Valproblematiek na CVA: mechanismen, risicofactoren en behandeling

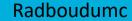
Alexander Geurts MD PhD

Sander.Geurts@Radboudumc.nl

Nijmegen, Netherlands

St Maartenskliniek Rehabilitation Center



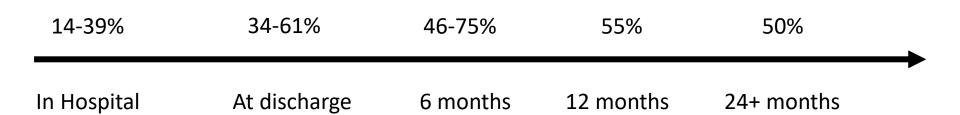








Fall incidence after stroke



Fall incidence after stroke

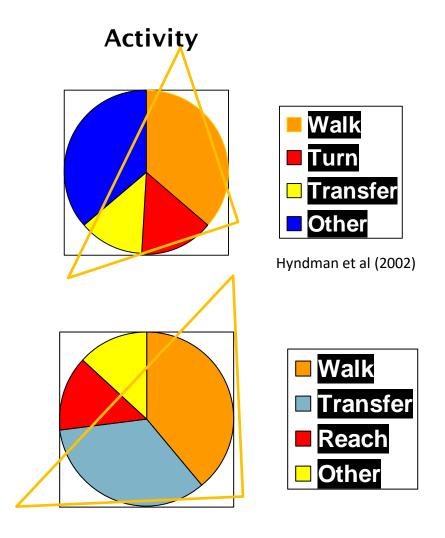


- 3-10 times greater fall rates than healthy
- 55% of all falls in PwS lead to injuries

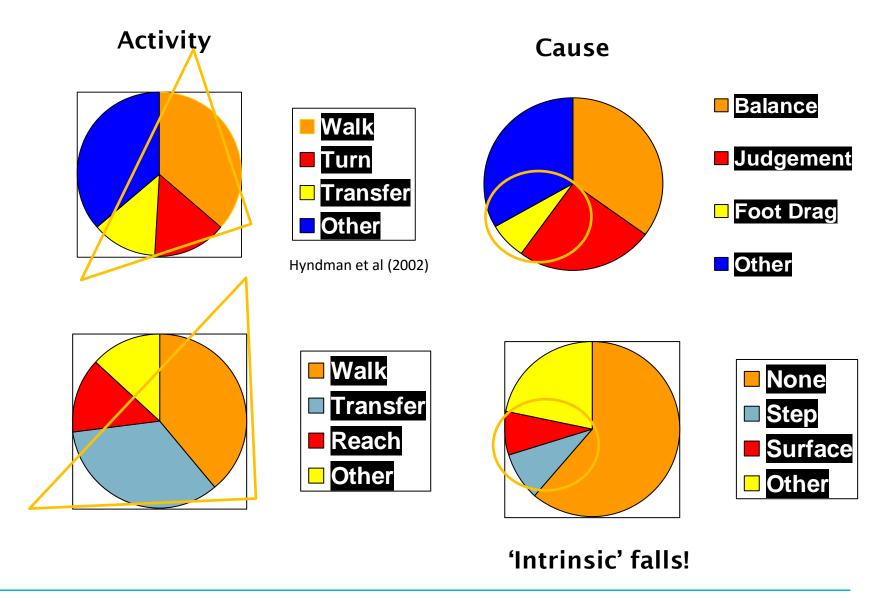


10% of all falls lead to severe injuries (e.g. fracture)

