Meditsiini UPDATE 2019

NEUROLOOGIA

Toomas Toomsoo MD, PhD

5. detsember 2019
Swissôtel Tallinn konverentsikeskus

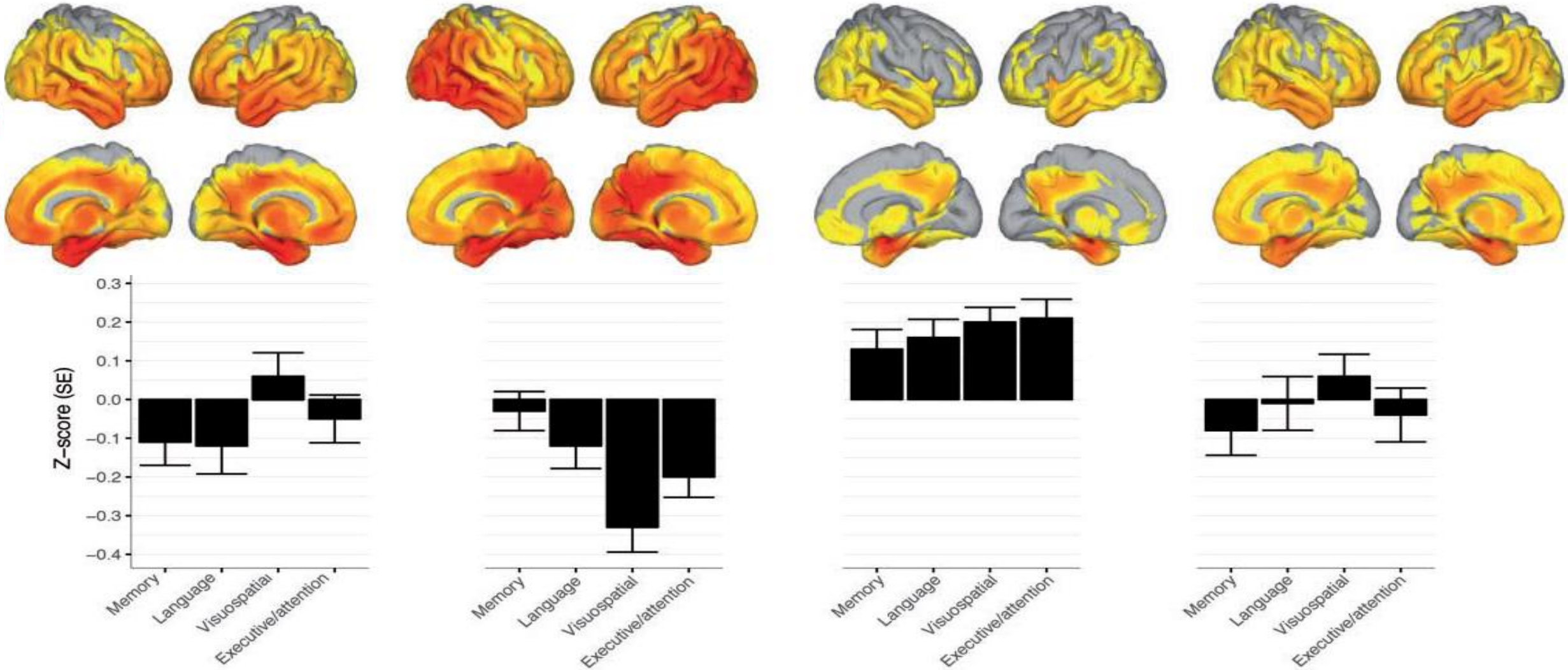
Aju ja kognitsiooni languse kiirus

doi:10.1093/brain/awy264 BRAIN 2018: Page 1 of 14 | 1

BRAIN
A JOURNAL OF NEUROLOGY

Atrophy subtypes in prodromal Alzheimer's disease are associated with cognitive decline

Mara ten Kate,[1] Ellen Dicks,[1] Pieter Jelle Visser,[1,2] Wiesje M. van der Flier,[1,3] Charlotte E. Teunissen,[4] Frederik Barkhof,[5,6] Philip Scheltens[1] and Betty M. Tijms,[1] for the Alzheimer's Disease Neuroimaging Initiative* and Amsterdam Dementia Cohort


Z-score (SE)
0.3
0.2
0.1
0.0
−0.1
−0.2
−0.3
−0.4
Memory
Language
Visuospatial
Executive/attention

Prodromaalne Alzheimeri tõbi

Temporo- mediaalne atroofia

- Halb mälu, keelelised oskused
- Vanem iga, madal liikvori Tau kontsentratsioon ja enam vaskulaarseid koldeid

Parieto-oktsipitaalne atroofia

- Halvad täidesaatvad funktsioonid, tähelepanu
- Kõrge liikvori Tau sisaldus

Kerge atroofia

- Noorem iga
- Väga kõrge liikvori Tau sisaldus

Diffuusne atroofia

Dementsus – kuidas hoiduda

JAMA Psychiatry
JAMA Psychiatry. 2018 Jul; 75(7): 697–703.
Published online 2018 May 30. doi: 10.1001/jamapsychiatry.2018.0657: 10.1001/jamapsychiatry.2018.0657
PMCID: PMC6583858
PMID: 29847678

15 582 inimesest, vanuses 71-77 aastat, 1349 inimesel (8,7%) arenes 5 aasta jooksul dementsus

Vaimselt aktiivsetel oli dementsuse risk väiksem 0,71 (95% CI, 0.60-0.84; P < .001)

ARTICLE

Mediterranean diet and 3-year Alzheimer brain biomarker changes in middle-aged adults

Valentina Berti, MD, PhD, Michelle Walters, BS, Joanna Sterling, PhD, Crystal G. Quinn, PhD, Michelle Logue, BA, Randolph Andrews, PhD, Dawn C. Matthews, PhD, Ricardo S. Osorio, MD, Alberto Pupi, MD, Shankar Vallabhajosula, PhD, Richard S. Isaacson, MD, Mony J. de Leon, EdD, and Lisa Mosconi, PhD

