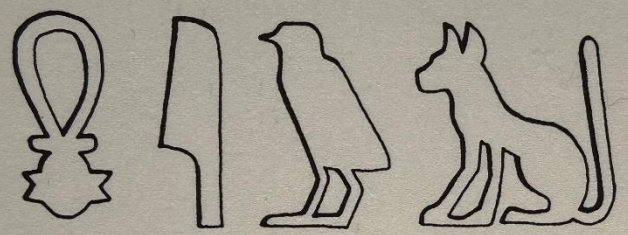
Pieter Nederveen
neuroloog

DIJKLANDER ZIEKENHUIS

Steen van Rosetta

Egyptian word for cat is written:



mi + i + w + picture sign

The first three signs record the sounds 'miw' (perhaps derived from a cat's 'miaow'), followed by a sign depicting the animal to enhance the meaning of the word.

Special fares apply
Chesham
Amersham
Chalfont & Latimer
Chorleywood
Rickmansworth
Watford
Croxley
Moor Park
Northwood
Northwood Hills
Pinner
North Harrow
Harrow-on-the-Hill
West Harrow
Uxbridge
Hillingdon
Ickenham
Ruislip
Ruislip Manor
Eastcote
West Ruislip
Ruislip Gardens
South Ruislip
Northolt
Greenford
Perivale
Hanger Lane
Rayners Lane
South Harrow
Sudbury Hill
Sudbury Town
Alperton
Park Royal
North Ealing
Ealing Broadway
Ealing Common
Acton Town
South Ealing
Northfields
Boston Manor
Osterley
Hounslow East
Hounslow Central
Hounslow West
Hatton Cross
Heathrow Terminals 1, 2, 3
Heathrow Terminal 4
Heathrow Terminal 5
Watford Junction
Watford High Street
Bushey
Carpenders Park
Hatch End
Headstone Lane
Harrow & Wealdstone
Kenton
Preston Road
Northwick Park
South Kenton
North Wembley
Wembley Central
Stonebridge Park
Harlesden
Willesden Junction
Kensal Green
Queen's Park
Stanmore
Canons Park
Queensbury
Kingsbury
Wembley Park
Neasden
Dollis Hill
Willesden Green
Kilburn
West Hampstead
Finchley Road
Swiss Cottage
St. John's Wood
Edgware
Burnt Oak
Colindale
Hendon Central
Brent Cross
Golders Green
Hampstead
Belsize Park
Chalk Farm
Camden Town
Mornington Crescent
High Barnet
Totteridge & Whetstone
Woodside Park
West Finchley
Mill Hill East
Finchley Central
East Finchley
Highgate
Archway
Tufnell Park
Kentish Town
Cockfosters
Oakwood
Southgate
Arnos Grove
Bounds Green
Wood Green
Turnpike Lane
Manor House
Finsbury Park
Arsenal
Holloway Road
Caledonian Road
King's Cross St. Pancras
Epping
Theydon Bois
Debden
Loughton
Buckhurst Hill
Roding Valley
Chigwell
Grange Hill
Hainault
Fairlop
Barkingside
Newbury Park
Woodford
South Woodford
Snaresbrook
Redbridge
Wanstead
Gants Hill
Leytonstone
Leyton
Stratford
Upminster
Upminster Bridge
Hornchurch
Elm Park
Dagenham East
Dagenham Heathway
Becontree
Upney
Barking
East Ham
Upton Park
Plaistow
West Ham
Paddington
Edgware Road
Marylebone
Baker Street
Great Portland Street
Euston
Euston Square
Warren Street
Regent's Park
Oxford Circus
Bond Street
Marble Arch
Lancaster Gate
Queensway
Notting Hill Gate
Holland Park
Shepherd's Bush
White City
East Acton
North Acton
West Acton
Bayswater
Ladbroke Grove
Latimer Road
Westbourne Park
Royal Oak
Warwick Avenue
Maida Vale
Kilburn Park
Goodge Street
Tottenham Court Road
Holborn
Chancery Lane
St. Paul's
Bank
Liverpool Street
Moorgate
Barbican
Farringdon
Angel
Old Street
Aldgate
Aldgate East
Tower Hill
Monument
Cannon Street
Mansion House
Blackfriars
Temple
Embankment
Charing Cross
Covent Garden
Leicester Square
Piccadilly Circus
Green Park
Hyde Park Corner
Knightsbridge
South Kensington
Gloucester Road
High Street Kensington
Earl's Court
West Kensington
Barons Court
Hammersmith
Goldhawk Road
Shepherd's Bush Market
Wood Lane
Ravenscourt Park
Stamford Brook
Turnham Green
Chiswick Park
Gunnersbury
Kew Gardens
Richmond
West Brompton
Fulham Broadway
Parsons Green
Putney Bridge
East Putney
Southfields
Wimbledon Park
Wimbledon
Sloane Square
Victoria
St. James's Park
Westminster
Waterloo
Lambeth North
Southwark
Borough
London Bridge
Elephant & Castle
Kennington
Oval
Stockwell
Vauxhall
Pimlico
Brixton
Clapham North
Clapham Common
Clapham South
Balham
Tooting Bec
Tooting Broadway
Colliers Wood
South Wimbledon
Morden
Canary Wharf
Canada Water
Bermondsey
Rotherhithe
Wapping
Shadwell
Whitechapel
Stepney Green
Mile End
Bow Road
Bow Church
Bromley-by-Bow
Limehouse
Westferry
Poplar
All Saints
Devons Road
Langdon Park
Blackwall
East India
Canning Town
West India Quay
Heron Quays
South Quay
Crossharbour
Mudchute
Island Gardens
Cutty Sark for Maritime Greenwich
Greenwich
Deptford Bridge
Elverson Road
Lewisham
North Greenwich
West Silvertown
Pontoon Dock
London City Airport
King George V
Woolwich Arsenal
Royal Victoria
Custom House for ExCeL
Prince Regent
Royal Albert
Beckton Park
Cyprus
Gallions Reach
Beckton
Surrey Quays
New Cross
New Cross Gate
Brockley
Honor Oak Park
Forest Hill
Sydenham
Penge West
Anerley
Crystal Palace
Norwood Junction
West Croydon
Imperial Wharf
Clapham Junction
River Thames

Indeling

-inleiding
-eigen regie
-nieuwe ontwikkelingen
-samenvatting
-tijd voor vragen

Inleiding

-chronische aandoening
-progressieve aandoening
-behandelbare aandoening
-ziekteverschijnselen zijn zeer divers
-er is niet één ziekte van Parkinson

The Parkinson's Iceberg

IN THIS TOGETHER parkinson's NSW

Parkinson Monitor

DATUM: (DD/MM/JJ)
.....