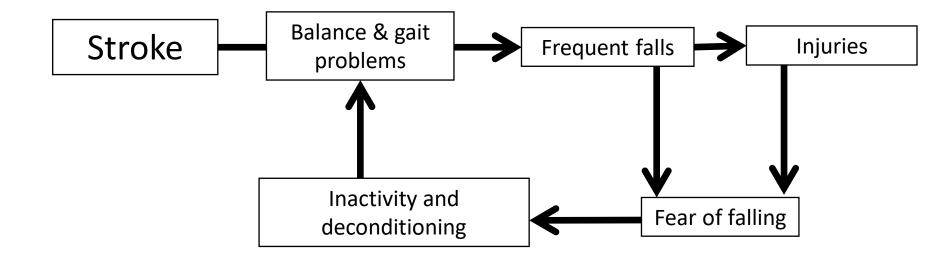
Circumstances of falls after stroke



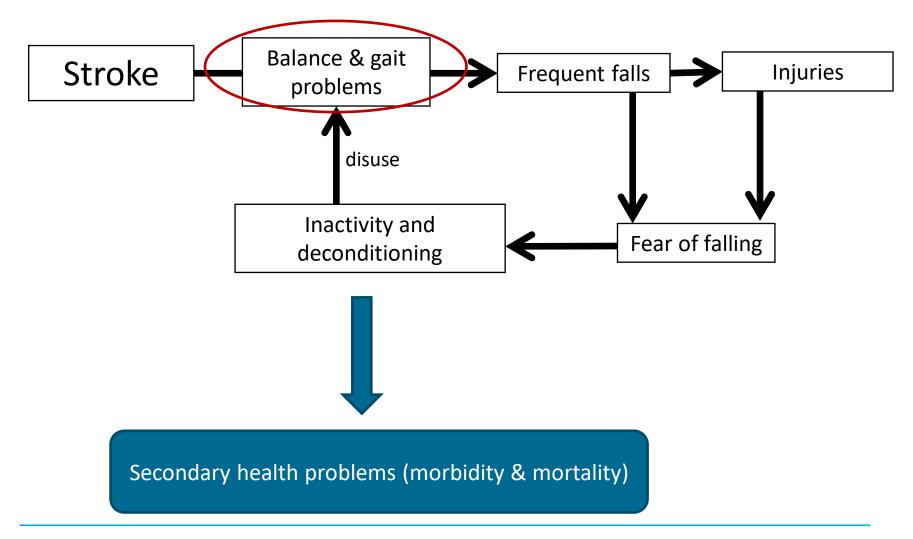
Circumstances of falls after stroke



Vicious circle

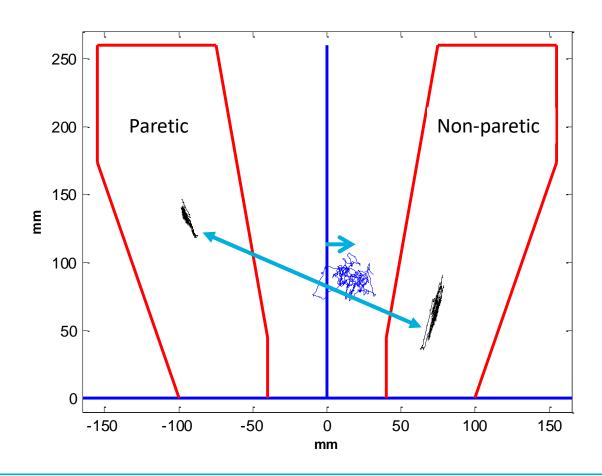


Vicious circle

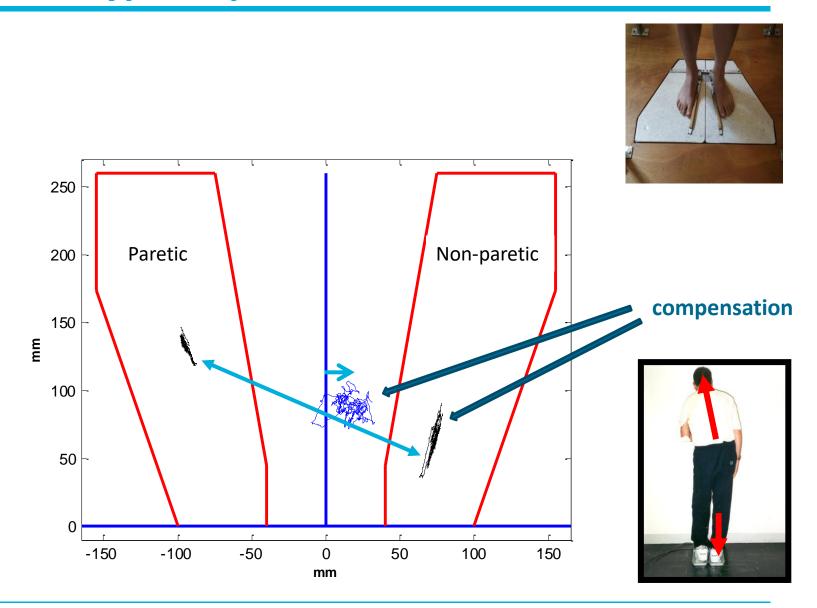


Typical quiet stance in stroke



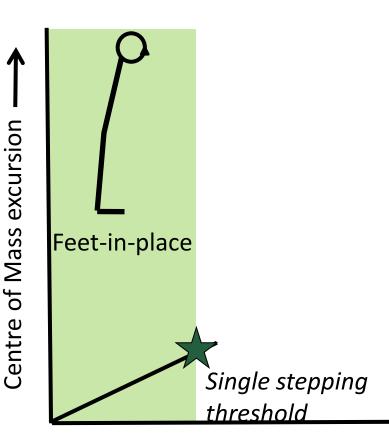


Typical quiet stance in stroke



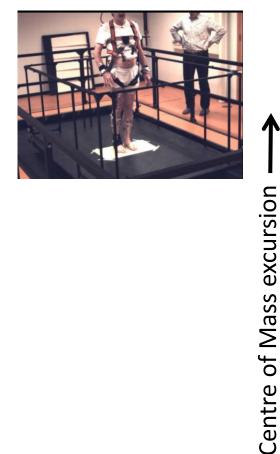
Balance recovery from perturbation