Correspondence
Dr. Mosconi
lim2035@med.cornell.edu

Neurology® 2018;90:e1789-e1798. doi:10.1212/WNL.0000000000005527

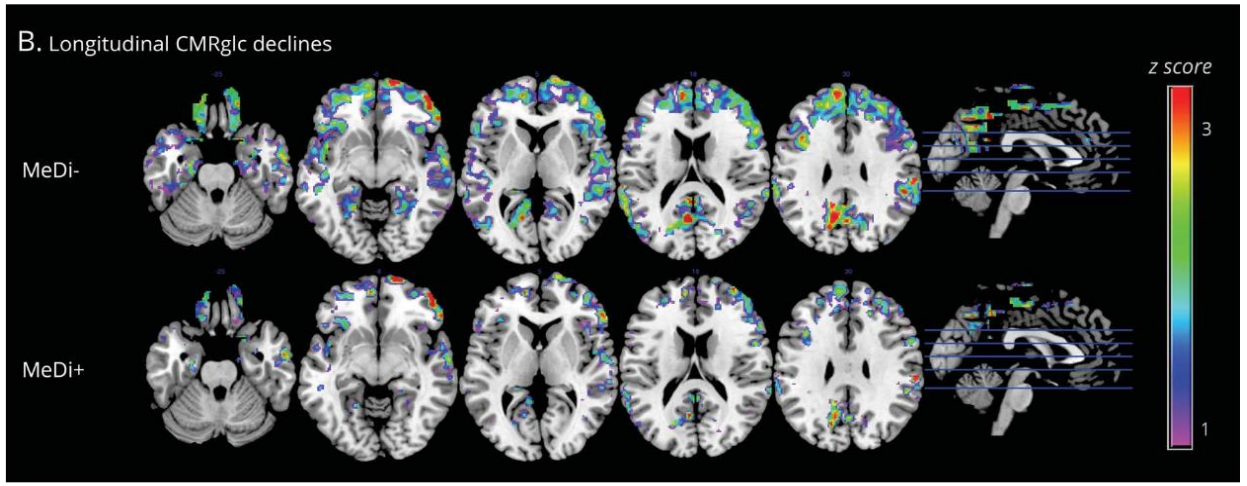
Methods

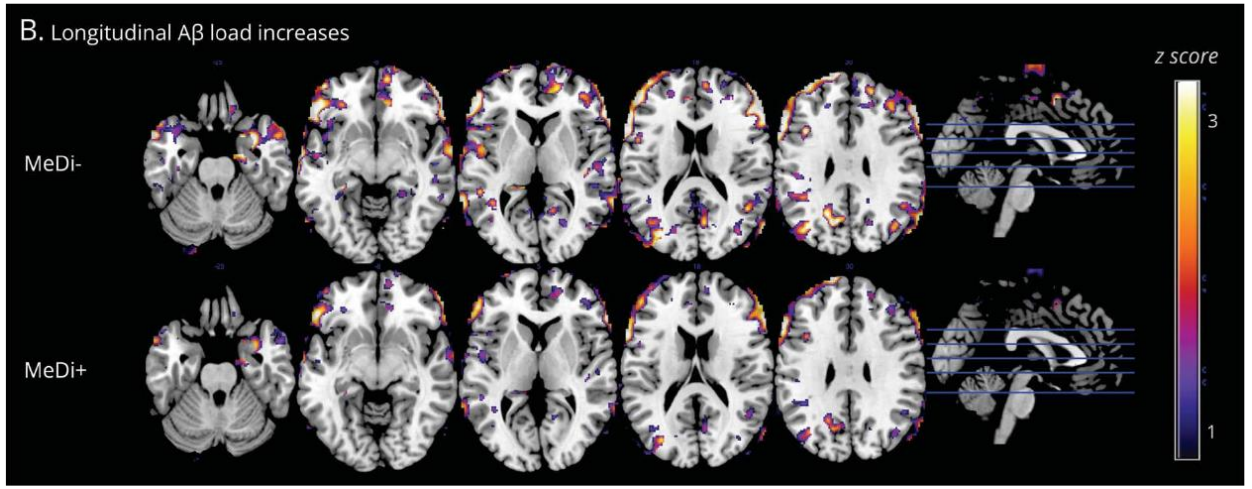
Seventy 30- to 60-year-old cognitively normal participants with clinical, neuropsychological, and dietary examinations and imaging biomarkers at least 2 years apart were examined. These included 34 participants with higher (MeDi+) and 36 with lower (MeDi−) MeDi adherence. Statistical parametric mapping and volumes of interest were used to compare AD biomarkers between groups at cross section and longitudinally.

Results

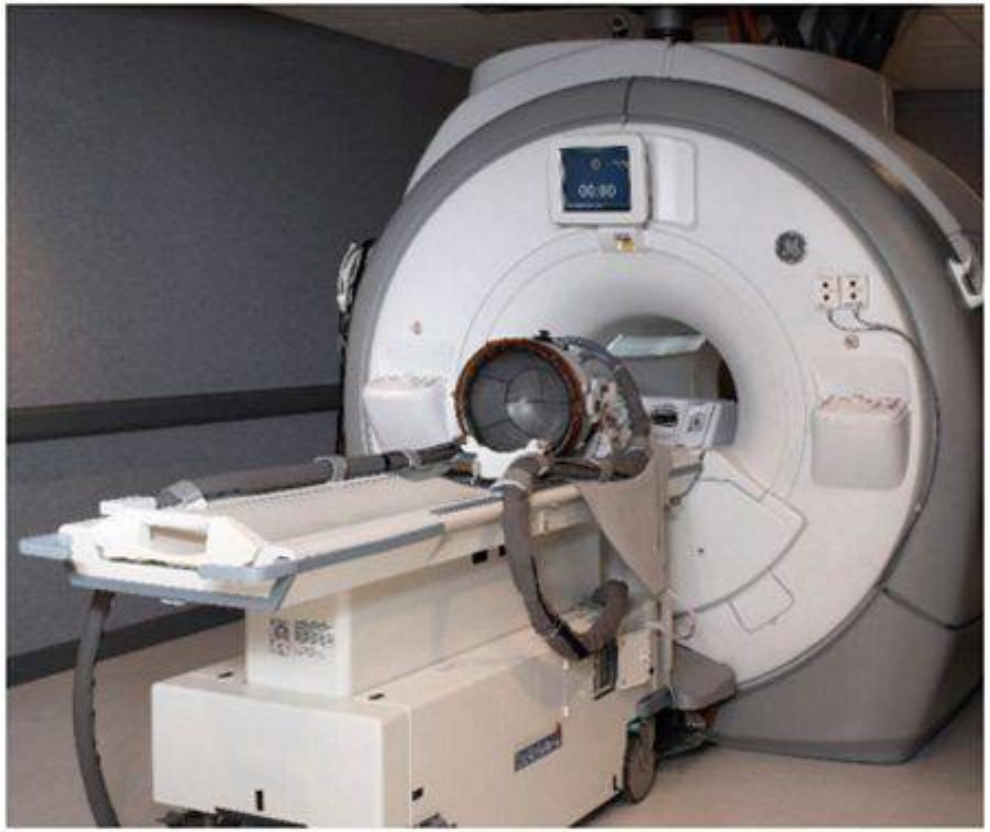
MeDi groups were comparable for clinical and neuropsychological measures. At baseline, compared to the MeDi+ group, the MeDi− group showed reduced FDG-PET glucose metabolism (CMRglc) and higher PiB-PET deposition in AD-affected regions ($p < 0.001$). Longitudinally, the MeDi−-group showed CMRglc declines and PiB increases in these regions, which were greater than those in the MeDi+ group ($p_{interaction} < 0.001$). No effects were observed on MRI. Higher MeDi adherence was estimated to provide 1.5 to 3.5 years of protection against AD.