Markeer het cijfer in het diagram dat het beste aangeeft hoeveel last u van uw klachten heeft.
U geeft een cijfer aan de categorie in zijn geheel (bijv. slaapstoornissen), niet aan de afzonderlijke klachten.
0 Geen last 1 Weinig last 2 Last 3 Veel last 4 Zeer veel last

Stemming

- ☐ Ik heb steeds minder interesse in dingen
- ☐ Ik heb minder/geen plezier meer in de dingen die ik voorheen leuk vond
- ☐ Ik voel me ongelukkig
- ☐ Ik ben nerveus, angstig of raak in paniek
- ☐ Ik ben depressief
- ☐ Ik pieker veel
- ☐ Ik heb problemen in de relationele sfeer/met gezinsleden
- ☐ Andere: .....

Slaapstoornissen

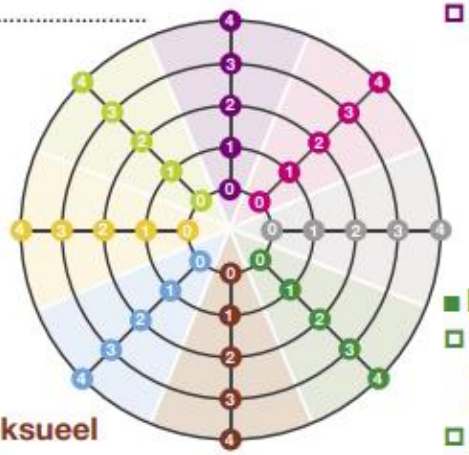
- ☐ Ik heb problemen om 's avonds in slaap te vallen
- ☐ Ik heb problemen met doorslapen
- ☐ Ik heb problemen om weer in slaap te vallen zodra ik wakker ben geworden
- ☐ Ik ben 's ochtends moe
- ☐ Ik ben gedurende de dag vermoeid
- ☐ Ik dut regelmatig in op ongewenste momenten
- ☐ Andere: .....

Aandacht/Geheugen

- ☐ Ik kan mij niet concentreren gedurende activiteiten
- ☐ Ik spreek traag
- ☐ Ik ben vergeetachtig
- ☐ Ik heb problemen met het herinneren van namen, getallen, gebeurtenissen
- ☐ Ik heb moeite om op woorden te komen
- ☐ Ik heb moeite met initiatief nemen
- ☐ Andere: .....

Spijsvertering

- ☐ Ik heb moeite met slikken
- ☐ Ik heb last van overvloedig speeksel
- ☐ Ik moet vaak overgeven of voel mij ziek (misselijk)
- ☐ Ik heb last van constipatie (verstopping)
- ☐ Ik heb last van diarree
- ☐ Ik heb last van mijn maag
- ☐ Andere: .....



Andere niet-motorische symptomen

- ☐ Ik heb een licht gevoel in mijn hoofd/ben duizelig als ik opsta vanuit een liggende positie
- ☐ Ik val als gevolg van een flauwte
- ☐ Ik merk een wijziging in mijn vermogen om te ruiken/proeven
- ☐ Ik merk een wijziging in gewicht (niet te wijten aan een wijziging in dieet)
- ☐ Ik zweet overmatig
- ☐ Ik zie/hoor dingen die er niet zijn
- ☐ Andere: .....

Blaas en seksueel functioneren

- ☐ Ik voel aandrang om te plassen terwijl ik niet hoef te plassen
- ☐ Ik moet 's nachts vaker plassen
- ☐ Ik heb last van incontinentieproblemen
- ☐ Ik heb een gewijzigde interesse in seks
- ☐ Ik heb problemen bij het hebben van seks
- ☐ Andere: .....

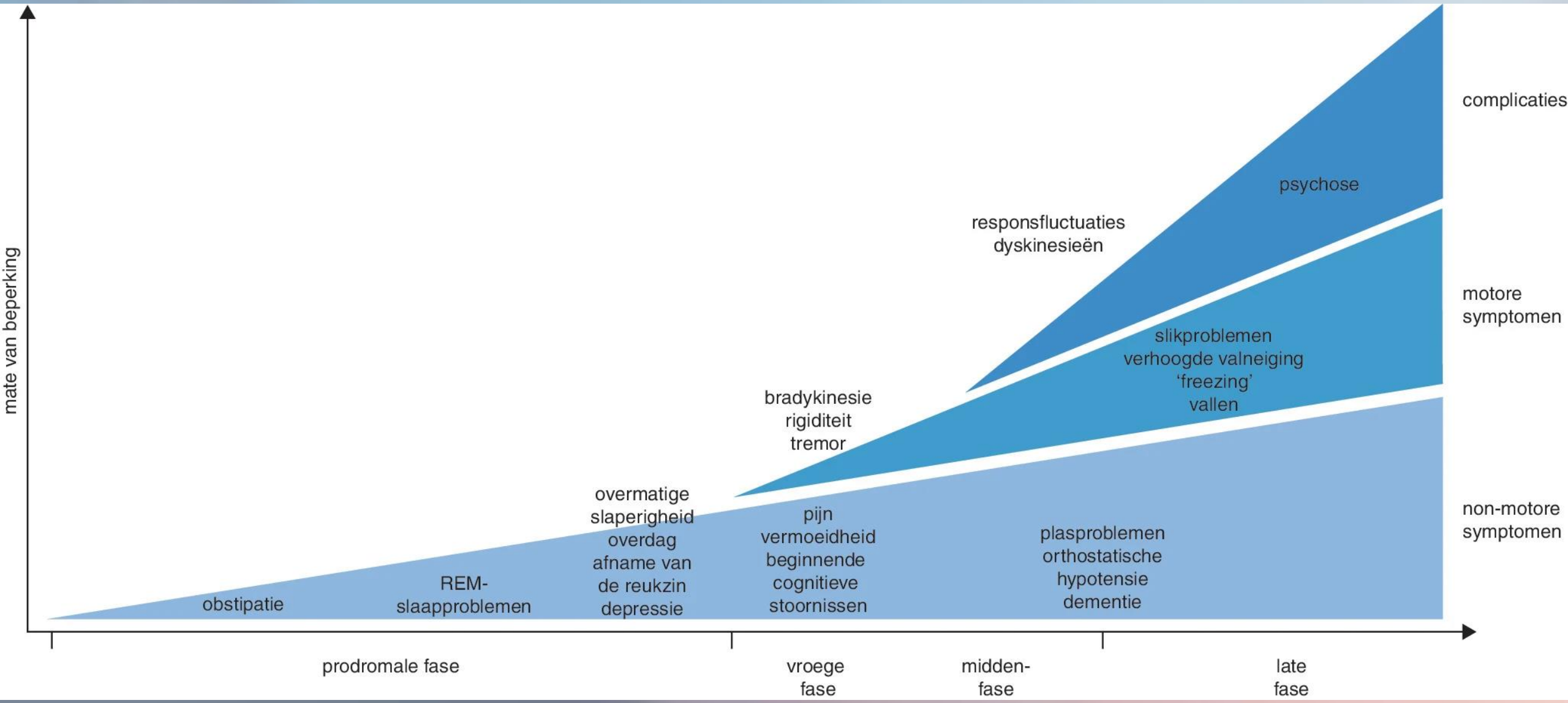
Pijn

- ☐ Ik heb vroeg in de ochtend pijnlijke krampen in mijn tenen, vingers, enkels en polsen, waar ik wakker van word
- ☐ Ik heb pijnlijke, stijve ledematen gedurende de dag
- ☐ Ik heb pijnlijke, stijve ledematen gedurende de nacht
- ☐ Ik heb pijnschokken, -scheuten in mijn ledematen
- ☐ Ik heb pijn door abnormale ongewenste bewegingen
- ☐ Ik heb pijn door rusteloosheid of nerveus bewegen 's nachts
- ☐ Ik heb zware hoofdpijn
- ☐ Andere: .....

