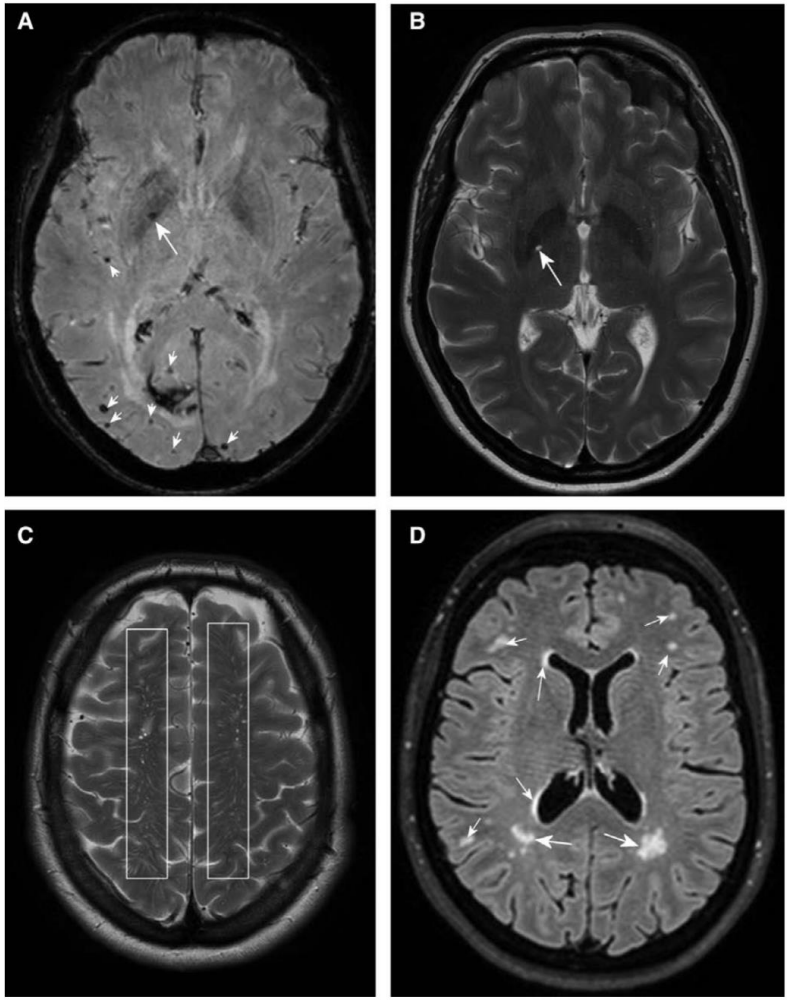
DÉPRESSION VASCULAIRE

Toulouse, Mars 2019



Thomas Desmidt
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Imaging & Brain

CONSULTATION INTERSECTORIELLE DE GÉRONTOPSYCHIATRIE

Historique Dépression Vasculaire

The American Journal of Psychiatry, VOL. 93, No. 5

ARTICLE | March 01, 1937

MORTALITY AMONG PATIENTS WITH INVOLUTION MELANCHOLIA

Benjamin Malzberg

Abstract

Patients with involution melancholia had an average annual crude death rate of 132.4 per 1000 exposures. This is almost twice the rate for patients with manic-depressive psychoses, and four times the rate for patients with dementia præcox. It is the highest rate of any of the functional group of psychoses. On the basis of standardized death rates, patients with involution melancholia had a death rate in excess of that of the general population in the ratio of 6.2 to 1. Among males and females the corresponding ratios were 6.2 to 1 and 6.8 to 1, respectively. Males have higher death rates than females, though the difference is not significant with respect to the probable error.Diseases of the heart constitute the leading cause of death, being responsible for almost 40 per cent of all the deaths. The death rate from these diseases is almost eight times the corresponding rate in the general population, when both are corrected for age. Pneumonia was responsible for only a third as many deaths as diseases of the heart. Tuberculosis ranked third as a cause of death. It is noteworthy, however, that the death rate from tuberculosis exceeded that of patients with dementia præcox.

Historique Dépression Vasculaire

Global Burden OF Disease STUDY

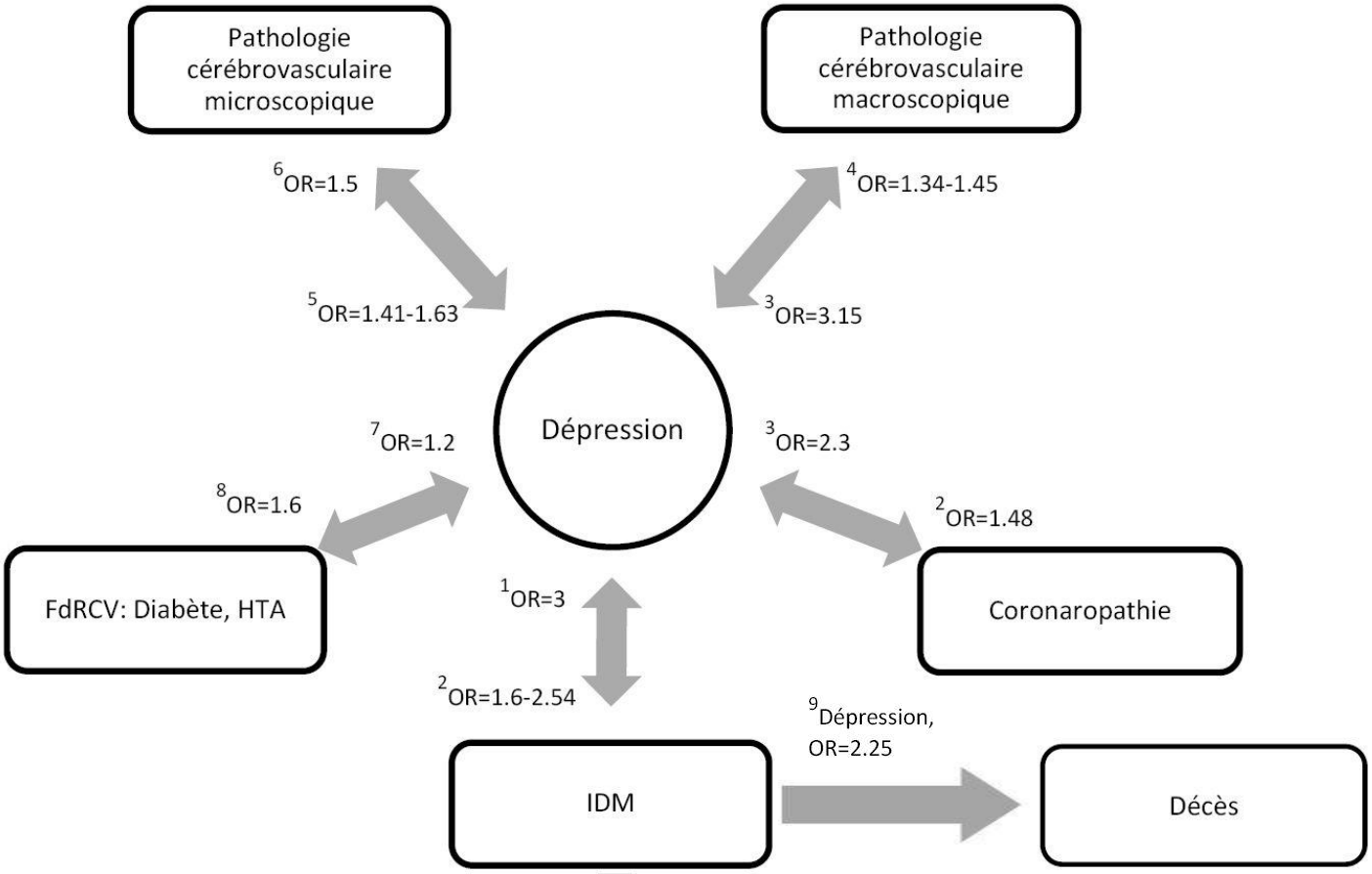
Should Global Burden of Disease Estimates Include Depression as a Risk Factor for Coronary Heart Disease?