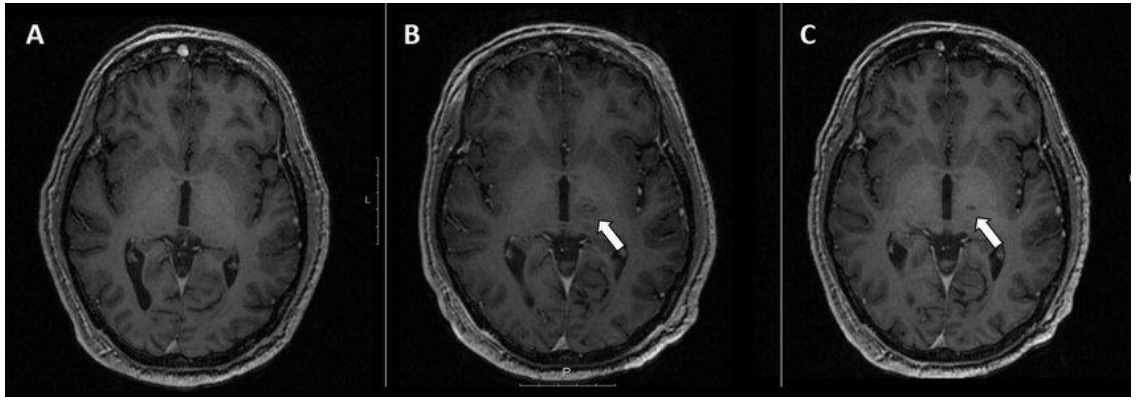
Dementsuse risk ja Vahemere dieet





Treemori ravi – uued võimalused

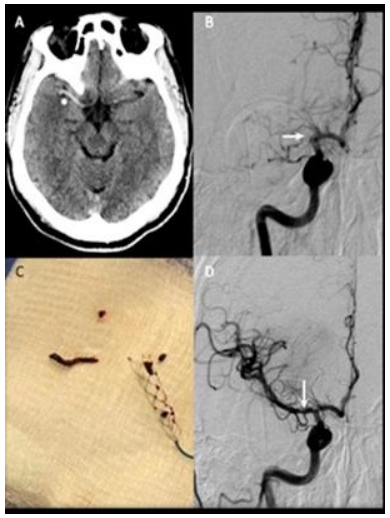


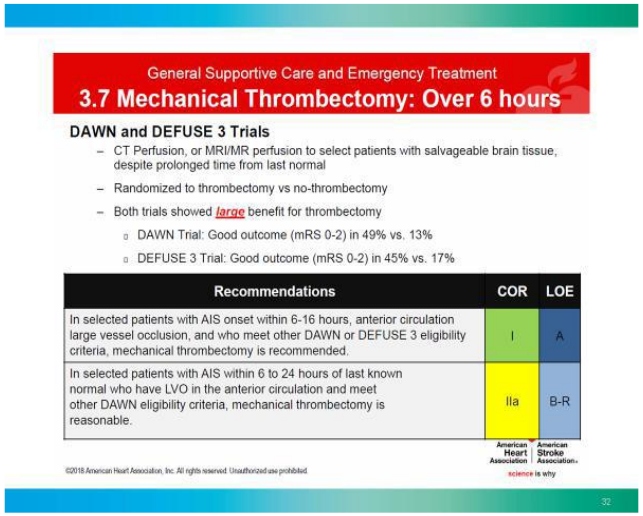


Chang 2018

A Prospective Trial of Magnetic Resonance guided Focused Ultrasound Thalamotomy for Essential Tremor: Results at the 2-year Follow-up
Running head: 2-year Follow-up Results of Magnetic Resonance guided Focused Ultrasound Thalamotomy for Essential Tremor

Insult- aeg on aju





2018

The NEW ENGLAND JOURNAL of MEDICINE

Thrombolysis Guided by Perfusion Imaging up to 9 Hours after Onset of Stroke

2019

Insuldi käsitlus – sekundaarne preventsioon

thebmj

RAPID RECOMMENDATIONS

Dual antiplatelet therapy with aspirin and clopidogrel for acute high risk transient ischaemic attack and minor ischaemic stroke: a clinical practice guideline

Kameshwar Prasad,[1] Reed Siemieniuk,[2 3] Qiukui Hao,[2 4] Gordon Guyatt,[2 5] Martin O'Donnell,[6] Lyubov Lytvyn,[2] Anja Fog Heen,[7] Thomas Agoritsas,[2 8] Per Olav Vandvik,[7 9] Sankar Prasad Gorthi,[10] Loraine Fisch,[11] Mirza Jusufovic,[12] Jennifer Muller,[13 14] Brenda Booth,[13] Eleanor Horton,[15] Auxiliadora Fraiz, Jillian Siemieniuk,[16] Awah Cletus Fobuzi,[17] Neelima Katragunta,[18] Bram Rochwerg[2 5]

Insuldi tekkimise risk
ABCD2 skoor

Transitoorne isheemiline atakk

Vanus ≥ 60	1
AVR ≥ 140/90	1
Kõnehäire	1
Ühepoolne halvatus	2
Kestvus 10 min – 1 t	1
Kestvus > 1 t	2
Diabeet	1

Kerge insult

NIHSS ≤ 3
RISK:
TIA risk saamaks uue insuldi 7 pv jooksul

1-3 risk 1,2 % 7 päeva jooksul
4-5 risk 5,9% 7 päeva jooksul
6-7 risk 11,7% 7 päeva jooksul

Table 1 | Current recommendations for antiplatelet therapy for secondary prevention of stroke

Guideline	Antiplatelet to be used	Statement
AHA/ASA 2018[6]	• Aspirin • DAPT	Aspirin (50 to 325mg) monotherapy, combination of aspirin and extended-release dipyridamole, and clopidogrel monotherapy are all acceptable options for initial therapy for patients with non-cardioembolic stroke or TIA. For patients with minor stroke, treatment for 21 days with DAPT begun within 24 hours can be beneficial for early secondary stroke prevention for up to 90 days from symptom onset
Canadian Stroke Best Practice guideline 2017[7]	• Aspirin • Combined aspirin and dipyridamole • Clopidogrel	Aspirin 80-325 mg daily, combined aspirin 25 mg and extended-release dipyridamole 200 mg twice daily, or clopidogrel 75 mg daily are appropriate options and selection should depend on clinical circumstances
Australian Clinical Guidelines for Stroke Management 2017[12]	• Low dose aspirin • Clopidogrel • Combined low dose aspirin and modified release dipyridamole • DAPT	Long term antiplatelet therapy (low dose aspirin, clopidogrel, or combined low dose aspirin and modified release dipyri… c attack who are not prescr… For hig… used in the first three weeks… DAPT should not be used for long term secondary prevention of cerebrovascular disease in people who do not have acute coronary disease or recent coronary stent
NICE 2016[13]	• Clopidogrel • Aspirin with modified release dipyridamole • Modified release dipyridamole	For long term vascular prevention in people with ischaemic stroke or transient ischaemic attack without paroxysmal or permanent atrial fibrillation, clopidogrel 75 mg daily should be standard antithrombotic treatment. Aspirin 75 mg daily with modified-release dipyridamole 200 mg twice daily should be used for those who are unable to tolerate clopidogrel. Aspirin 75 mg daily should be used if both clopidogrel and modified release dipyridamole are contraindicated or not tolerated. Modified release dipyridamole 200 mg twice daily should be used if both clopidogrel and aspirin are contraindicated or not tolerated. The combination of aspirin and clopidogrel is not recommended unless there is another indication (such as acute coronary syndrome, recent coronary stent)

AHA/ASA=American Heart Association/American Stroke Association. NICE=National Institute for Health and Care Excellence. DAPT=dual antiplatelet therapy of clopidogrel plus aspirin.