Beweging

- ☐ Ik heb last van stijfheid in de vroege ochtend
- ☐ Ik heb last van stijfheid
- ☐ Ik tril
- ☐ Ik beweeg traag
- ☐ Ik ben beperkt in mijn bewegingen
- ☐ Ik heb evenwichtsproblemen/valneigingen
- ☐ Ik heb een gewijzigde lichaamshouding
- ☐ Ik heb problemen met spreken
- ☐ Ik heb een klein handschrift
- ☐ Ik heb last van bevriezen (freezing)
- ☐ Andere: .....

Dit diagram en de gesommeerde klachten zijn niet gevalideerd.


mate van beperking
complicaties
motore symptomen
non-motore symptomen
psychose
responsfluctuaties
dyskinesieën
slikproblemen
verhoogde valneiging
'freezing'
vallen
bradykinesie
rigiditeit
tremor
overmatige slaperigheid overdag
afname van de reukzin
depressie
pijn
vermoeidheid
beginnende cognitieve stoornissen
plasproblemen
orthostatische hypotensie
dementie
obstipatie
REM-slaapproblemen
prodromale fase
vroege fase
midden-fase
late fase

Eigen regie


W. RAY JOHNSTON presents
"THE WHEEL OF DESTINY"
RAYART PICTURES

-informatie Parkinson
-contact met lotgenoten
-leefstijl
-”shared decision making”
-

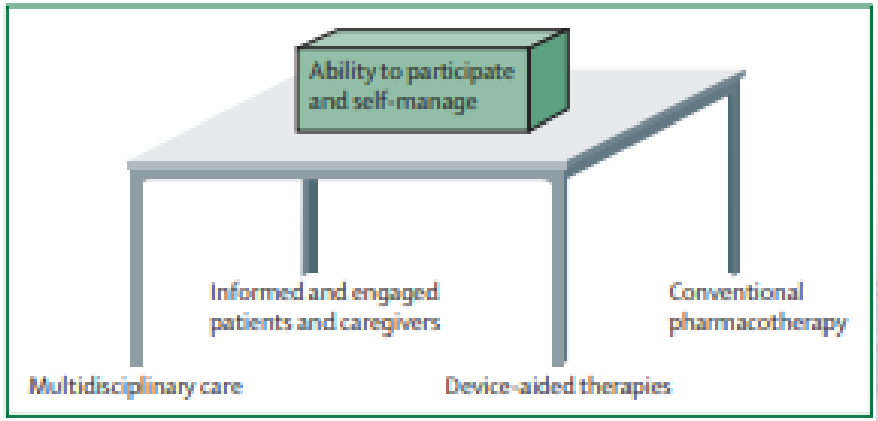


***Figure 5*: Overall management approach of Parkinson's disease**
The overall management approach of Parkinson's disease can be visualised as a table resting on four legs that are needed for all people with Parkinson's disease, except for neurosurgery, which is indicated for only a subgroup. In line with a modern definition of health,[16] the ultimate goal is to support people with Parkinson's disease in their ability to participate in activities that are meaningful to them, and to support them in self-management.