Charlson *et al. BMC Medicine* 2011, **9**:47
http://www.biomedcentral.com/1741-7015/9/47

Abstract

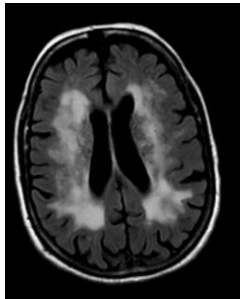
The 2010 Global Burden of Disease Study estimates the premature mortality and disability of all major diseases and injuries. In addition it aims to quantify the risk that diseases and other factors play in the aetiology of disease and injuries. Mental disorders and coronary heart disease are both significant public health issues due to their high prevalence and considerable contribution to global disease burden. For the first time the Global Burden of Disease Study will aim to assess mental disorders as risk factors for coronary heart disease. We show here that current evidence satisfies established criteria for considering depression as an independent risk factor in development of coronary heart disease. A dose response relationship appears to exist and plausible biological pathways have been proposed. However, a number of challenges exist when conducting a rigorous assessment of the literature including heterogeneity issues, definition and measurement of depression and coronary heart disease, publication bias and residual confounding. Therefore, despite some limitations in the available data, it is now appropriate to consider major depression as a risk factor for coronary heart disease in the new Global Burden of Disease Study.

Historique Dépression Vasculaire



Historique Dépression Vasculaire

- Atherosclerotic depression, Gaupp, 1905
- Vascular Depression, Alexopoulos, 1997
  - Cerebrovascular disease, including small vessel ischemic changes, may predispose, precipitate, or perpetuate some geriatric depressive symptoms as a consequence of structural damage to frontal–subcortical circuits, with disruption of cortico–striato–pallido–thalamo–cortical pathways as their underlying systems
- Depressive–executive dysfunction syndrome, Alexopoulos
- MRI-defined Vascular Depression



JAMA Psychiatry | Original Investigation | META-ANALYSIS

Association of Microvascular Dysfunction With Late-Life Depression

A Systematic Review and Meta-analysis

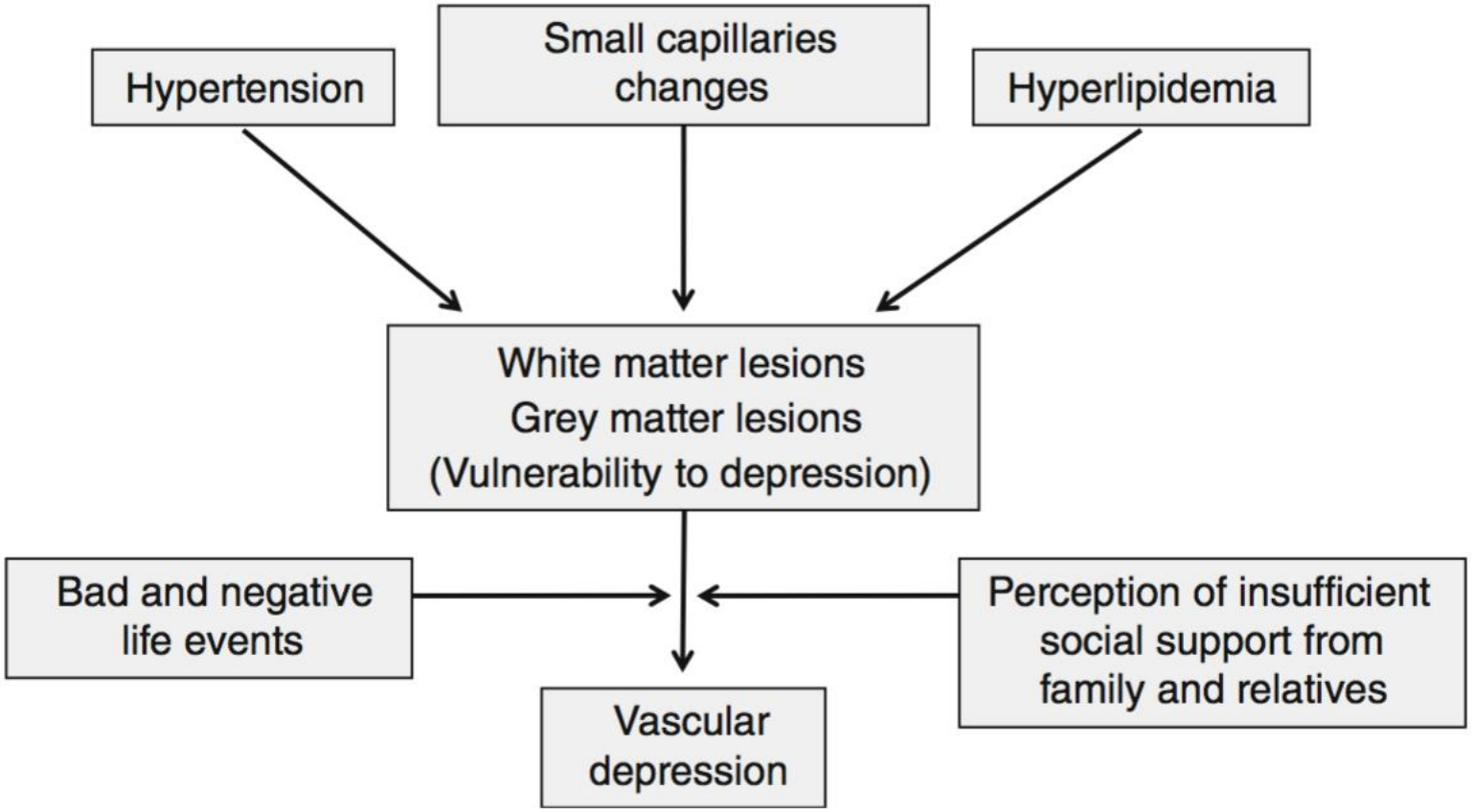
Marnix J. M. van Agtmaal, MD; Alfons J. H. M. Houben, PhD; Frans Pouwer, PhD; Coen D. A. Stehouwer, MD, PhD; Miranda T. Schram, MD