DAPT kuni 3 nädalat

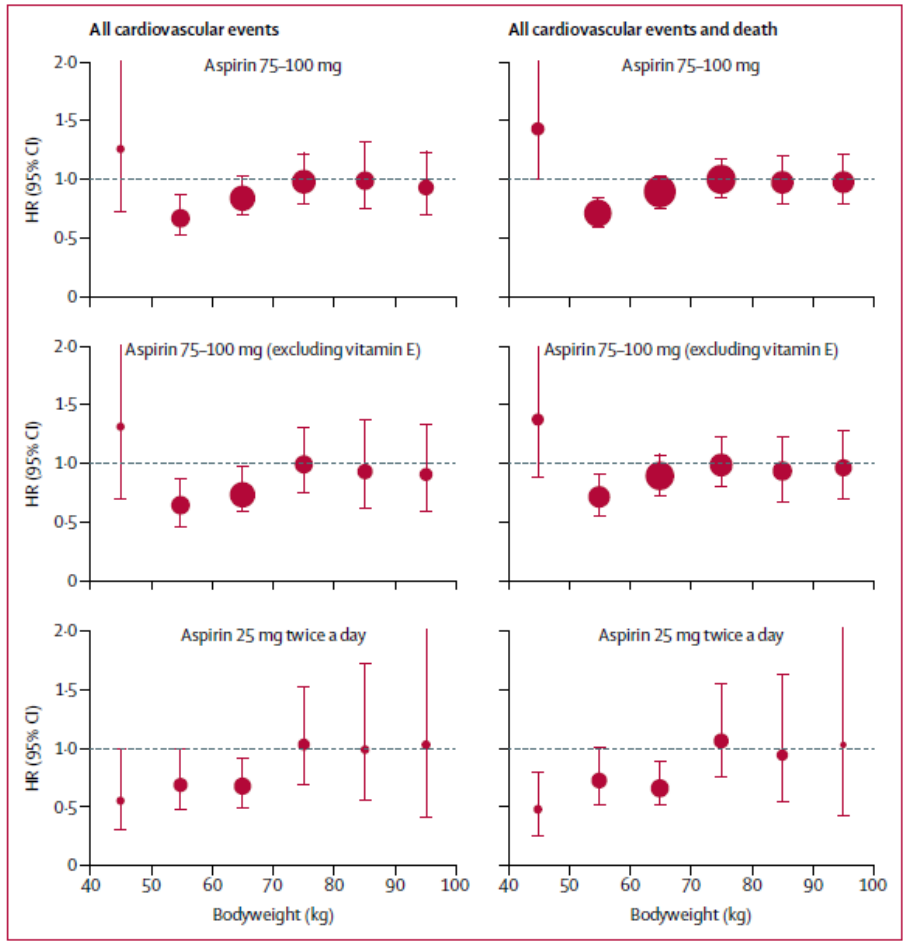
ANTIAGREGANTRAVI

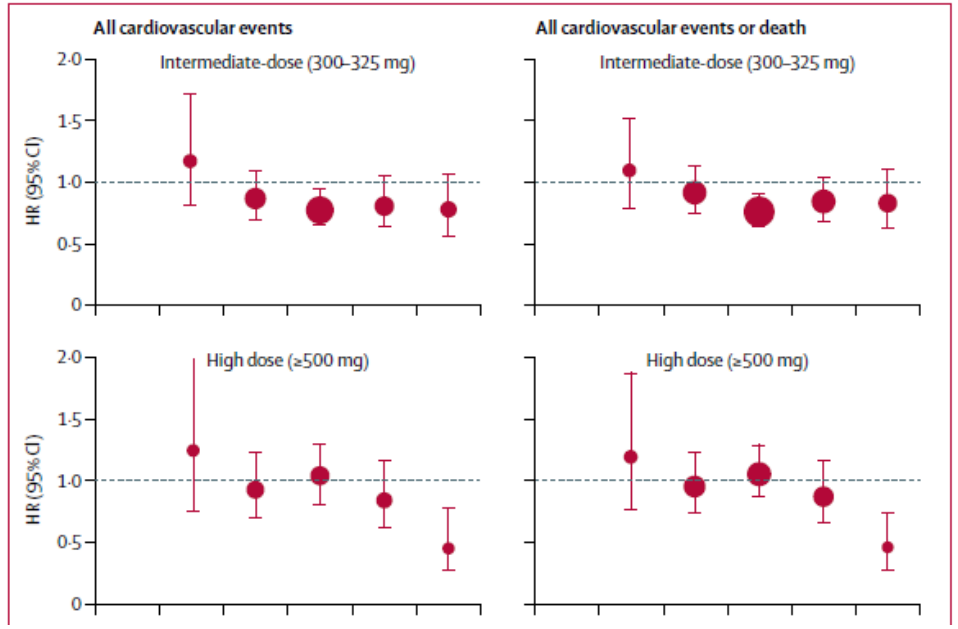
Effects of aspirin on risks of vascular events and cancer according to bodyweight and dose: analysis of individual patient data from randomised trials

Peter M Rothwell, Nancy R Cook, J Michael Gaziano, Jacqueline F Price, Jill F F Belch, Maria Carla Roncaglioni, Takeshi Morimoto, Ziyah Mehta

August 4, 2018

Aspiriini mõju KV sündmuse ärahoidmiseks





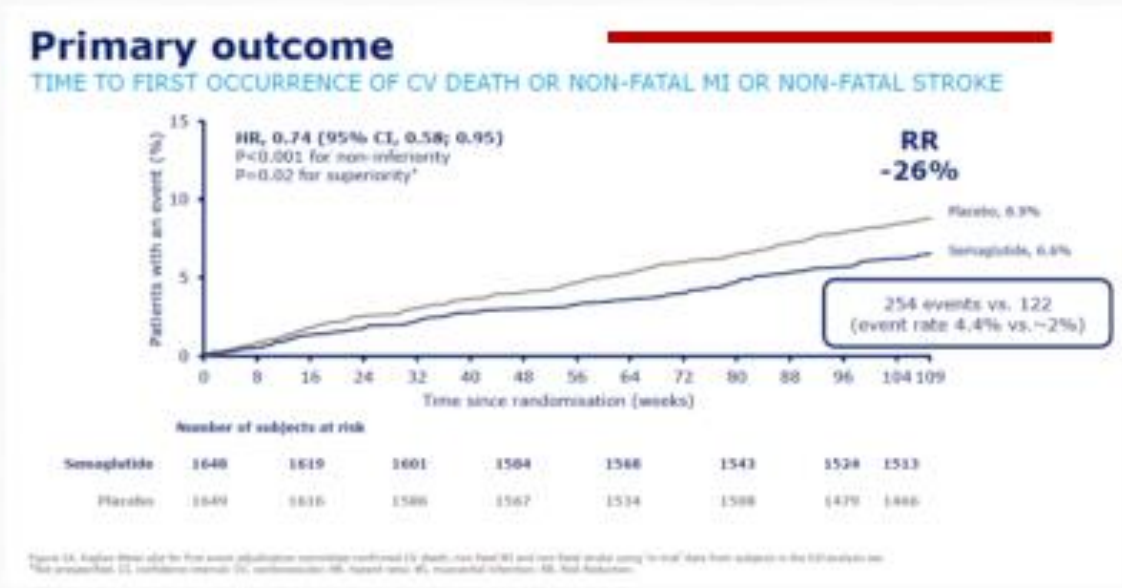
Diabeet ja insult

Drug	Risk for AF	Risk for Stroke
Insulin	Increased [12]	Increased [6,13]
Metformin	Reduced [12,15]	Reduced [17,18]
Sulfonylureas	Unchanged [12]	Reduced [22], unchanged [23], or increased [20,24]
Thiazolidinediones	Reduced [12,28,29,31,34] or unchanged [32,33]	Reduced [35–37]
DPP-4 inhibitors	Reduced [38] or unchanged [12]	Reduced [39] or unchanged [40–46]
GLP-1 receptor agonists	Increased with albiglutide [50], unchanged with semaglutide, liraglutide, and dulaglutide, or in meta-analyses [51–54]	Reduced in meta-analyses [46] and with semaglutide [53], unchanged with liraglutide, albiglutide, and dulaglutide [55–57]
SGLT-2 inhibitors	Data not available	Increased in some meta-analyses [62], unchanged in others [46,64]

