Crescenzo[a], Mario Ciliberto[b], Deny Menghini[c], Giorgio Treglia[d], Klaus P. Ebmeier[e] and Luigi Janiri[a]

Results: Eleven articles comprising 128 patients were included. We extracted data on glucose uptake of depressed patients and controls at baseline and after different types of intervention (total sleep deprivation followed by a recovery sleep and treatment with selective serotonin reuptake inhibitors).
Conclusions: ^{18}F-FDG-PET showed significant alterations of glucose uptake in several brain areas, in particular the anterior cingulate cortex, which showed reduced metabolism after treatment, and was a predictor of treatment response.

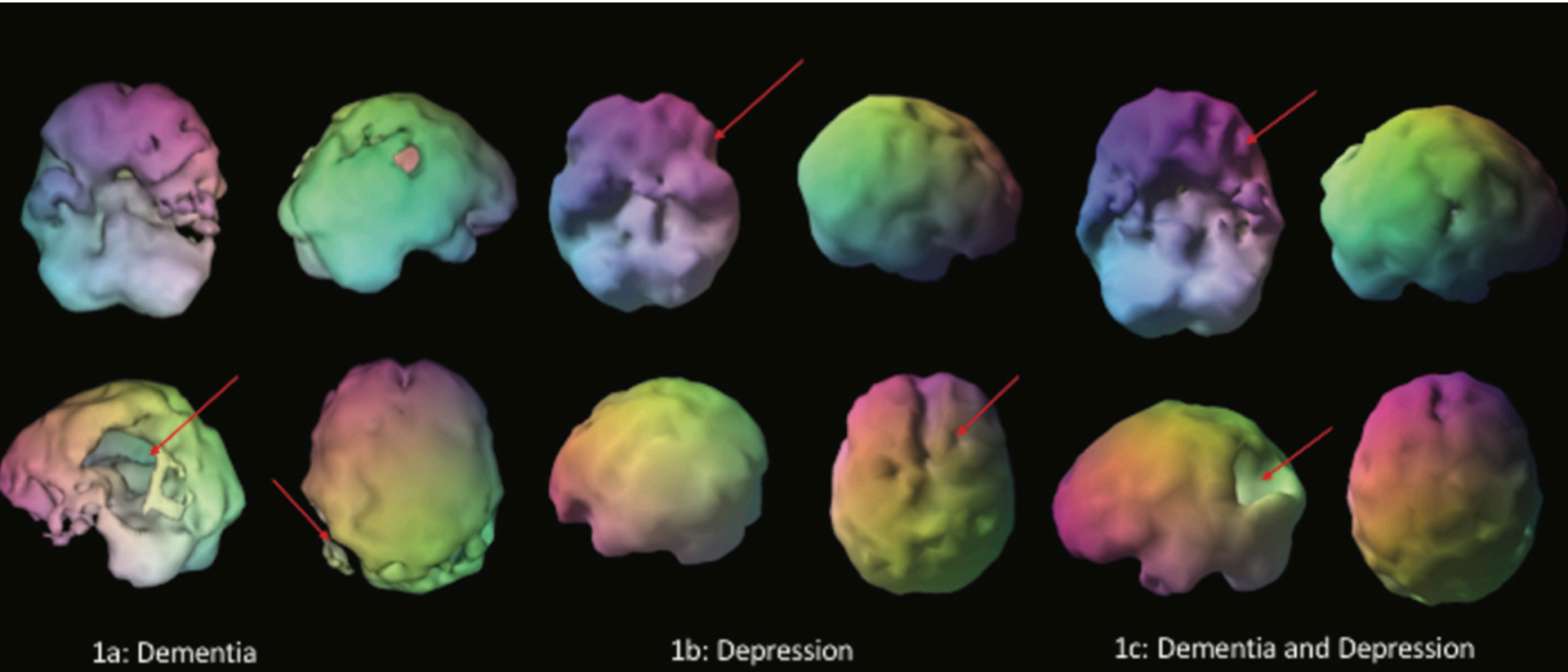
Classification of Depression, Cognitive Disorders, and Co-Morbid Depression and Cognitive Disorders with Perfusion SPECT Neuroimaging

Daniel G. Amen[a,*], Pavitra Krishnamani[b], Somayeh Meysami[c], Andrew Newberg[b] and Cyrus A. Raji[d]