Informatie Parkinson

-www.parkinson-vereniging.nl

-www.parkinsontv.nl

-

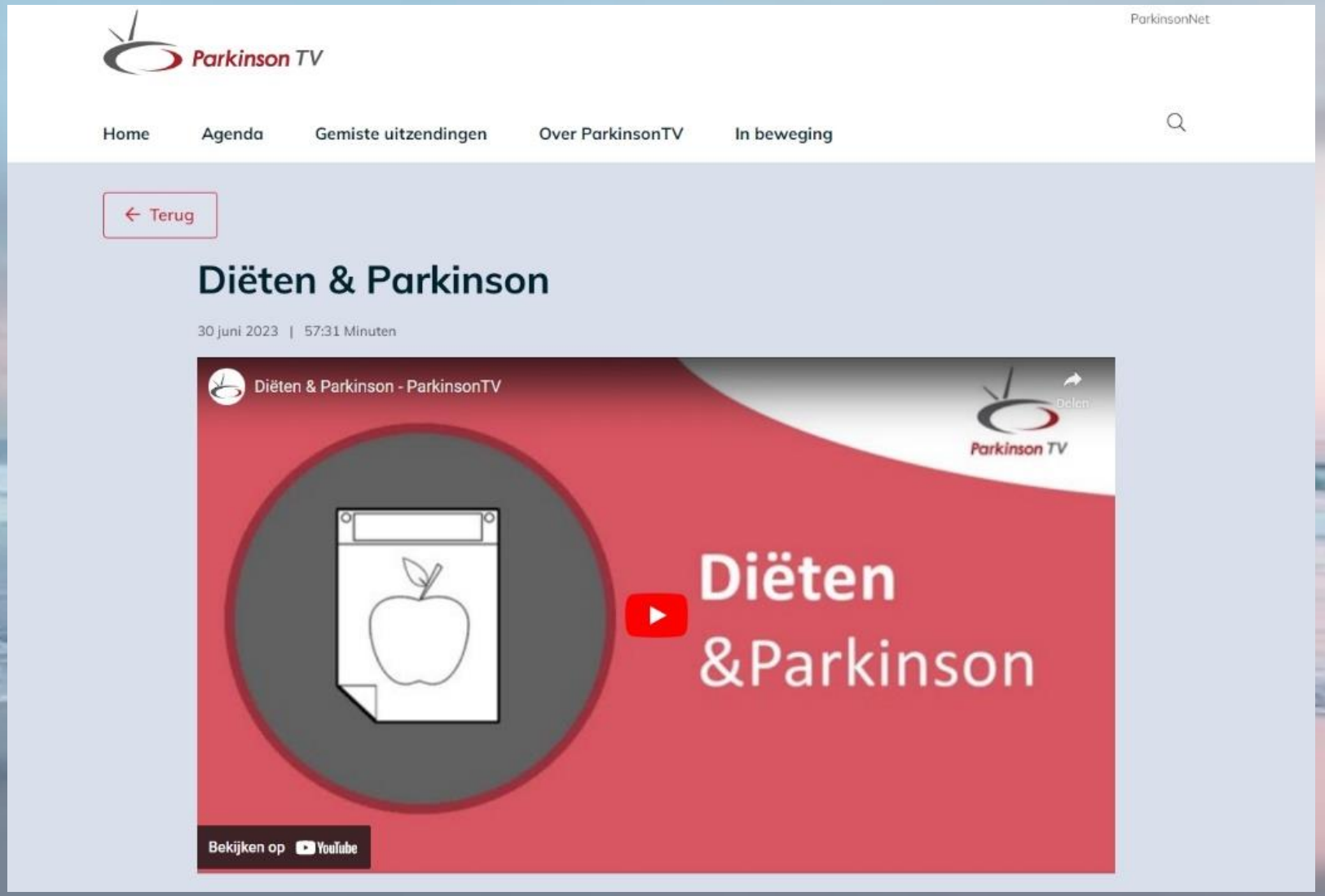
-

PARKINSONISME
VERENIGING

Parkinson TV

Informatie Parkinson

Informatie Parkinson



Contact met lotgenoten

-www.parkinson-vereniging.nl
-Parkinsoncafé
-bij de therapeut (trainen in groepen)
-boksen, dansen…
-

Contact met lotgenoten

Leefstijl

Voeding

Beweging

Verbinding

Ontspannen

Middelen

Slaap

“Shared decision making”

Op basis van informatie en eigen wensen samen met een medisch team uw eigen behandeling vorm geven

Nieuwe ontwikkelingen

14000! artikelen Parkinson

-antilichamen alfa-synucleine

-alfa-synucleine bloed/CSF

-nieuwe toedieningsvormen

-FUS PD

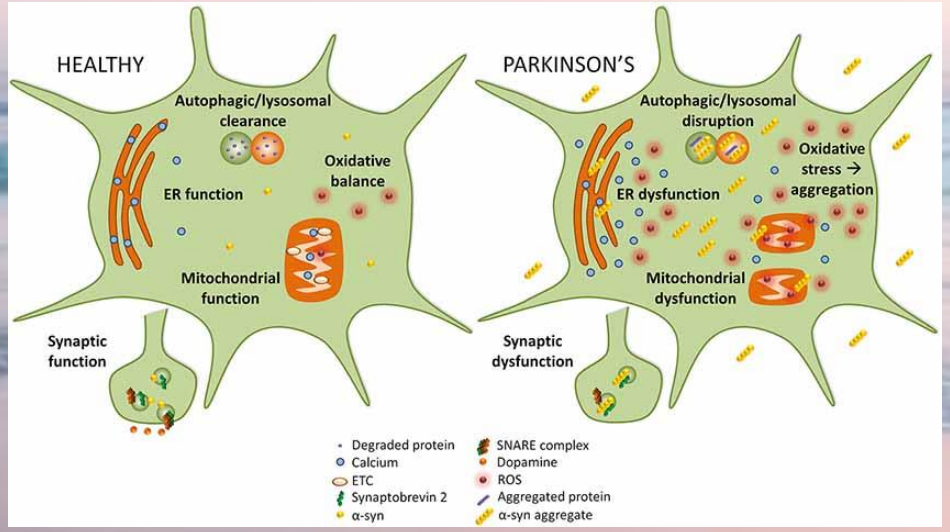
-GBA1 studie

Wat gaat er mis bij Parkinson

-alfa synucleine rol

-samenklonteren afwijkend alfa synucleine

-”prionziekte”



RESEARCH SUMMARY

Trial of Prasinezumab in Early-Stage Parkinson's Disease

Pagano G et al. DOI: 10.1056/NEJMoa2202867

CLINICAL PROBLEM

Aggregated α-synuclein has a prominent role in the pathogenesis of Parkinson's disease. Prasinezumab, a humanized monoclonal antibody that binds to aggregated α-synuclein, has been proposed as a potential treatment for Parkinson's disease, but clinical trial data are needed.

CLINICAL TRIAL

Design: A phase 2, multinational, double-blind, randomized, placebo-controlled trial examined the efficacy and safety of low- and high-dose prasinezumab in patients with early-stage Parkinson's disease.

Intervention: 316 patients who had not previously received treatment for symptoms of Parkinson's disease or who were receiving stable doses of a monoamine oxidase B inhibitor were assigned to receive intravenous prasinezumab (1500 mg or 4500 mg) or placebo every 4 weeks for 52 weeks. The primary end point was the change from baseline to week 52 in the Movement Disorder Society–sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) total score; scores range from 0 to 236, with higher scores indicating greater symptom severity.

RESULTS

Efficacy: The mean change in the MDS-UPDRS score at week 52 did not differ significantly between either prasinezumab dose and placebo.

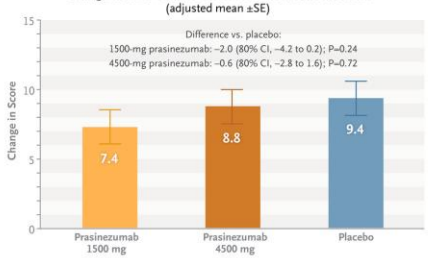
Safety: Infusion reactions were common and were reported most frequently in the 4500-mg group. Serious adverse events occurred more often with prasinezumab than with placebo.

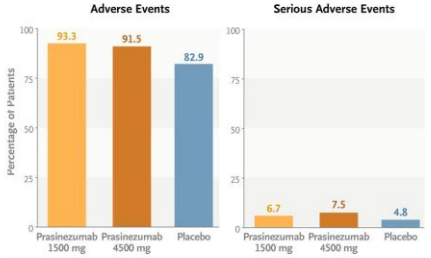
LIMITATIONS AND REMAINING QUESTIONS

- Nearly one third of the participants were excluded from the 52-week efficacy analysis because they had started treatment for symptoms of Parkinson's disease.
- Non-White and non-U.S. or non-European populations were underrepresented in the trial.
- Testing for target engagement of prasinezumab was not performed.

Links: Full Article | NEJM Quick Take | Editorial

Change in MDS-UPDRS Score from Baseline to Week 52
(adjusted mean ±SE)





CONCLUSIONS

The monoclonal antibody prasinezumab, as compared with placebo, did not slow disease progression in patients with early-stage Parkinson's disease over a 52-week treatment period.

RESEARCH SUMMARY

Trial of Cinpanemab in Early Parkinson's Disease

Lang AE et al. DOI: 10.1056/NEJMoa2203395

CLINICAL PROBLEM

Existing therapies for Parkinson's disease are limited. The targeting of α-synuclein aggregates has been proposed as a potential disease-modifying strategy. Cinpanemab, a human-derived monoclonal antibody that binds to aggregated α-synuclein, showed promise in a mouse model and in a phase 1 study of Parkinson's disease.