Mihai 2019

GLP-1, diabeet ja insult

SEMAGLUTIID ja mõju mitte fataalsele insuldile



Interaktiivne seminar: „Ideaalne diabeediravi – kui lähedale me oleme jõudnud?" 5/2019

Kodade virvendus ja insult

A Simple Clinical Risk Score (C_2HEST) for Predicting Incident Atrial Fibrillation in Asian Subjects

Derivation in 471,446 Chinese Subjects, With Internal Validation and External Application in 451,199 Korean Subjects

Yan-Guang Li, MD, PhD; Daniele Pastori, MD, PhD; Alessio Farcomeni, PhD; Pil-Sung Yang, MD; Eunsun Jang, MD; Boyoung Joung, MD, PhD; Yu-Tang Wang, MD, PhD; Yu-Tao Guo, MD, PhD; and Gregory Y. H. Lip, MD

Kodade virvendus ja insult

TABLE 4] Annual Incidence of AF by C_2HEST Score

Score	No. of Subjects	No. of Incidents of AF	Incidence of AF[a]	Hazard Ratio	95% CI
0	310,117	246	0.18	1.00	...
1	88,825	378	0.82	4.31	3.67-5.06
2	19,270	148	2.31	12.8	10.4-15.6
3	8,253	68	3.73	22.6	17.2-29.6
4	1,373	68	16.1	97.0	74.1-127.0
5	90	6	28.7	187.4	83.3-421.6
≥ 6	45	7	59.8	332.0	156.6-704.0

See Table 1 legend for expansion of abbreviation.
[a]Per 1,000 person-years.

ORIGINAL RESEARCH

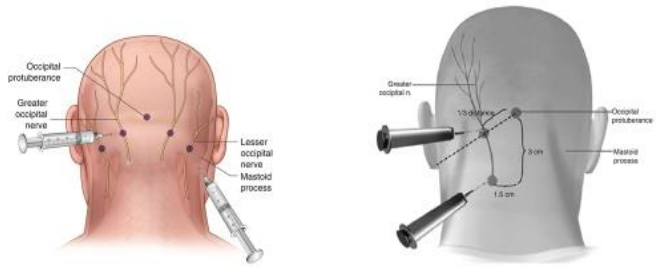
American Heart Association.

C_2HEST Score and Prediction of Incident Atrial Fibrillation in Poststroke Patients: A French Nationwide Study

Yan-Guang Li, MD, PhD; Arnaud Bisson, MD; Alexandre Bodin, MD; Julien Herbert, MSc; Leslie Grammatico-Guillon, MD, PhD; Boyoung Joung, MD, PhD; Yu-Tang Wang, MD, PhD;* Gregory Y. H. Lip, MD;* Laurent Fauchier, MD, PhD*

Blokaadid peavalude ravis

Suure kuklanärvi blokaad



Accepted: 17 April 2018

DOI: 10.1111/ane.12952

ORIGINAL ARTICLE

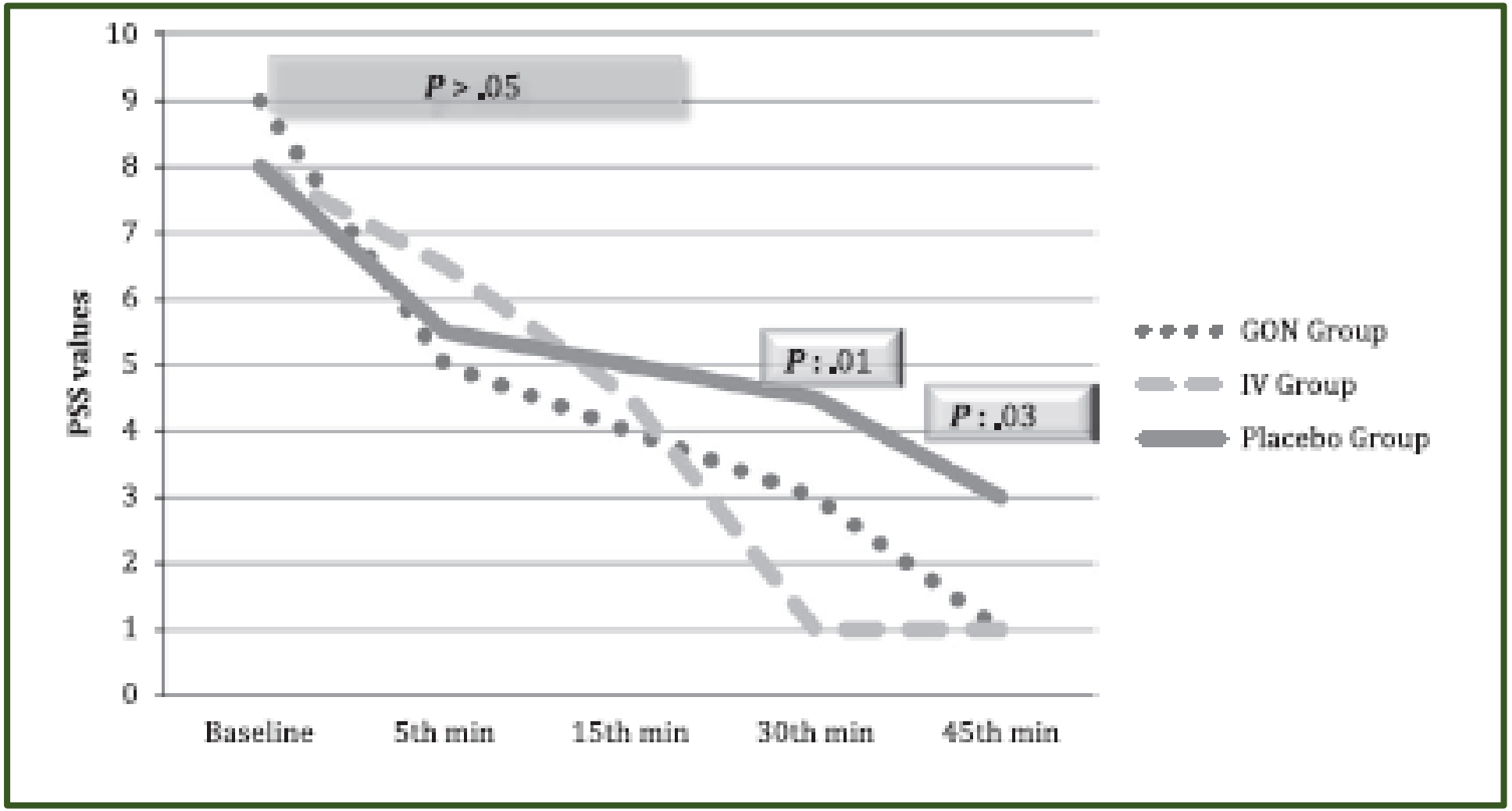
WILEY

Acta Neurologica Scandinavica

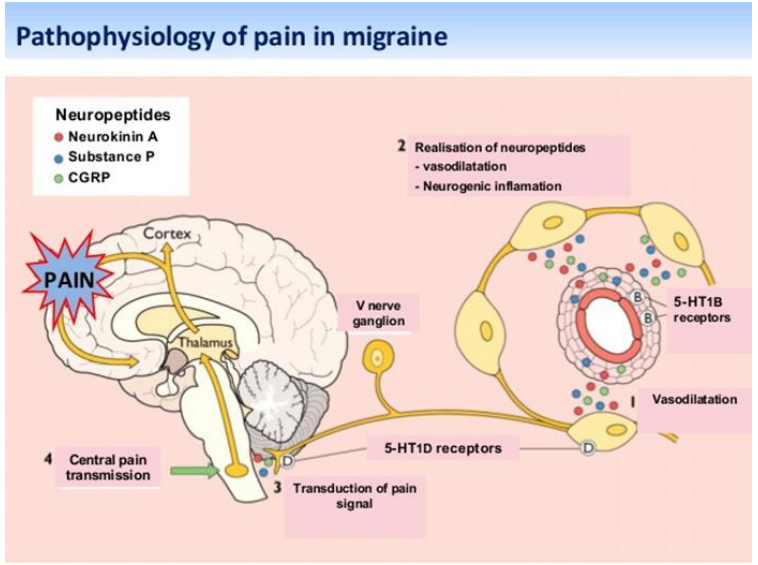
The effectiveness of greater occipital nerve blockade in treating acute migraine-related headaches in emergency departments