Journal of Alzheimer's Disease 57 (2017) 253–266

4a: Depression from Cognitive Disorders

1. Concentration Left Cerebellar Crus
2. Concentration Left Anterior Cingulate Gyrus
3. Concentration Vermis Subregion 9
4. Concentration Left Superior Frontal Gyrus
5. Concentration Left Inferior Parietal Cortex
6. Baseline Right Caudate
7. Concentration Right Insula
8. Concentration Left Cerebellum Subregion 6
9. Concentration Left Superior Anterior Temporal Cortex
10. Baseline Right Superior Orbital Frontal Cortex
11. Baseline Right Cerebellum Subregion 9
12. Concentration Left hippocampus
13. Baseline Left Caudate
14. Baseline Left Inferior Orbital Frontal Cortex



Brain [^{18}F]FDDNP Binding and Glucose Metabolism in Advanced Elderly Healthy Subjects and Alzheimer's Disease Patients

Clovis Tauber[a], Emilie Beaufils[a,b], Caroline Hommet[a,b], Maria Joao Ribeiro[a,b], Johnny Vercouillie[a], Emilie Vierron[a,d], Karl Mondon[a,b], Jean Philippe Cottier[a,b], Valérie Gissot[b,c], Denis Guilloteau[a,b,d] and Vincent Camus[a,b,*]

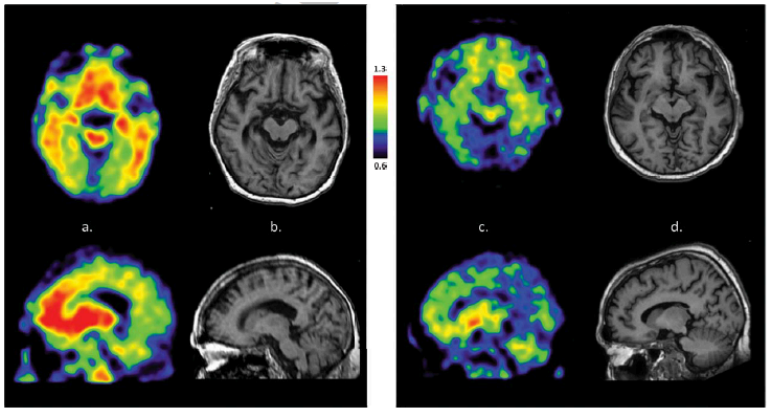
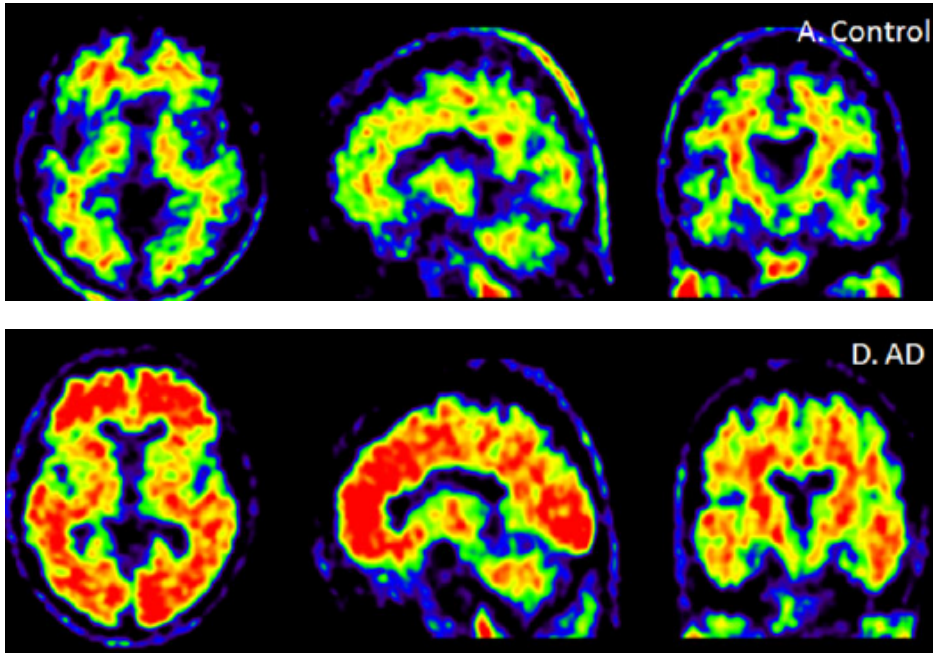


Fig. 1. Spatially normalized [^{18}F]FDDNP SUVr (a, c) and MRI (b, d) images obtained from an AD patient (a, b) and an HC subject (c, d). The cerebellum was used as the reference region.