CLINICAL TRIAL

Design: A phase 2, international, double-blind, randomized, placebo-controlled trial examined the efficacy and safety of cinpanemab in persons with early-stage Parkinson's disease.

Intervention: 357 participants who were not receiving treatment for Parkinson's symptoms were assigned to receive intravenous cinpanemab at one of three doses (250 mg, 1250 mg, or 3500 mg) or placebo (control) every 4 weeks for 52 weeks, after which placebo recipients switched to cinpanemab. The primary end points included the change from baseline to weeks 52 and 72 in the total score on the Movement Disorder Society–sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS); scores range from 0 to 236, with higher scores indicating greater symptom severity.

RESULTS

Efficacy: At 52 weeks, the change in MDS-UPDRS total score did not differ significantly between any cinpanemab dose and placebo. Results at 72 weeks, when the trial was stopped early for lack of efficacy, were consistent with the results at 52 weeks.

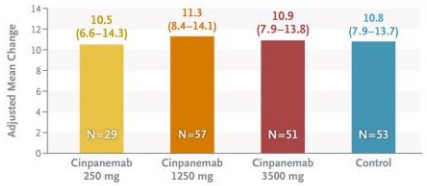
Safety: Adverse events occurred in similar proportions of cinpanemab and placebo recipients and were usually mild to moderate in severity. The most common adverse events with cinpanemab included headache, nasopharyngitis, falls, and back pain.

LIMITATIONS AND REMAINING QUESTIONS

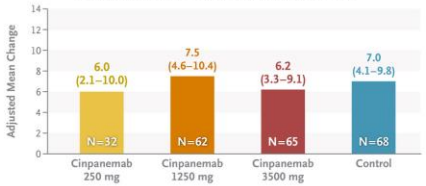
- 40% of the participants were not included in the 52-week analysis because they had started other treatments for Parkinson's symptoms.
- Clearance of α-synuclein in cinpanemab recipients could not be verified.

Links: Full Article | NEJM Quick Take | Editorial

Change in MDS-UPDRS Score, Baseline to Week 52



Change in MDS-UPDRS Score, Baseline to Week 72



Adverse Events to Week 52

Adverse Event	Cinpanemab 250 mg (N=55)	Cinpanemab 1250 mg (N=102)	Cinpanemab 3500 mg (N=100)	Control (N=100)
Any adverse event	42 (76)	83 (81)	86 (86)	80 (80)
Adverse events occurring in ≥5% of participants				
Headache	6 (11)	19 (19)	21 (21)	18 (18)
Nasopharyngitis	10 (18)	10 (10)	13 (13)	12 (12)
Fall	5 (9)	6 (6)	15 (15)	5 (5)
Back pain	3 (5)	8 (8)	13 (13)	9 (9)

Data are no. of participants (%).

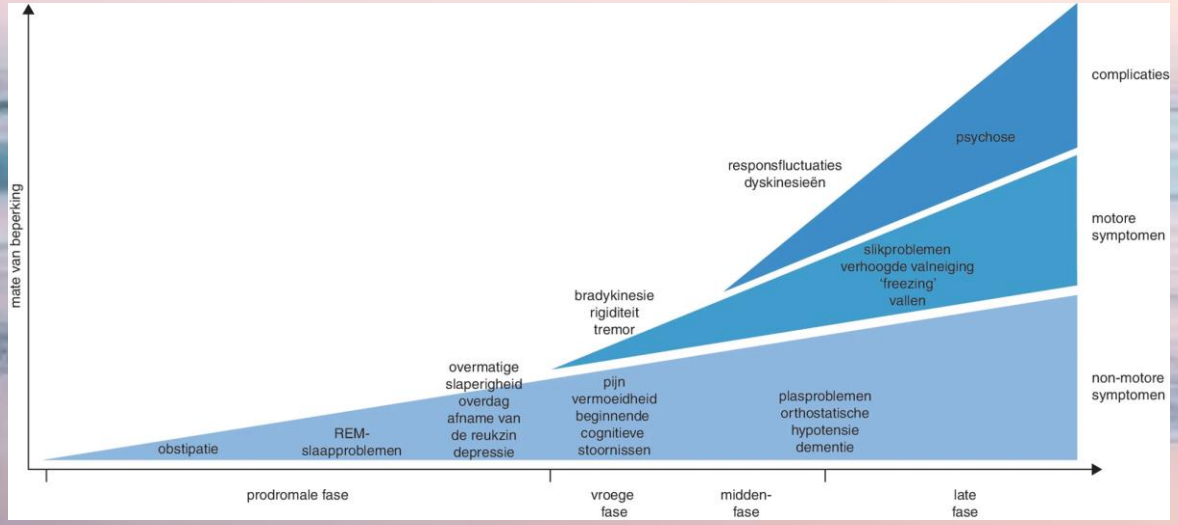
CONCLUSIONS

The monoclonal antibody cinpanemab, as compared with placebo, did not slow progression of Parkinson's disease in patients with early-stage disease.

Opmerkingen bij deze studies

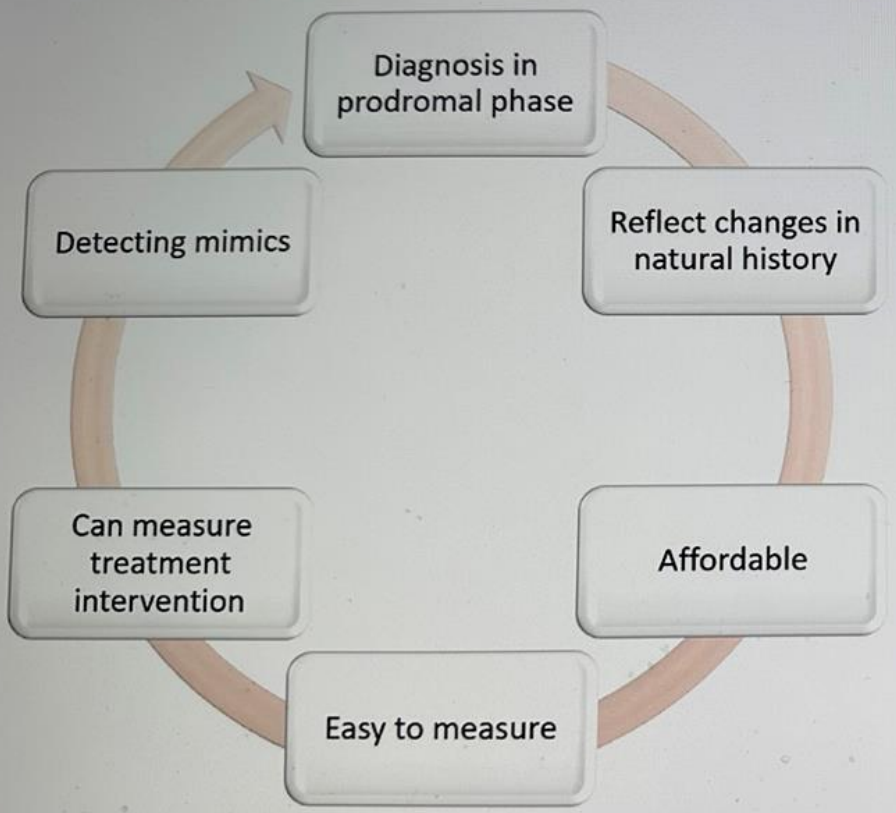
-mogelijk wel effect prodromale fase?