O. Korucu[1] | S. Dagar[2] | Ş. K. Çorbacioglu[2] | E. Emektar[2] | Y. Cevik[2]

Suure kuklanärvi blokaad- äge migreeniatakk



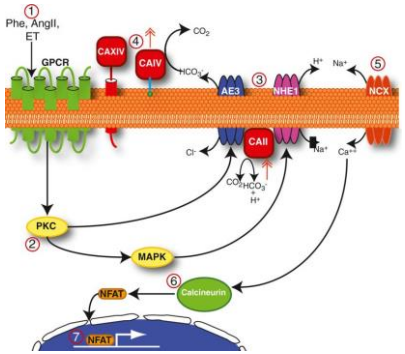
CGRP muudab kõik peapiirkonna sensoorsed **närvid ülitundlikuks**



Valu leevendumine

1. **Triptaanid** seonduvad serotoniiniretseptoritega ja blokeerivad CGRP vabanemise
2. **CGRP seonduvad** TG ganglioni retseptoritega, ja valk ei saa närviga seonduda
3. **CGRP antikeha** tunneb ara CGRP, seondub sellega ja VALK kaotab oma mõju

- **Östrogeenide tase mõjutab rakumembraane**
- **Naised kannatavad migreenide all enam**
- **Naised reageerivad ka migreeniravile halvemini**



- NHE1 —- mille ülesanne on transportida vesiniku ja Na ioone läbi rakumembraani
- NHE1 tase on madal või on funktsioon häiritud – põhjustab see valu tekke
- NHE 1 tase (madal) loob halvenenud võimaluse migreeniravimite läbitavuse läbi HEB´i

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Uuriti naissoost ja meessoost rotte

Meessoost rottide NHE1 tase oli 4 korda kõrgem naissoost rottide NHE1 tasemest

Kõrgem östrogeenide tase oli heas korrelatsioonis madala NHE1 tasemega, kuid testosterooniga seos puudus

Galloway 2018, 2019

Kellele on näidustatud uued migreeniravimid (CGRP) ?

Rasked migreeniatakid, kellel eelnevad ravimid pole aidanud, raskusi ravireziimi kinnipidamisega, polüfarmakoteraapia erinevate komorbiidsete seisundite tõttu

Kellele ei ole näidustatud uued migreeniravimid (CGRP)?

Harvad migreenihood, rasedus, kõrge KV haiguse risk või olemasolev tõsine KV haigus

Loder 2018

Parkinsoni haiguse epidemioloogia Eestis

DISSERTATIONES MEDICINAE UNIVERSITATIS TARTUENSIS

LIIS KADASTIK-EERME

Parkinson's disease in Estonia: epidemiology, quality of life, clinical characteristics and pharmacotherapy

Parkinsoni haiguse epidemioloogia Eestis

The age-adjusted prevalence rate in all ages with PD on the 1st of October 2013 in the County of Tartu was 324/100,000 (adjusted to the European 2011 standard population) that is higher than reported in other population-based studies with similar case-finding methods and in-person examination, but lower than in several record-based studies without in-person screening. No significant difference in adjusted prevalence rates of PD was shown between urban and rural populations (RR= 1.02, p=0.83) that is in line with several other studies.

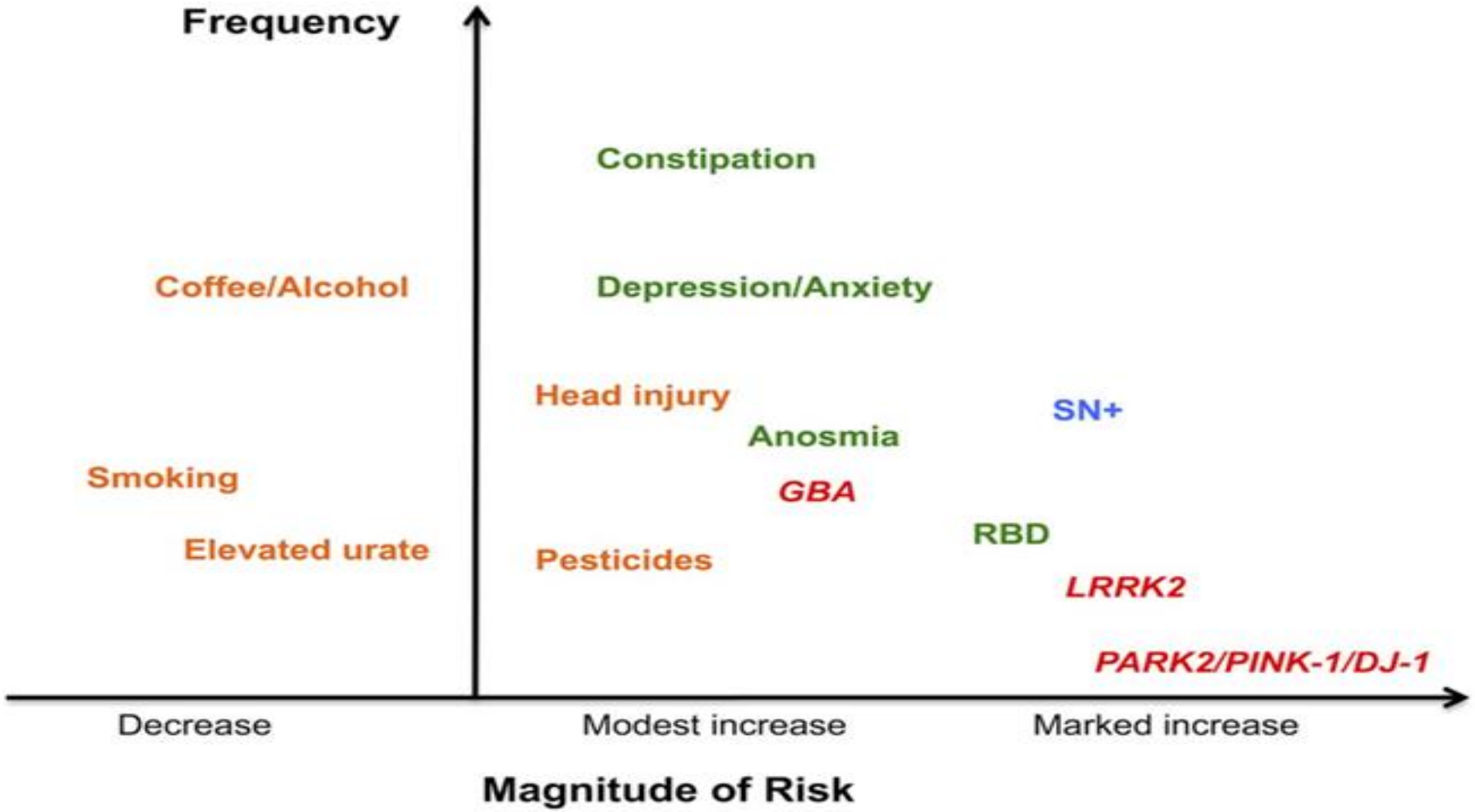
When comparing the current study with the previous epidemiological study on PD in the County of Tartu, we found that the overall age-adjusted prevalence rate was significantly higher in the current study (RR=1.30, p=0.004), a finding that is in line with other repeated prevalence studies of PD. The proportion of patients with more severe stages of the disease has increased.