JAMA Psychiatry Published online May 31, 2017

RESULTS A total of 712 studies were identified; 48 were included in the meta-analysis, of which 8 described longitudinal data. Data from 43 600 participants, 9203 individuals with depression, and 72 441 person-years (mean follow-up, 3.7 years) were available. Higher levels of plasma endothelial biomarkers (soluble intercellular adhesion molecule–1: OR, 1.58; 95% CI, 1.28-1.96), white matter hyperintensities (OR, 1.29; 95% CI, 1.19-1.39), cerebral microbleeds (OR, 1.18; 95% CI, 1.03-1.34), and cerebral (micro)infarctions (OR, 1.30; 95% CI, 1.21-1.39) were associated with depression. Among the studies available, no significant associations of albuminuria and retinal vessel diameters with depression were reported. Longitudinal data showed a significant association of white matter hyperintensities with incident depression (OR, 1.19; 95% CI, 1.09-1.30).

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]



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Clinical features of VaDep	Clinical features of non-VaDep
Depression occurring at age 65 years or later	Depression occurring at age 50 to 60 years
Absence of family history	Occasional family history
Executive dysfunctions, loss of energy, subjective feeling of sadness, anhedonia, psychomotor retardation, motivational problems, reduced processing speed and visuospatial skills, deficits in self-initiation, lack of insight; depressive symptomatology may not meet criteria for any mood disorder requested in DSM-V	Sadness, depression according to DSM-V diagnostic criteria, increased suicidality, reduced verbal fluency
Higher cardiac illness burden, increased rates of vascular risk factors (hypertension, etc.)	Lower or same cardiac illness burden and rates of vascular risk factors (hypertension, etc.)
Higher risk for cognitive decline and progression to dementia	Lower or similar risk for cognitive decline and progression to dementia
Fluctuating course of cognitive impairment due to progression of white matter hyperintensities	
Greater treatment resistance and poorer outcome	Lower or same treatment resistance and outcome(?)
Associated with increased mortality	

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]

Conclusion: The multifold pathogenesis of vascular depression as a possible subtype of late life depression needs further elucidation. There is a need for correlative clinical, intra vitam structural and functional MRI as well as postmortem MRI and neuropathological studies in order to confirm the relationship between clinical symptomatology and changes in specific brain regions related to depression. To elucidate the causal relationship between regional vascular brain changes and vascular depression, animal models could be helpful. Current treatment options include a combination of vasoactive drugs and antidepressants, but the outcomes are still unsatisfying.

Vascular Depression: Is an Old Research Construct Finally Ready for Clinical Prime Time?

David C. Steffens

Biological Psychiatry March 15, 2019; 85:441–442

- Major depression occurring in the context of clinical and/or neuroimaging evidence of subcortical ischemic cerebrovascular disease
- Clinical presentation including marked apathy, difficulty initiating thought and movement, psychomotor retardation, and impairment in executive function
- Occurrence in individuals ≥50 years of age, either as an initial episode of depression or as a recurrence of depression
- Decreased response to initial antidepressant monotherapy
- Increased risk of negative longitudinal outcomes, such as cognitive decline, dementia, and occurrence of cardiovascular and cerebrovascular events (e.g., myocardial infarction and stroke)

As such, this specifier should be strongly considered for inclusion in the next revision of our diagnostic nomenclature.

Lien Dépression/TNC

July 2017

Trajectories of Depressive Symptoms Before Diagnosis of Dementia

A 28-Year Follow-up Study

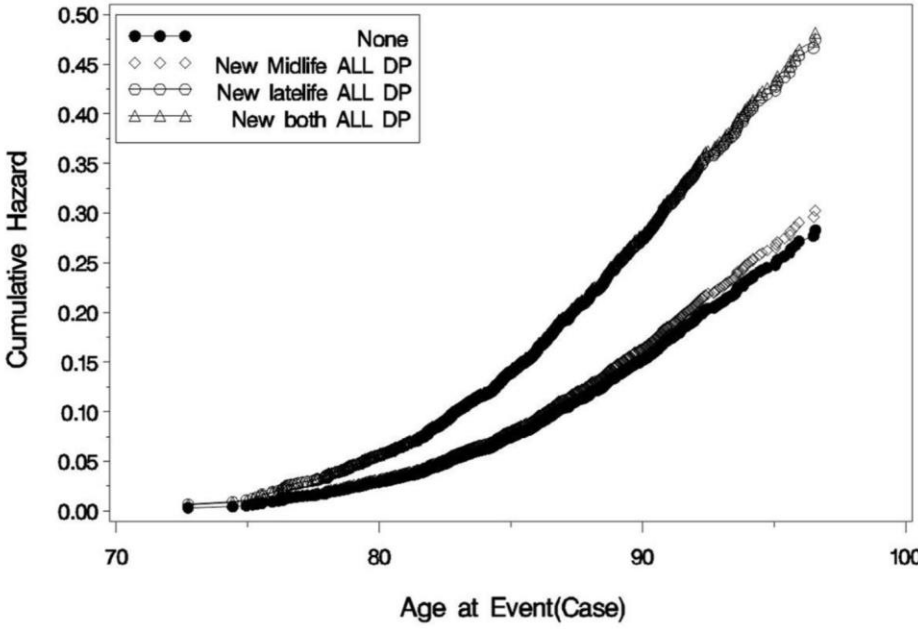
Archana Singh-Manoux, PhD[1,2]; Aline Dugravot, MSc[1]; Agnes Fournier, PhD[1]; et al