Journal of AD 2013; 36(2): 311-320

Using PET with ^{18}F-AV-45 (florbetapir) to quantify brain amyloid load in a clinical environment

V. Camus · P. Payoux · L. Barré · B. Desgranges · T. Voisin · C. Tauber · R. La Joie · M. Tafani · C. Hommet · G. Chételat · K. Mondon · V. de La Sayette · J. P. Cottier · E. Beaufils · M. J. Ribeiro · V. Gissot · E. Vierron · J. Vercouillie · B. Vellas · F. Eustache · D. Guilloteau



EJNMMI2012; 39(4): 621-631

The Amyloid Hypothesis: Is There a Role for Anti-amyloid Treatment in Late-Life Depression?

Nahla Mahgoub, M.D.[1] and **George S. Alexopoulos, M.D.**[1]

Am J Geriatr Psychiatry. 2016 March ; 24(3): 239–247

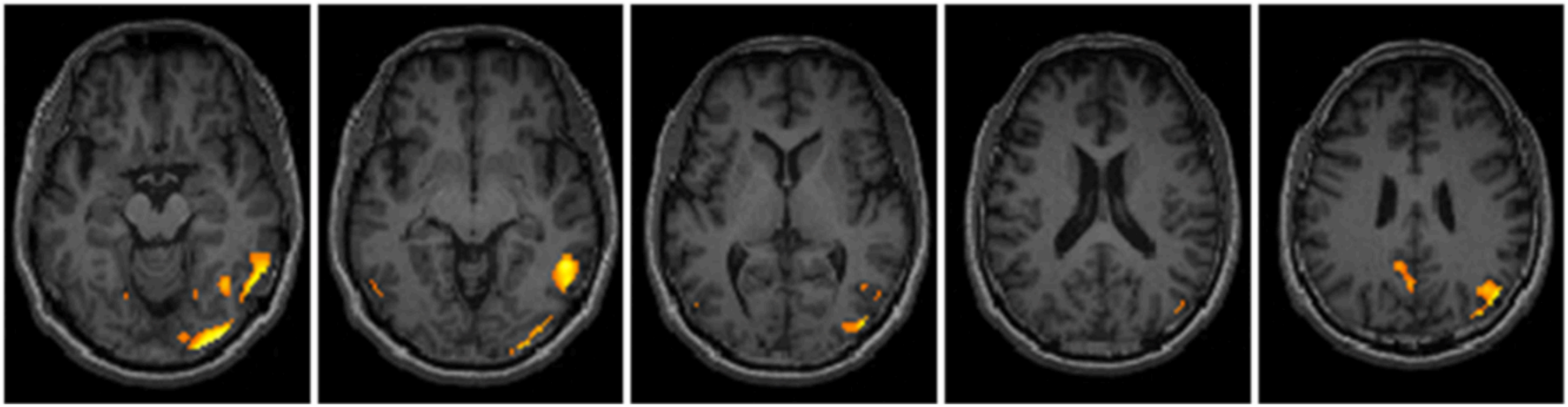
depression, part of the prodromal phase of AD. This assertion is based on the following observations: 1) Patients with lifetime history of depression have significant amyloid accumulation in brain regions related to mood regulation, an event conceivably related to the increased risk of AD conferred by recurrent depression (15). 2) Amyloid deposition occurs during a preclinical phase of dementia when depressive syndromes and symptoms of AD patients are prevalent (1, 16). 3) Amyloid deposition leads to neurobiological processes (vascular damage, degeneration, inflammation, blood brain barrier changes, abnormal functional connectivity) that can impair networks implicated in depression (10–12); 4) AD patients with history of depression have more amyloid plaques in the hippocampus than AD patients without depression (17). The amyloid hypothesis of late-life depression is timely

Beta-amyloid deposition in patients with major depressive disorder with differing levels of treatment resistance: a pilot study