The age-adjusted incidence rate in all ages with PD in the period of 2002 to 2012 was 28/100,000 (adjusted to the European 2011 standard population) that is slightly higher than in other studies with similar case-ascertainment methods but lower than in studies based on registers without the use of in-person validation of cases. Males had a slightly higher age-adjusted incidence rate than did females (RR=1.24; p=0.048), the higher risk of PD for males was not as high as that reported in most other studies. No significant difference in adjusted incidence rates of PD was shown between urban and rural populations (RR=1.0; p=0.97).

Study reference	Region	Ages (years)	Number of PD cases/ Study population	Crude prevalence rate/ 100,000	Adjusted prevalence rate/ 100,000
*Schrag et al. 2000b**	UK, London	All	156 / 121,608	128	168[a]
*Taba & Asser 2002**	Estonia, Tartu	All	270 / 153,240	176	152[a]
*Hobson et al. 2005**	UK, North Wales	All	112 / 77,388	144	105[a]
*Porter et al. 2006**	UK, North Tyneside	All	161 / 108,597	148	139[a]
*Wermuth et al. 2008**	Denmark, The Faroe Islands	All	100 / 48,371	206.7	218[a]
*Morgante et al. 2008**	Italy, Sicily	≥40	14 / 6494	215.6	151.7[a]
*Alrefai et al. 2009**	Jordan, Irbid Governorate	≥30	102/ 173,450	59	-
Newman et al. 2009	UK, West Scotland	All	610 / 511,927	119.2	129.5[a]
*Walker et al. 2010**	UK, North Northumberland	All	106 / 59,613	178	142[a]
*Yamawaki et al. 2009**	Japan, Yonago	All	254 / 140,911	180.3	166.8[a]
*Osaki et al. 2011**	Japan, Koban district	All	116 / 66,465	175	109[a]
Chillag-Talmor et al. 2011	Israel	20-84	7134 / 1,8 mil	170.8–260.6	334[a]
Bauso et al. 2012	Argentina, Buenos-Aires	All	-	219	-
Blin et al. 2015	France	All	200,273 / 65 mil	-	308[a]
Gordon et al. 2015	USA, Navajo Nation	All	316 / 217,158	146	261[b]
Riedel et al. 2016	Germany	≥65	10,596 / 815,573	1331	1680[a]
Liu et al. 2016	Taiwan	All	41,606 / 23 mil	179.1	147.7[a]
Moisan et al. 2016	France	All	149,672 / 64 mil	230.4	-
Nerius et al. 2017	Germany	≥50	4736-5751 / 491,038	-	797-961[a]
Myall et al. 2017	New Zealand	All	9340 / 4 mil	-	210[a]
Heinzel et al. 2018	Germany	All	27,714 / 82 mil	587.7	511.4[a]

Study reference	Country	Incidence period	Ages (years)	Number of PD cases/ Person-years at risk or study population	Crude incidence rate/ 100,000 person-years	Adjusted incidence rate/100,000 person-years
Morioka et al. 2000	Japan, Wakayama	1997	All	229 / 1 mil	16.9	10.5[a]
Van Den Eeden et al. 2003	USA, Northern California	1994–1995	All	588 / 4,7 mil	12.3	13.4[b]
Leentjens et al. 2003	The Netherlands	1990–2000	All	139 / -	22.4	-
Taba & Asser 2003	Estonia, Tartu	1990–1998	All	264 / 156,417	18.8	16.8[a]
Yamawaki et al. 2009	Japan, Yonago	2000–2004	All	34 / 140,911	18.4	10.3[a]
Hristova et al. 2010	Bulgaria, Plovdiv	2002–2004	≥40	244 / 2 mil	11.4	11.7[a]
Chillag-Talmor et al. 2011	Israel	2000–2007	20-84	5288 / 1.8 mil	33	45[a]
Jones et al. 2012	Canada, British Colombia	1992–2001	≥65	10,910 / 6 mil	252	-
Bauso et al. 2012	Argentina, Buenos-Aires	2003–2008	All	239 / 754,082	31.2	13.7[a]
Horsfall et al. 2013	UK	1999–2009	≥50	9051 / 10,8 mil	84	-
Blin et al. 2015	France	2005–2010	All	138 174 / 384 mil	-	36[a]
Gordon et al. 2015	USA, Navajo Nation	2001–2011	All	524 / 2,3 mil	22.5	35.9[c]
Liu et al. 2016	Taiwan	2011	All	8031 / -	34.7	28.8[a]
Moisan et al. 2016	France	2010	All	25,438 / 64 mil	39.3	-
Savica et al. 2016	USA, Minnesota	1976–2005	All	464 / 3,3 mil	14	17.2[b]
Nerius et al. 2017	Germany	2004–2010	≥50	3994 / 1,4 mil	270.2	222.8[a]
Myall et al. 2017	New Zealand	2006–2013	All	10,095 / 24 mil	-	31[a]
Heinzel et al. 2018	Germany	2015	All	3541 / 3,7 mil	95.8	84.1[a]
Valent et al. 2018	Italy, Friuli Venezia Giulia	2016	All	341 / 1,2 mil	28	-

Parkinsoni tõve risk



Parkinsoni tõbi – kes haigestuvad?

ABSTRACT: Background: Gut microbiota alterations have been found in prodromal and established Parkinson's disease (PD). Antibiotic exposure can have long-term effects on the composition of human intestinal microbiota, but a potential connection between antibiotic exposure and risk of PD has not been studied previously.

Objective: To evaluate the impact of antibiotic exposure on the risk of PD in a nationwide, register-based, case-control study.

Methods: We identified all patients who were diagnosed with PD in Finland during the years 1998 to 2014. Information was obtained on individual purchases of orally administered antibiotics during the years 1993 to 2014. We assessed the association between prior antibiotic exposure and PD using conditional logistic regression.

Results: The study population consisted of 13,976 PD cases and 40,697 controls. The strongest connection with PD risk was found for oral exposure to macrolides and lincosamides (adjusted odds ratio up to 1.416; 95% confidence interval, 1.053–1.904). After correction for multiple comparisons, exposure to antianaerobics and tetracyclines 10 to 15 years before the index date, sulfonamides and trimethoprim 1 to 5 years before the index date, and antifungal medications 1 to 5 years before the index date were positively associated with PD risk. In post hoc analyses, further positive associations were found for broad-spectrum antibiotics.

Conclusions: Exposure to certain types of oral antibiotics seems to be associated with an elevated risk of PD with a delay that is consistent with the proposed duration of a prodromal period. The pattern of associations supports the hypothesis that effects on gut microbiota could link antibiotics to PD, but further studies are needed to confirm this.