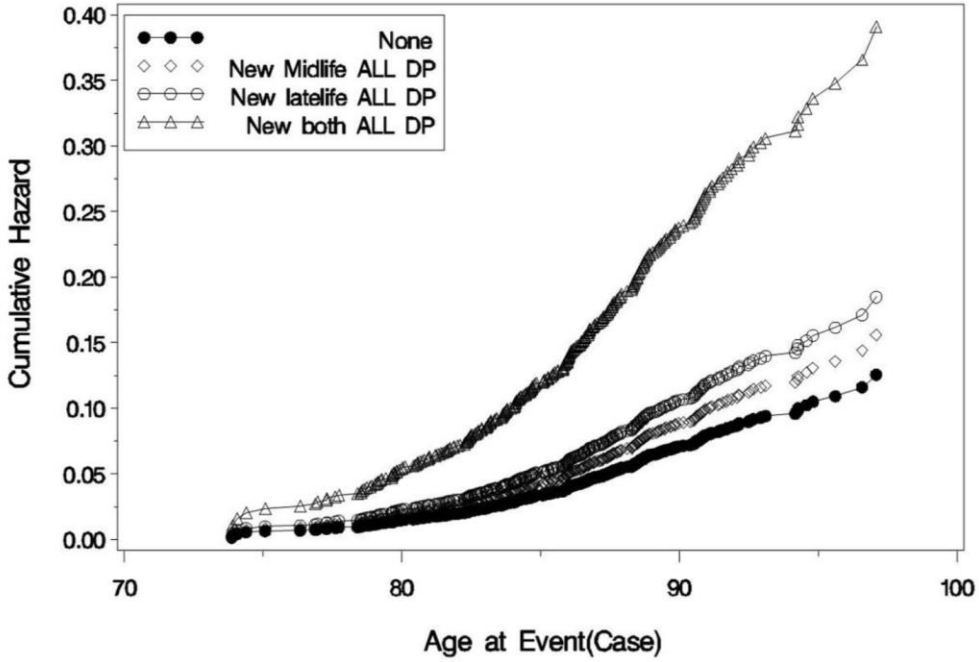
- EDM augmente le risque de MA de 65% et de VD de 150%

- EDM=FdR ou prodrome?

Arch Gen Psychiatry. 2012 May ; 69(5): 493–498. doi:10.1001/archgenpsychiatry.2011.1481.

Mid-life versus late-life depressive symptoms and risk of dementia: Differential effects for Alzheimer's disease and vascular dementia





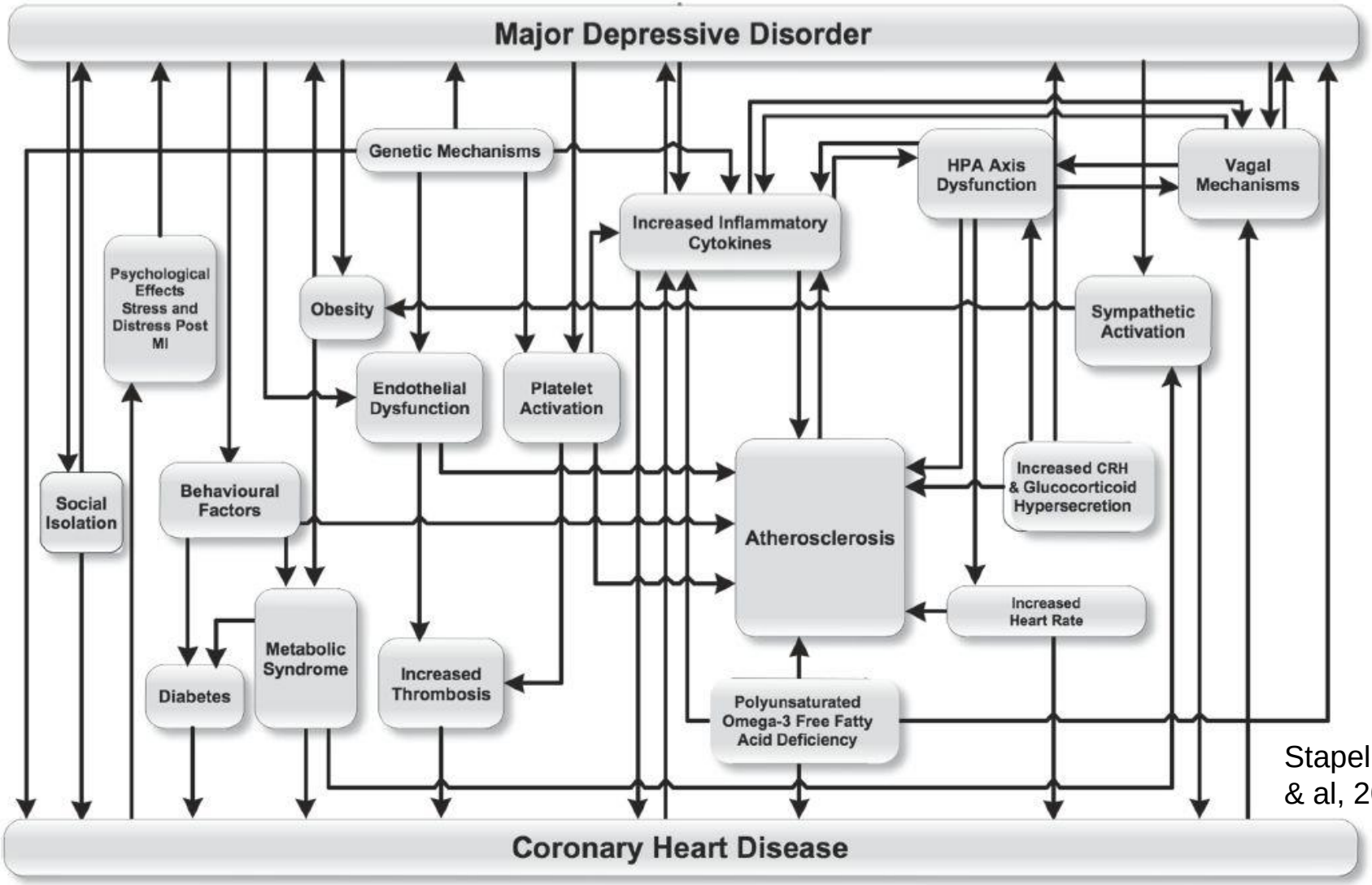
Perspectives on the Management of Vascular Depression

Warren D. Taylor, M.D., Susan K. Schultz, M.D., Vanessa Panaite, Ph.D., David C. Steffens, M.D., M.H.S.

Am J Psychiatry 175:12, December 2018

- Dépression vasculaire = Dépression résistante?
  - Seulement 33% de rémission sous Sertraline bien conduite
  - Sévérité des lésions cérébrovasculaires et sévérité du trouble exécutif = Facteurs de Résistance
  - CAT: Plusieurs lignes d'ADP et/ou dose plus élevée
- Thérapie qui cible spécifiquement les fonctions cognitives?
  - Certaines formes de TCC
- rTMS efficacité modeste
- ECT efficace indépendamment de la présence des facteurs de risques vasculaires
- Vasodilatateurs Cérébraux? Inhibiteurs Calciques?
- Béta Bloquants à risque d'accentuer les symptômes?