Peng Li[1†], Ing-Tsung Hsiao[2,3†], Chia-Yih Liu[1], Chia-Hsiang Chen[1], She-Yao Huang[2,3], Tzu-Chen Yen[2,3], Kuan-Yi Wu[1*] and Kun-Ju Lin[3,4*]

Li *et al. EJNMMI Research* (2017) 7:24

Conclusions: This study provided preliminary evidence that region-specific Aβ deposition was present in some (but not all) MDD patients, especially in those with moderate-to-severe treatment resistance, and their depressive symptoms may represent prodromal manifestations of Alzheimer's disease (AD). Depressive symptomatology in old age, particularly in subjects with a poor treatment response, may underscore early changes of AD-related pathophysiology.



ULTRASONS?

Ultrasound and dynamic functional imaging in vascular cognitive impairment and Alzheimer's disease

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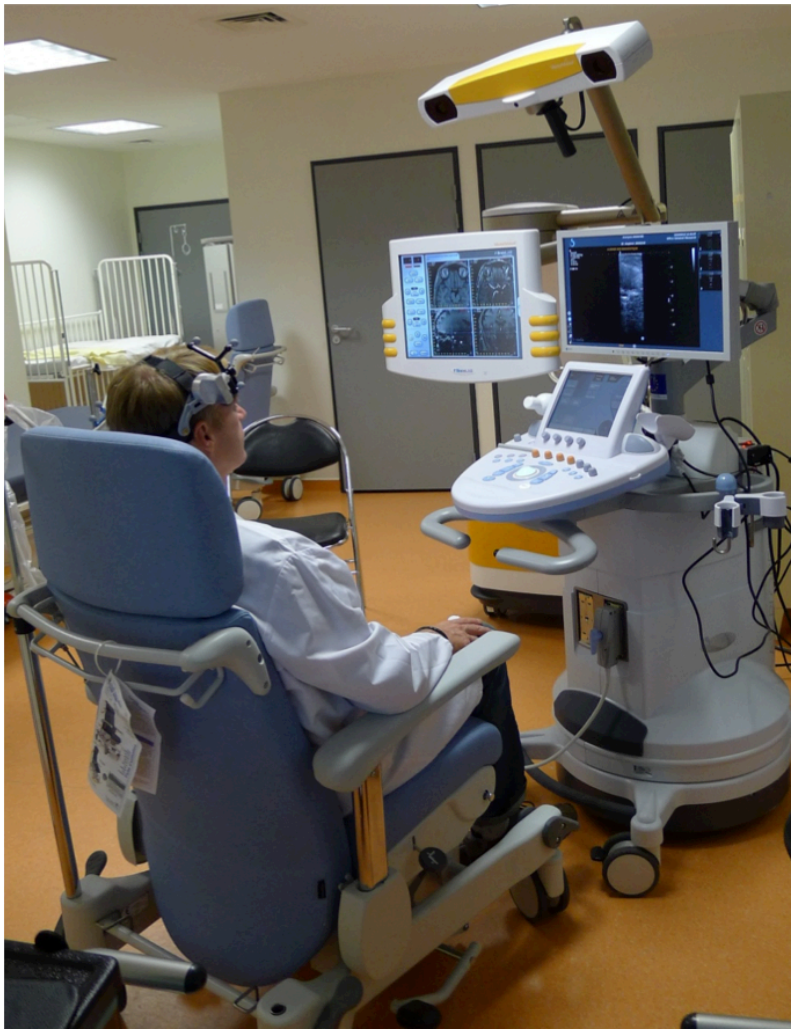
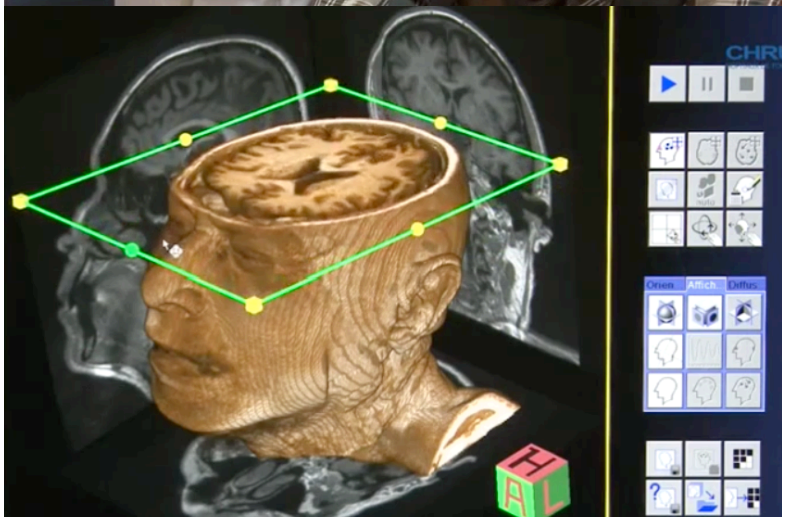
Table 1 Potential applications of extracranial ultrasound in vascular dementia (VaD) and Alzheimer's disease (AD)