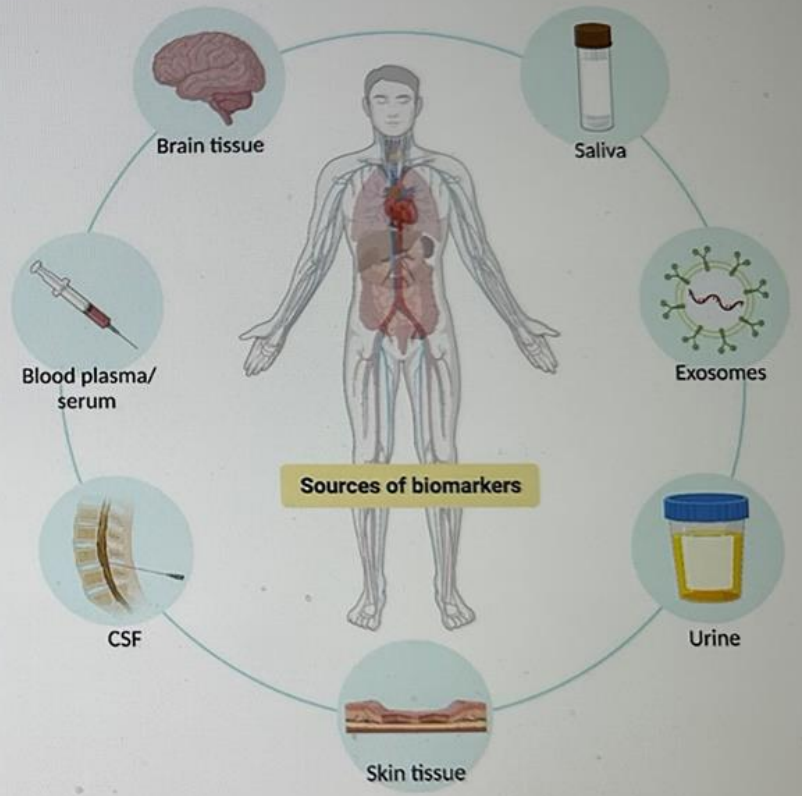
-mogelijk langer behandelen?




Biomarker

Ideal Biomarker





Berg D, Klein C. α-synuclein seed amplification and its uses in Parkinson's disease. Lancet Neurol. 2023 May;22(5):369-371.

Chopra A, Outeiro TF. Aggregation and beyond: alpha-synuclein-based biomarkers in synucleinopathies. Brain. 2023 Aug 1:awad260.

https://doi.org/10.1093/brain/awac115 BRAIN 2022: 145; 3058–3071 | 3058

BRAIN
ORIGINAL ARTICLE

Detection of neuron-derived pathological α-synuclein in blood

Annika Kluge,[1] Josina Bunk,[2] Eva Schaeffer,[1] Alice Drobny,[3] Wei Xiang,[3] Henrike Knacke,[1] Simon Bub,[3] Wiebke Lückstädt,[4] Philipp Arnold,[5] Ralph Lucius,[4] Daniela Berg[1,†] and Friederike Zunke[3,†]

[†]These authors contributed equally to this work.

See Martinez-Valbuena *et al.* (https://doi.org/10.1093/brain/awac292) for a scientific commentary on this article.

To date, no reliable clinically applicable biomarker has been established for Parkinson's disease. Our results indicate that a long anticipated blood test for Parkinson's disease may be realized. Following the isolation of neuron-derived extracellular vesicles of Parkinson's disease patients and non-Parkinson's disease individuals, immunoblot analyses were performed to detect extracellular vesicle-derived α-synuclein. Pathological α-synuclein forms derived from neuronal extracellular vesicles could be detected under native conditions and were significantly increased in all individuals with Parkinson's disease and clearly distinguished disease from the non-disease state. By performing an α-synuclein seeding assay these soluble conformers could be amplified and seeding of pathological protein folding was demonstrated. Amplified α-synuclein conformers exhibited β-sheet-rich structures and a fibrillary appearance. Our study demonstrates that the detection of pathological α-synuclein conformers from neuron-derived extracellular vesicles from blood plasma samples has the potential to evolve into a blood-biomarker of Parkinson's disease that is still lacking so far. Moreover, the distribution of seeding-competent α-synuclein within blood exosomes sheds a new light of pathological disease mechanisms in neurodegenerative disorders.

Assessment of heterogeneity among participants in the Parkinson's Progression Markers Initiative cohort using α-synuclein seed amplification: a cross-sectional study

Prof Andrew Siderowf, MD * • Luis Concha-Marambio, PhD * • David-Erick Lafontant, MS • Carly M Farris, MS • Yihua Ma, MS • Paula A Urenia, BA • et al. Show all authors • Show footnotes

α-synuclein SAA analysis of CSF
1123 participants
Parkinson's disease=545
Healthy controls= 163
SWEDD=54
Prodromal participants= 51
Non-manifesting carriers= 310

- Specificity for healthy controls and SWEDD were high
- Sensitivity for Parkinson's disease was 87·7%
- PD with the typical olfactory deficit had high sensitivity
- LRRK2 mutation had low sensitivity compared with GBA
- Prodromal participants with RBD or hyposmia had high positivity for α-synuclein SAA

	N	Specificity (95% CI)	Sensitivity (95% CI)
Healthy controls	163	96·3% (93·4–99·2)	NA
SWEDD	54	90·7% (83·0–98·5)	NA
All Parkinson's disease cases	545	NA	87·7% (84·9–90·5)
Hyposmic	390	NA	97·2% (95·5–98·8)
Normosmic	146	NA	63·0% (55·2–70·8)
Sporadic Parkinson's disease	373	NA	93·3% (90·8–95·8)
LRRK2 mutation Parkinson's disease	123	NA	67·5% (59·2–75·8)
GBA mutation Parkinson's disease	49	NA	95·9% (90·4–100·0)
LRRK2 mutation Parkinson's disease			
Male participants	65	NA	78·5% (68·5–88·5)
Female participants	58	NA	55·2% (42·4–68·0)
Hyposmic	69	NA	89·9% (82·7–97·0)
Normosmic	49	NA	34·7% (21·4–48·0)
Normosmic and female participants	24	NA	12·5% (4·3–31·0)

Behandeling

Toedieningsvormen

International Congress of Parkinson's Disease and Movement Disorders®

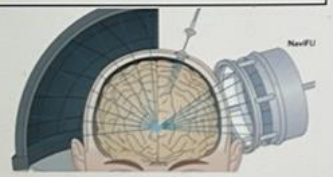
August 27-31, 2023 Copenhagen DENMARK

Device-aided treatments

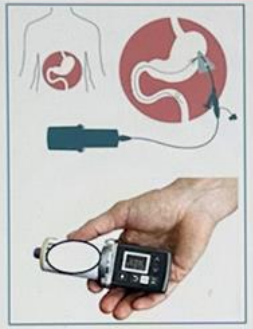
Identical indication for DBS and infusions: persistent motor fluctuations despite optimised oral/transdermal treatment. Additional indication for DBS: refractory tremor.