Liens dépression/maladies cardiovasculaires: physiopathologie



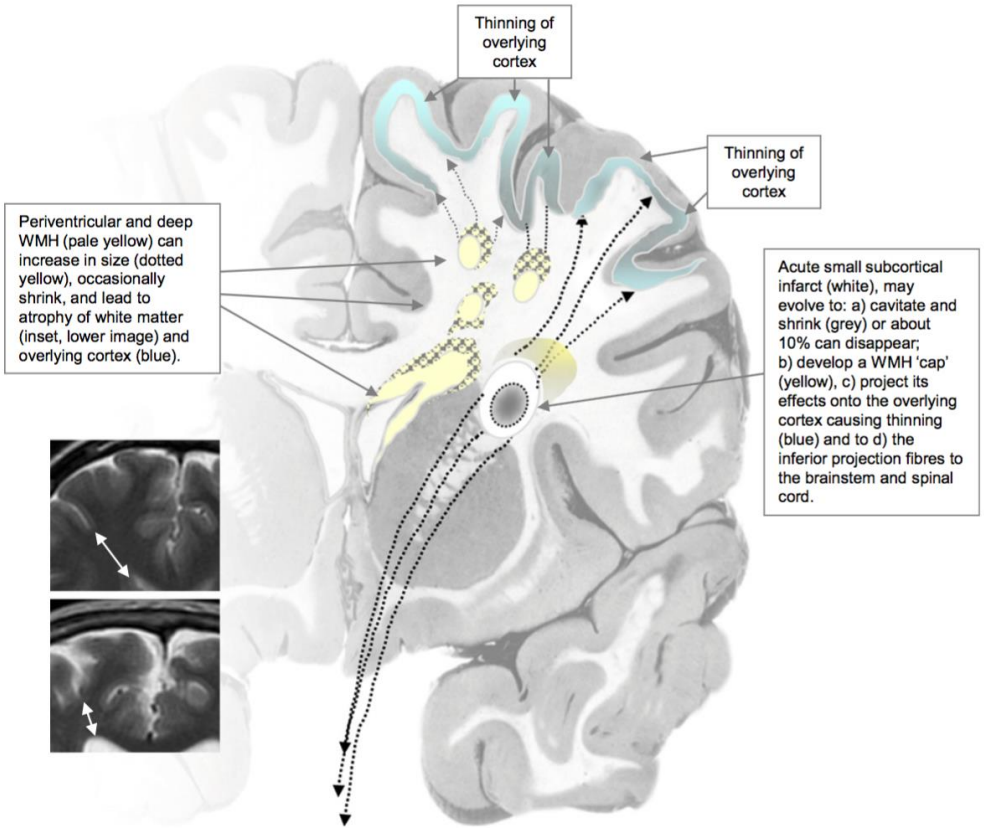
Stapelberg & al, 2011

American Heart Association | American Stroke Association

What are White Matter Hyperintensities Made of?

Relevance to Vascular Cognitive Impairment

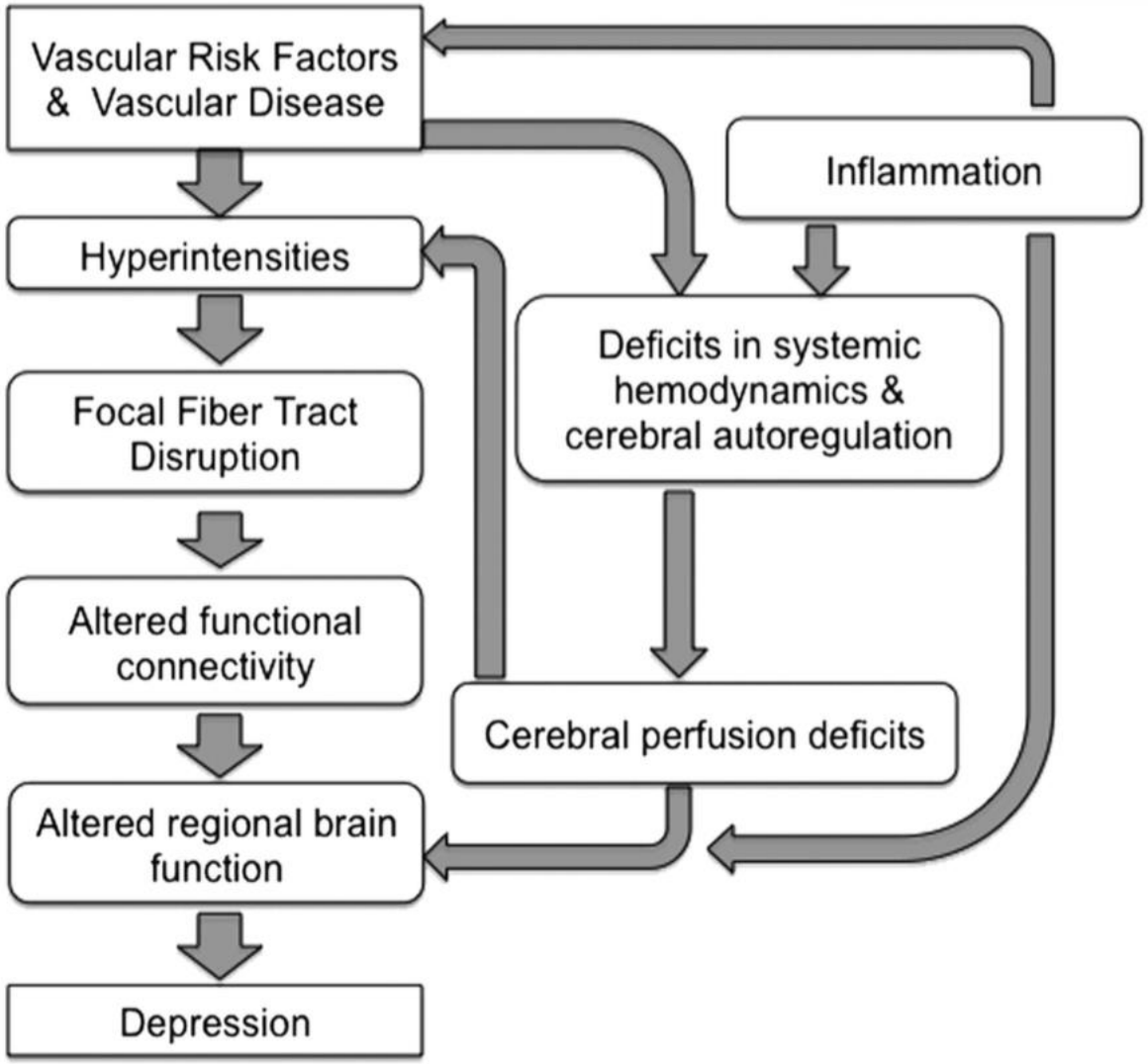
Joanna M. Wardlaw, MD, FRCR, FMedSci, FRSE; Maria C. Valdés Hernández, BSc, PhD; Susana Muñoz-Maniega, BSc, PhD