Carotid ultrasound method	Finding	References
Aortic stiffness (carotid–femoral pulse wave velocity)	Increased aortic stiffness in VaD	Poels et al., 2012 [142] Mitchell et al., 2011 [131] Webb et al., 2012 [132]
Carotid stiffness index	Greater CCA stiffness indexes in VaD	Morovic et al., 2009 [180] Jurasic et al., 2009 [181] Turk et al., 2015 [149]
Carotid pulsatility and resistance index	Higher ICA pulsatility in patients with WMH	Mitchell et al., 2011 [131] Webb et al., 2012 [132] Tanaka et al., 2009 [133] Aribisala et al., 2014 [134]
Carotid diameter	CCA diameter increase in VaD	Morovic et al., 2009 [180] Heliopoulos et al., 2012 [18]
Carotid BFV	Higher ICA pulsatility and lower BFV in VaD patients	Tanaka et al., 2009 [133] Aribisala et al., 2014 [134] Heliopoulos et al., 2012 [18]
Cerebral blood flow	Lower CBF in VaD and AD patients compared to controls Longer CCT in VaD and AD patients compared to controls	Schreiber et al., 2005 [136]
	Similar CBF in VaD and AD patients compared to controls	Turk et al., 2015 [149]
Plaque instability: Ultrasound strain imaging	Increased strain in plaque correlated with WMH	Berman et al., 2015 [137]
Intima media thickness and plaque burden	Positive correlation between intima media thickness and plaque burden with WMH lesion burden	Casado-Naranjo et al., 2015 [138] Heliopoulos et al., 2012 [18] Kearney-Schwartz et al., 2009 [182] Shrestha et al., 2009 [140]

BFV blood flow velocity, *CBF* cerebral blood flow, *CCA* common carotid artery, *ICA* internal carotid artery, *WMH* white matter hyperintensities, *CCT* cerebral circulation time