DBS

MRI guided focussed ultrasound: lesion

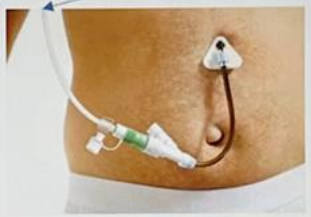


Krishna NEJM 2023

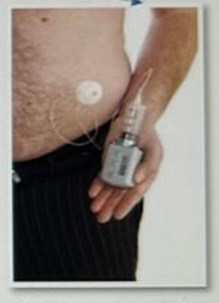


Levodopa/ carbidopa/ entacapone infusion

Infusions



Levodopa/ carbidopa intestinal gel infusion LCIG



Subcutaneous apomorphine infusion

Poewe MDS 2021; Giladi Eur J Neurol; Olanow Mov Disord 2020; Rosebraugh Park Relat Disord 2022; Soileau Lancet Neurol 2022

Odin Park Relat Disord 2015; Politis Mov Disord 2017; Othman Clin Pharmacokinet 2015; Natera-Villalba Curr Op Neurol 2022

Nieuwe toedieningsvormen

International Congress of Parkinson's Disease and Movement Disorders®

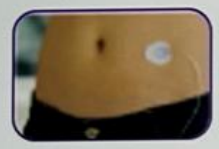
August 27-31, 2023 Copenhagen DENMARK

Subcutaneous foslevodopa/foscarbidopa

Pump system not approved by FDA or EMA

Pro-drug; more soluble than levodopa, enzymatic conversion
⇒ less volume.

Facheris Neurology 2020; Rosebraugh Ann Neurol 2021



Worn for 72 hours.

Randomised comparison with oral levodopa; double-dummy

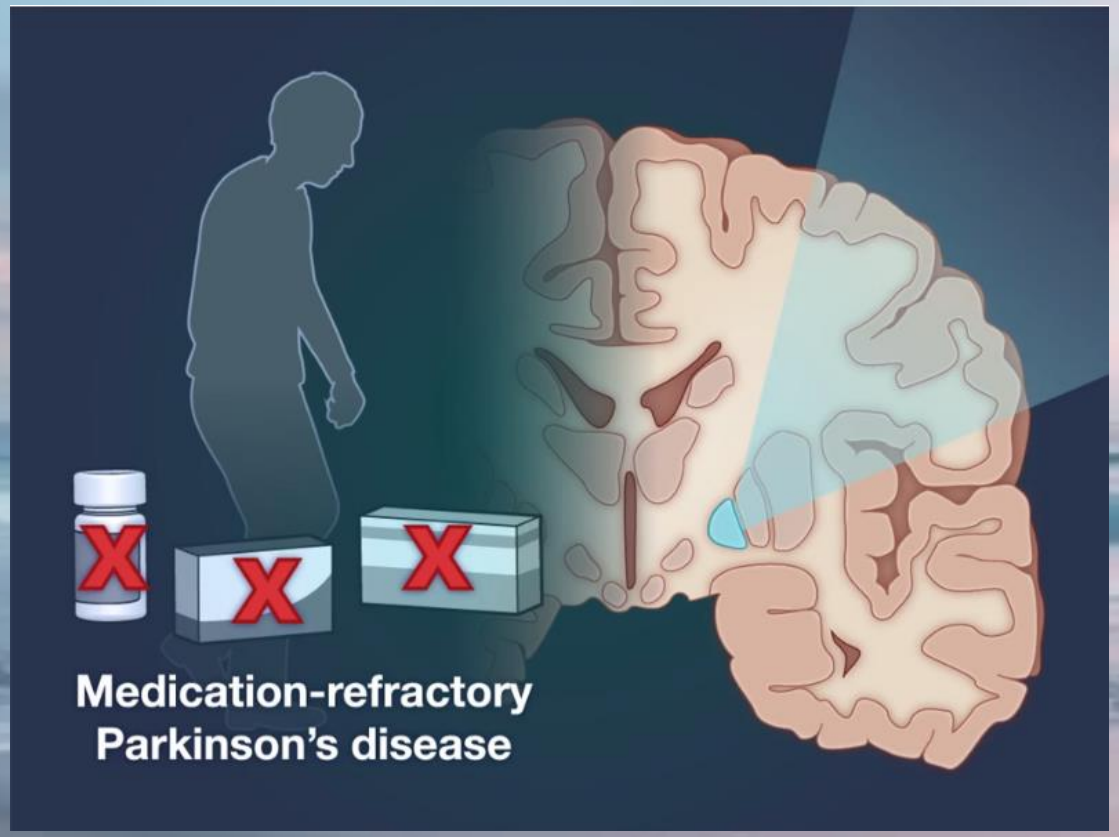
Screening: n=174; device training - levodopa drugs converted to immediate-release levodopa-carbidopa
Double-blind phase: n=141; 12-weeks: dose adjustments during first 4 weeks.

Safety and efficacy of continuous subcutaneous foslevodopa-foscarbidopa in patients with advanced Parkinson's disease: a randomised, double-blind, active-controlled, phase 3 trial

Michael J Soileau, Jason Aldred, Kumar Budur, Nahome Fisseha, Victor SC Fung, Anna Jeong, Thomas E Kimber, Kevin Klos, Irene Litvan, Daniel O'Neill, Weining Z Robieson, Meredith A Spindler, David G Standaert, Saritha Talapala, Eleni Okeanis Vaou, Hui Zheng, Maurizio F Facheris, Robert A Hauser

Soileau Lancet Neurology 2022

“FUS”


Medication-refractory
Parkinson’s disease


Focused
Ultrasound

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Trial of Globus Pallidus Focused Ultrasound Ablation in Parkinson's Disease

Krishna V et al. DOI: 10.1056/NEJMoa2202721

CLINICAL PROBLEM

In patients with Parkinson's disease, focused ultrasound ablation of the internal segment of the globus pallidus has been associated with reductions in motor symptoms and dyskinesias in small, open-label studies. Additional data are needed.

CLINICAL TRIAL

Design: A multicenter, prospective, double-blind, randomized, sham-controlled trial assessed the efficacy and safety of unilateral focused ultrasound ablation of the globus pallidus internus in patients with medication-refractory idiopathic Parkinson's disease.