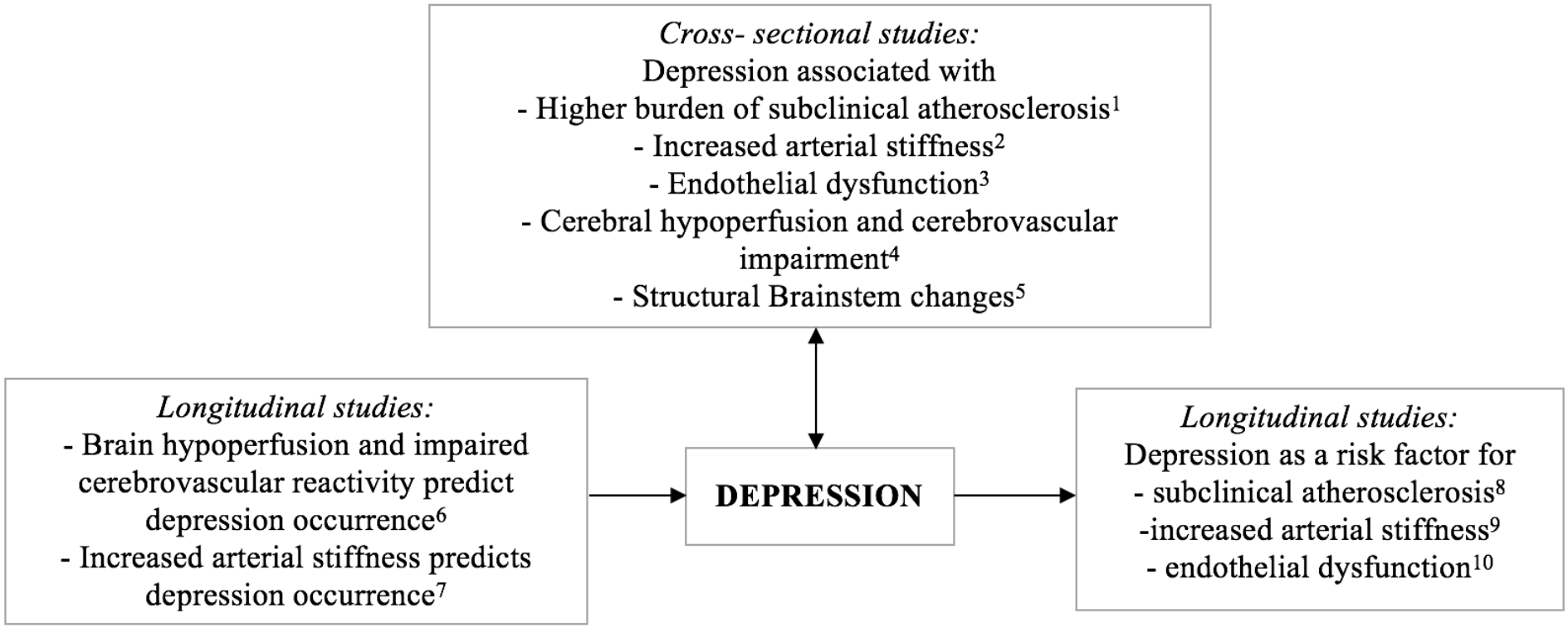
The vascular depression hypothesis: mechanisms linking vascular disease with depression

WD Taylor[1], HJ Aizenstein[2] and GS Alexopoulos[3]

Molecular Psychiatry (2013) 18, 963–974



Ultrasound Studies



Cerebral Hemodynamics and Incident Depression: The Rotterdam Study

BIOL PSYCHIATRY 2012;72:318–323

Nese Direk, Peter J. Koudstaal, Albert Hofman, M. Arfan Ikram, Witte J. Hoogendijk, and Henning Tiemeier

Background: According to the vascular depression hypothesis, subclinical cerebrovascular disease can cause depression in older adults. To test this hypothesis, several cross-sectional studies have assessed structural brain parameters, but few have examined hemodynamic alterations in the brain.

Methods: From the Rotterdam Study, we studied a cohort of 1494 participants (65+ years of age) free of depression, dementia, and stroke at baseline. In the middle cerebral artery blood flow velocities and vasomotor reactivity were measured with transcranial Doppler ultrasonography. All participants were repeatedly assessed for depressive symptoms with Centre for Epidemiological Studies-Depression scale (CES-D). Participants with depressive symptoms (CES-D $\geq$16) had a semi-structured interview, to classify the depression according to DSM-IV criteria. All analyses were adjusted for sociodemographic data, vascular risk factors, and incident stroke.

Results: Lower peak-systolic, end-diastolic, and mean blood flow velocities at baseline were associated with higher CES-D scale scores at follow-up. Mean blood flow velocity predicted incident depressive symptoms (odds ratio [OR]: .74, 95% confidence interval [CI]: .60–.91, p = .004) and depressive disorders (OR: .83, 95% CI: .69–.98, p = .032), whereas decreased baseline vasomotor reactivity predicted incident depressive disorders only (OR: .66, 95% CI: .53–.83, $p < .001$).

Conclusions: Lower blood flow velocity, indicating reduced cerebral metabolism, predicted depressive symptoms and depressive disorders. Reduced vasomotor reactivity, which might indicate cerebral microangiopathy, predicted depressive disorders only, in healthy older adults. These findings provide prospective evidence for vascular depression hypothesis.

Carotid Artery Stiffness and Incident Depressive Symptoms: The Paris Prospective Study III

Thomas T. van Sloten, Pierre Boutouyrie, Muriel Tafflet, Lucile Offredo, Frédérique Thomas, Catherine Guibout, Rachel E. Climie, Cédric Lemogne, Bruno Pannier, Stéphane Laurent, Xavier Jouven, and Jean-Philippe Empana

Biological Psychiatry March 15, 2019; 85:498–505

ABSTRACT

BACKGROUND: Arterial stiffness may contribute to late-life depression via cerebral microvascular damage, but evidence is scarce. No longitudinal study has evaluated the association between arterial stiffness and risk of depressive symptoms. Therefore, we investigated the association between carotid artery stiffness and incident depressive symptoms in a large community-based cohort study.