Pulsatilité Cérébrale par Ultrasons

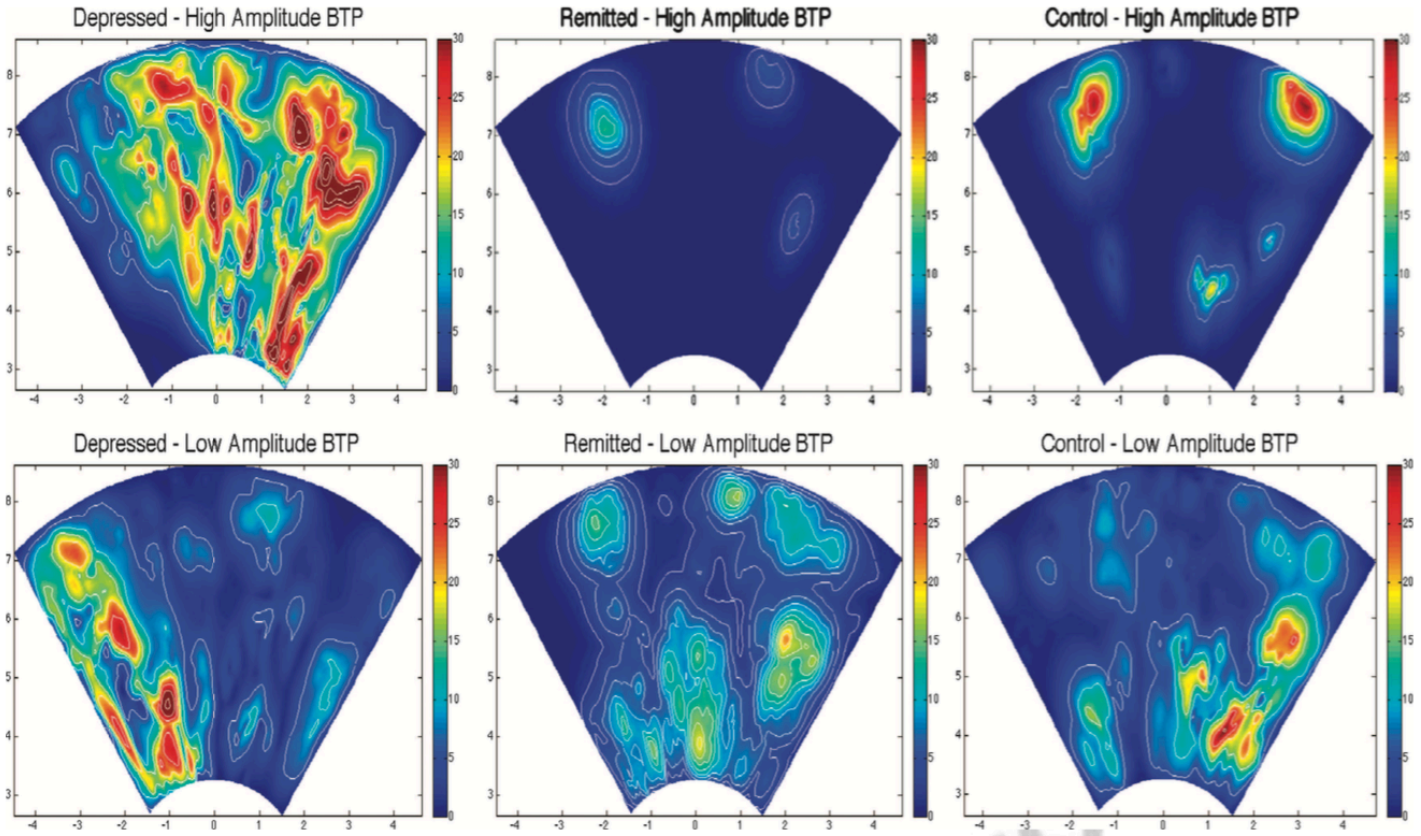


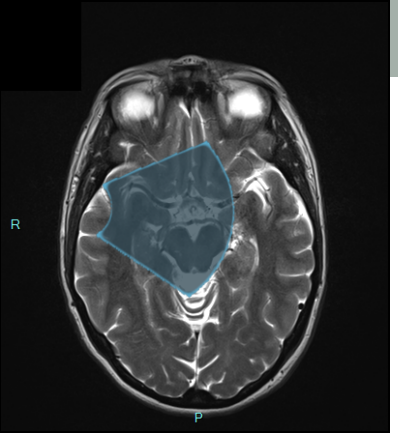


Brain Tissue Pulsatility is Increased in Midlife Depression: a Comparative Study Using Ultrasound Tissue Pulsatility Imaging

Thomas Desmidt*[,1,2], Bruno Brizard[2], Paul-Armand Dujardin[3], Redouane Ternifi[2], Jean-Pierre Réméniéras[2,3], Frédéric Patat[2,3], Frédéric Andersson[2], Jean-Philippe Cottier[2,4], Emilie Vierron[2,3], Valérie Gissot[3], Kang Kim[5], Howard Aizenstein[6], Wissam El-Hage[1,2,3] and Vincent Camus[1,2]

Neuropsychopharmacology (2017), 1–8

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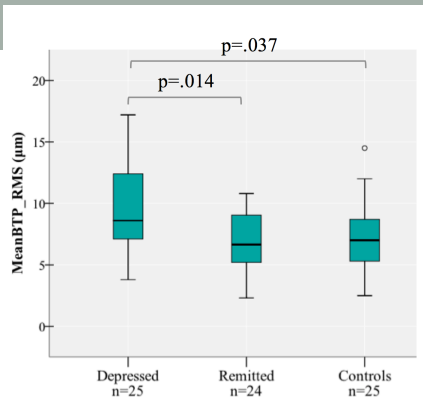
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p=.014
MeanBTP_RMS (µm)
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15
10
5
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Depressed
n=25
Remitted
n=24
Controls
n=25

MERCI!