Intervention: 94 patients ≥30 years of age with dyskinesias or motor impairment while receiving levodopa were assigned in a 3:1 ratio to undergo either focused ultrasound ablation of the globus pallidus internus (active treatment) or a sham procedure, delivered opposite the side with greater impairment. Patients were awake and treated in the off-medication state. The primary outcome was a response, defined as a reduction (improvement) of ≥3 points on either a motor-impairment scale for the treated side in the off-medication state or on a dyskinesia scale in the on-medication state, without a clinically meaningful worsening in either scale, at 3 months.

RESULTS

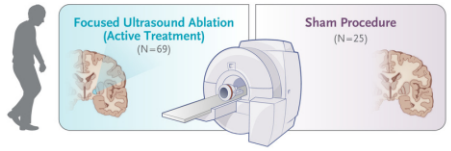
Efficacy: Among 87 patients who could be evaluated at 3 months, the percentage who had a response was more than twice as high in the active-treatment group as in the control group.

Safety: Pallidotomy-related adverse events at 3 months were uncommon but included dysarthria, gait disturbance, loss of taste, visual disturbance, and facial weakness.

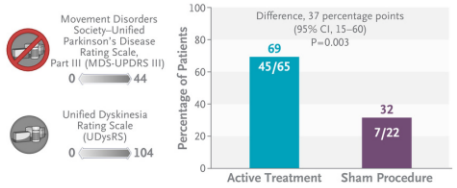
LIMITATIONS AND REMAINING QUESTIONS

- Primary-outcome data were missing for approximately 7% of patients.
- Blinding of the trial-group assignments was unsatisfactory.
- Longer and larger trials are needed to determine the efficacy and safety of this intervention in Parkinson's disease.

Links: Full Article | NEJM Quick Take | Editorial



Response (≥3-Point Improvement) at 3 Mo



Response (≥3-Point Improvement) at 12 Mo

30/39
Patients in the active-treatment group maintained treatment response

Pallidotomy-Related Adverse Events at 3 Mo

	Active Treatment (N=68)	Sham Procedure (N=24)
Dysarthria	1	0
Visual disturbance	1	0
Facial weakness	1	0

CONCLUSIONS

In patients with medication-refractory Parkinson's disease, those who underwent unilateral focused ultrasound ablation of the globus pallidus internus were significantly more likely to have a reduction in motor symptoms or dyskinesias over a period of 3 months than those who underwent a sham procedure.

-gevorderde PD
-geen DBS kandidaat
-veelbelovend
-lange termijn resultaten
-niet omkeerbaar
-invloed QoL?

GBA 1 geassocieerde ziekte van Parkinson

-varianten GBA1 gen => genetische risicofactor Parkinson (bij ongeveer 10% PD)
-GBA 1 gen codeert voor glucocerebrosidase
-mechanisme?: accumulatie glucosylceramide?
-Venglustat glucosylceramide synthase remmer

Safety and efficacy of venglustat in *GBA1*-associated Parkinson's disease: an international, multicentre, double-blind, randomised, placebo-controlled, phase 2 trial

Lancet Neurol 2023; 22: 661–71

Nir Giladi, Roy N Alcalay, Gary Cutter, Thomas Gasser, Tanya Gurevich, Günter U Höglinger, Kenneth Marek, Claudio Pacchetti, Anthony H V Schapira, Clemens R Scherzer, Tanya Simuni, Pascal Minini, S Pablo Sardi, M Judith Peterschmitt

- phase 2 MOVES-PD trial
- the safety, efficacy, and pharmaco- dynamics of venglustat 15 mg/day in people with GBA1-associated Parkinson's disease
- This part of the study consisted of a 52-week, placebo-controlled, double- blinded treatment period, which was followed by a 104-week open-label extension period, in which participants in the placebo group switched to venglustat treatment
- In people with GBA1-associated Parkinson's disease in our study, venglustat had a satisfactory safety profile but showed no beneficial treatment effect compared with placebo

THE LANCET
Neurology
Volume 22, Issue 8, August 2023, Pages 644-645

Comment

Lessons and future directions for *GBA1*-targeting therapies

Ziv Gan-Or [a]

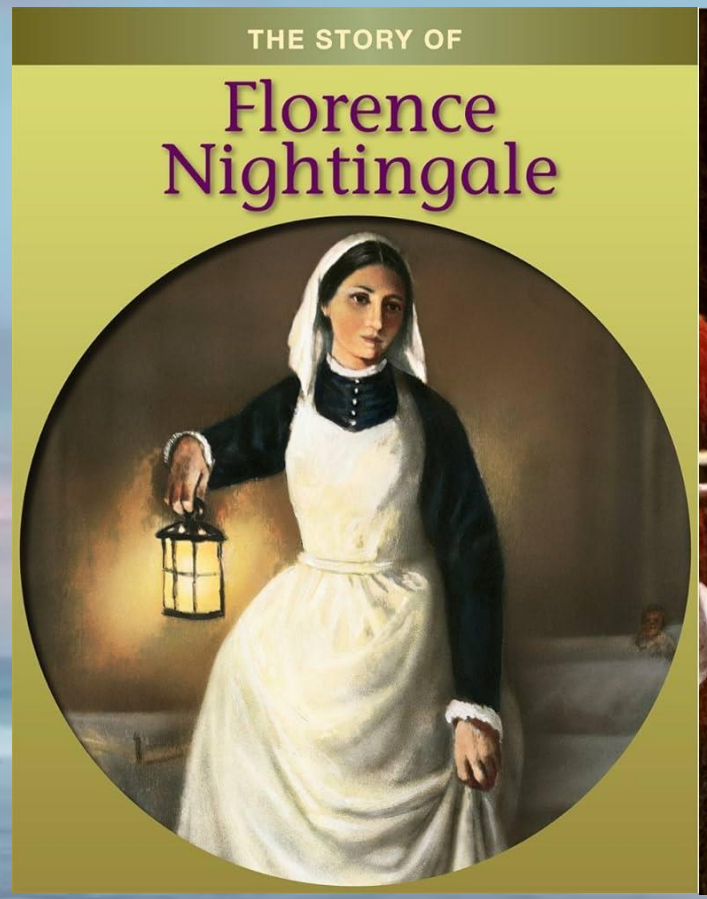
- The study hypothesis was wrong
- Participants were recruited at too advanced stage for the drug to have an effect
- GBA1 variants can be classified as severe or mild
- In this study, a small imbalance in severe and mild GBA1 variants was noted between groups

Samenvatting

-Parkinson is een multisysteem ziekte
-goed geïnformeerd passende zorg
-veel lopend onderzoek
-biomarkers Parkinson komen eraan
-nieuwe toedieningsvormen

Vragen?

Vragen?



Voorlichtingsavond over
de ziekte van Parkinson