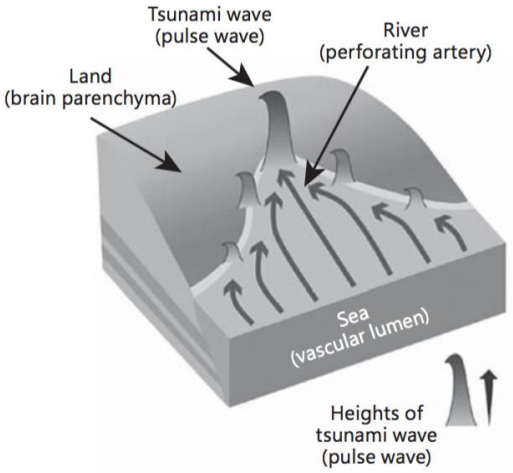
METHODS: This longitudinal study included 7013 participants (mean age 59.7 ± 6.3 years; 35.8% women) free of depressive symptoms at baseline. Carotid artery stiffness (high-resolution echo tracking) was determined at baseline. Presence of depressive symptoms was determined at baseline and at 4 and 6 years of follow-up, and was defined as a score ≥7 on the validated Questionnaire of Depression, Second Version, Abridged and/or new use of antidepressant medication. Logistic regression and generalized estimating equations were used.

RESULTS: In total, 6.9% (n = 484) of the participants had incident depressive symptoms. Individuals in the lowest tertile of carotid distensibility coefficient (indicating greater carotid artery stiffness) compared with those in the highest tertile had a higher risk of incident depressive symptoms (odds ratio: 1.43; 95% confidence interval: 1.10–1.87), after adjustment for age, sex, living alone, education, lifestyle, cardiovascular risk factors, and baseline Questionnaire of Depression, Second Version, Abridged scores. Results were qualitatively similar when we used carotid Young's elastic modulus as a measure of carotid stiffness instead of carotid distensibility coefficient, and when we used generalized estimating equations instead of logistic regression.

CONCLUSIONS: Greater carotid stiffness is associated with a higher incidence of depressive symptoms. This supports the hypothesis that carotid stiffness may contribute to the development of late-life depression.

Magnetic Resonance Imaging of Cardiovascular Function and the Brain

Is Dementia a Cardiovascular-Driven Disease?



(These modifications of figures are approved by the Japan Meteorological Agency)

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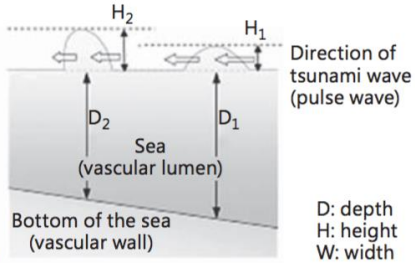

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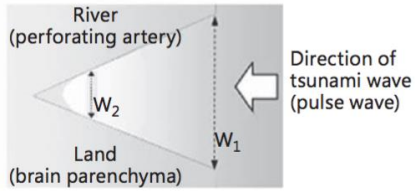

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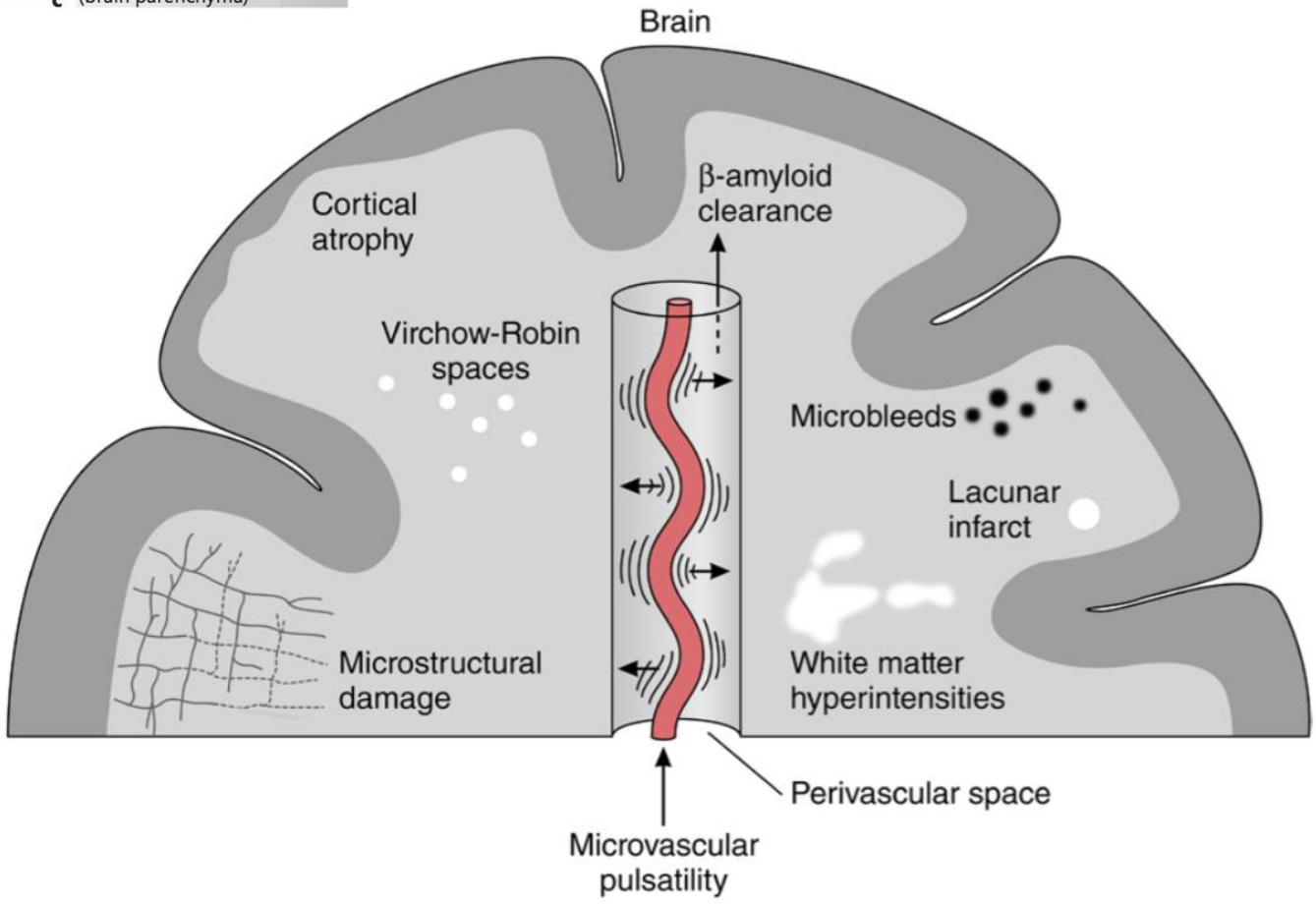