Key Words: antibiotic exposure; epidemiology; microbiota; Parkinson's disease; risk factors

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Transcranial Brain Sonography in the Estonian Cohort of Parkinson's Disease

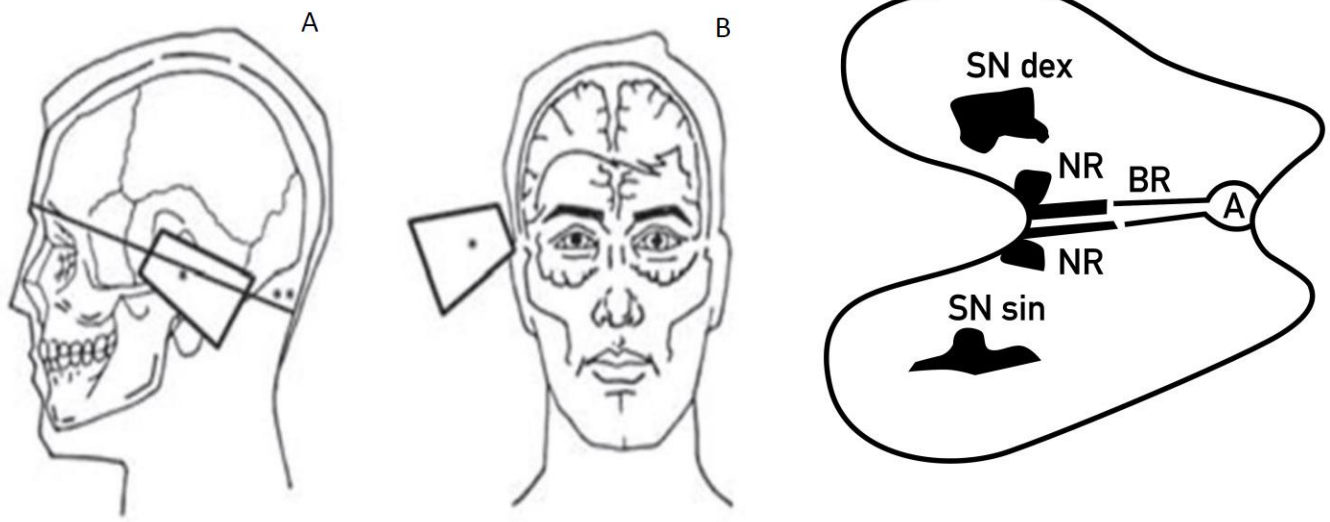
Ph.D. Dissertation Defense

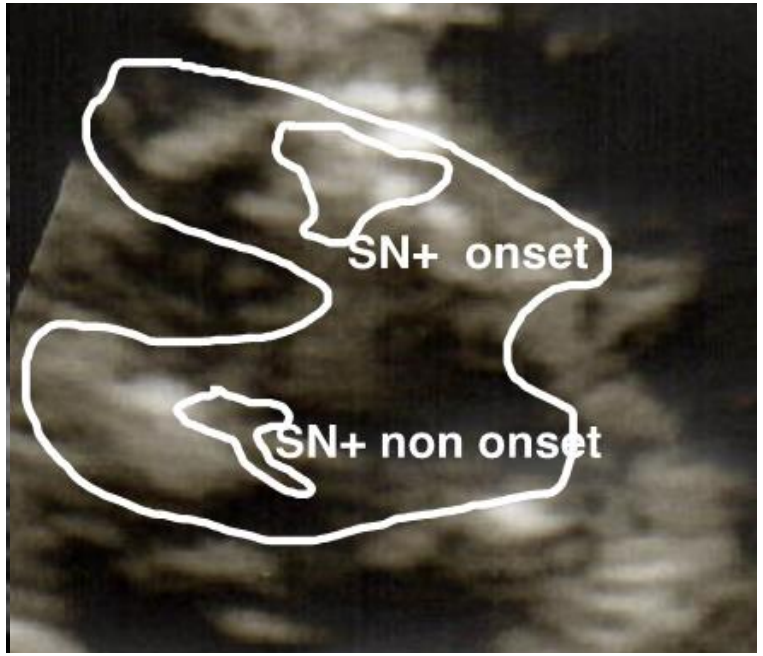
Supervisors: prof. P.Taba, prof. T. Asser, prof. D. Berg

TOOMAS TOOMSOO

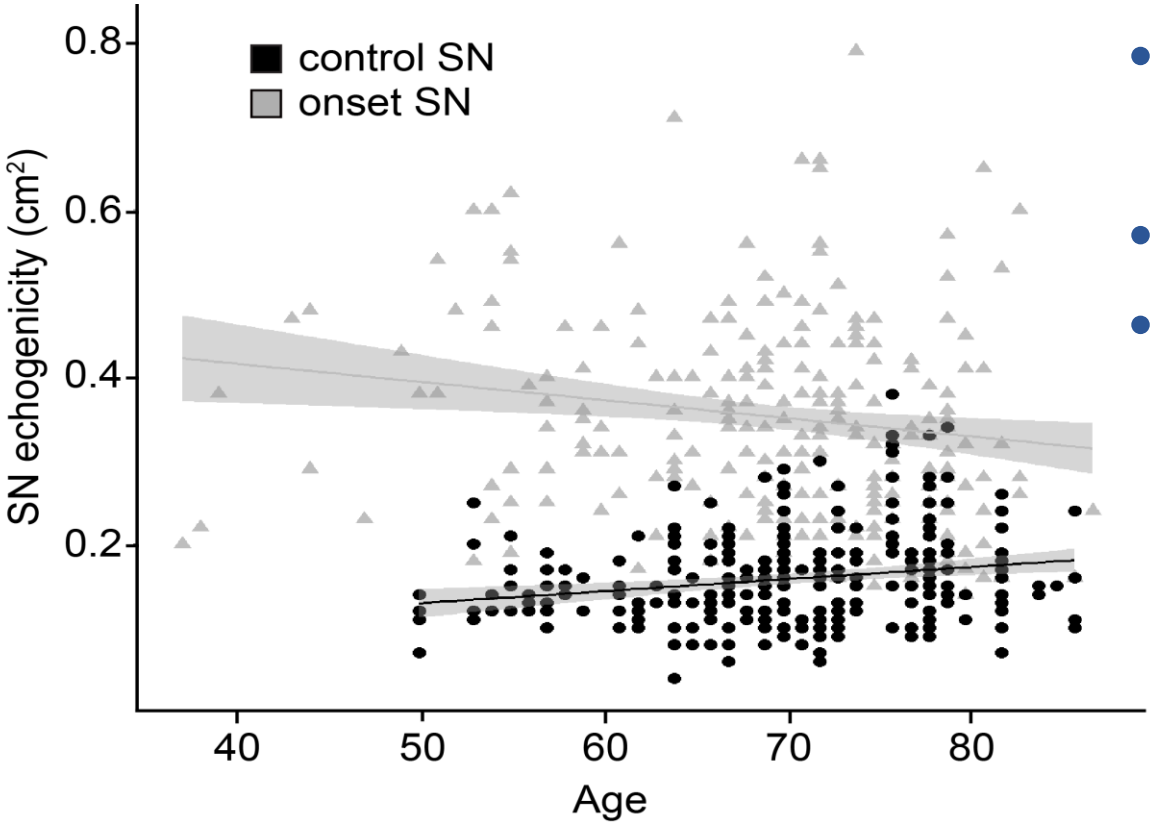
University of Tartu, 14.10. 2019

Transkraniaalne aju ultraheli





Vanuse mõju SN hüperehhogeensusele



- **Kõrgem iga tervetel on seotud SN+ suurenemisega** (p<0.0001)
-
- **Kõrgem iga PT patsientidel on seotud SN+ vähenemisega** (p=0.0049)