Brain Tissue Pulsatility is Increased in Midlife Depression: a Comparative Study Using Ultrasound Tissue Pulsatility Imaging

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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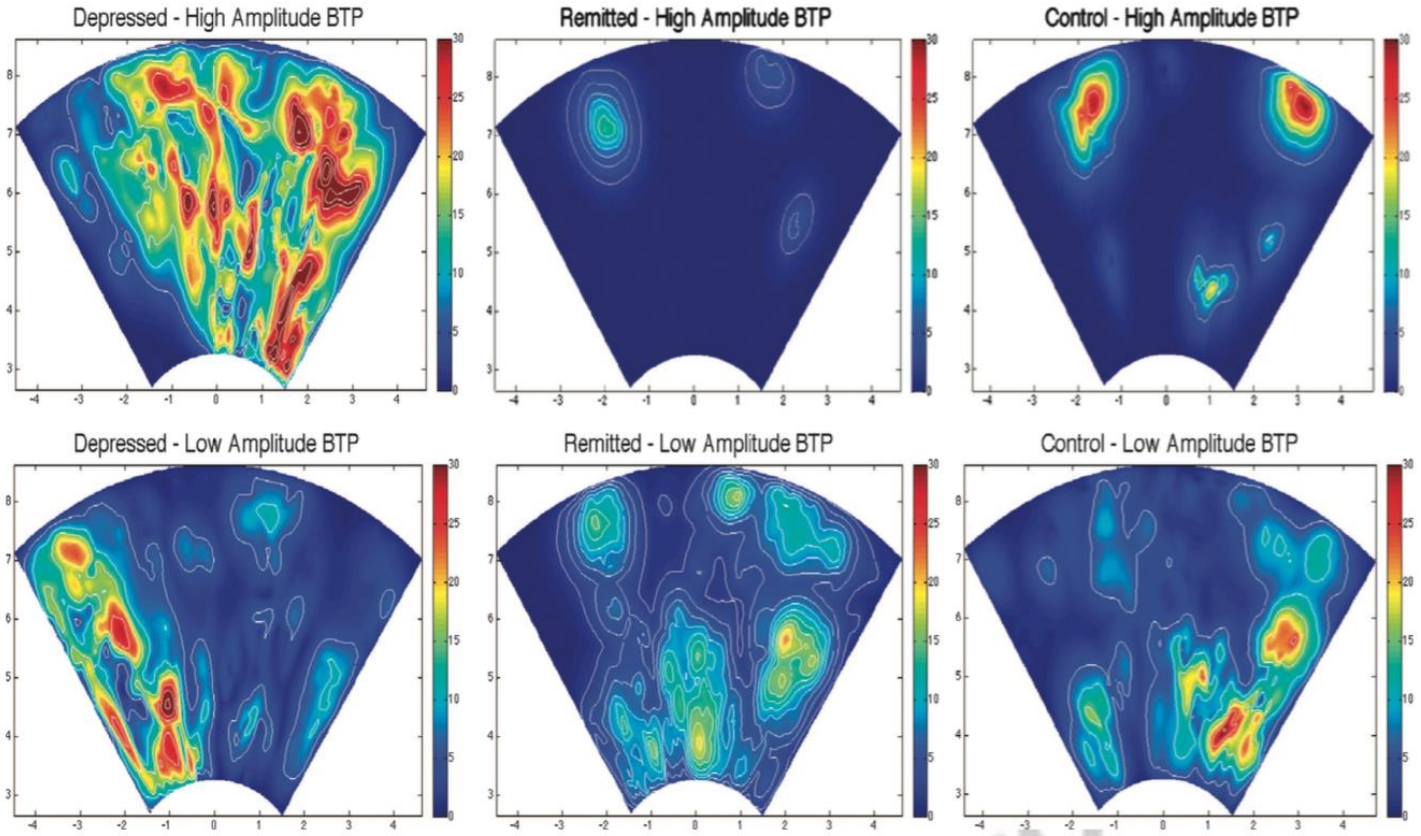

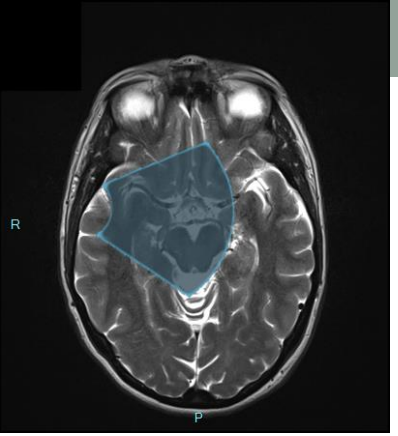
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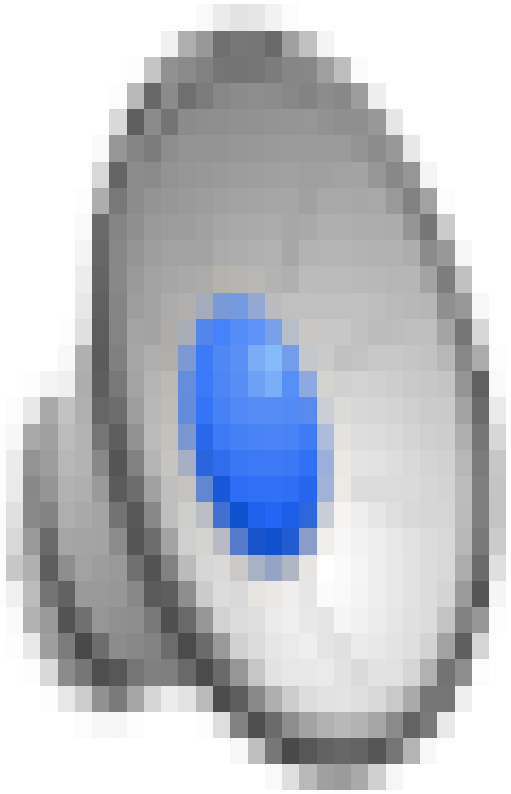

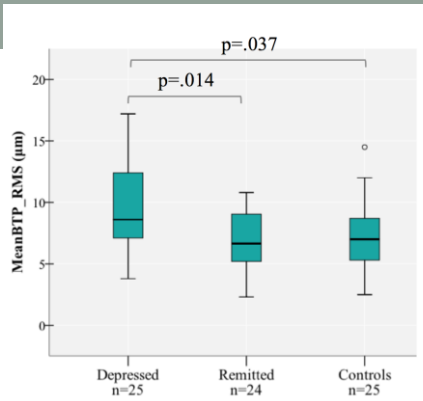
p=.037
p=.014
MeanBTP_RMS (µm)
20
15
10
5
0
Depressed
n=25
Remitted
n=24
Controls
n=25