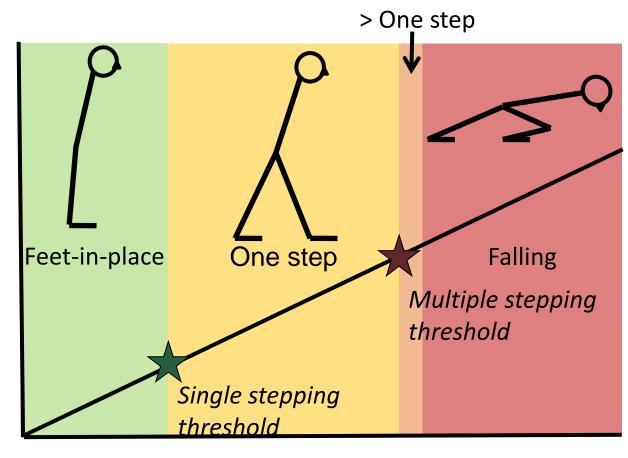




Perturbation intensity ->

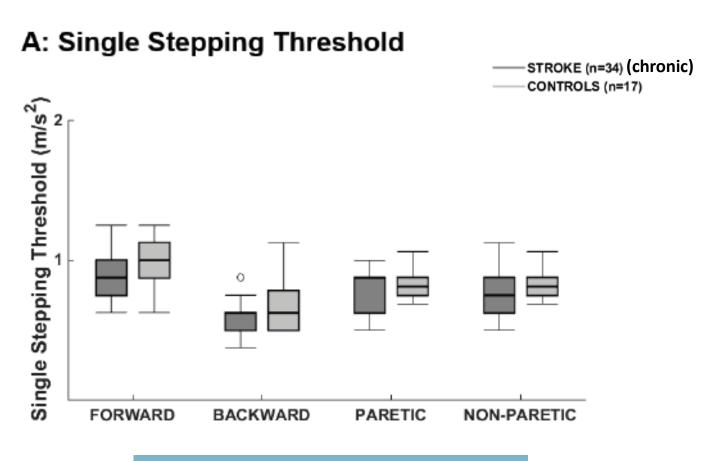
Balance recovery from perturbation





Perturbation intensity ->

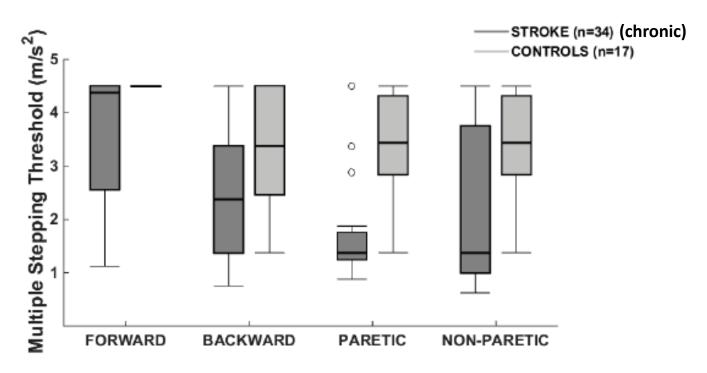
"Feet in place"



No significant group differences

"Recover in one step"

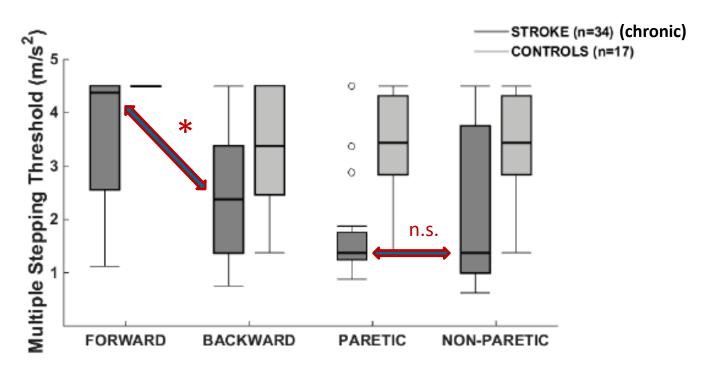
B: Multiple Stepping Threshold



Significant group differences all directions (p<.01)

"Recover in one step"

B: Multiple Stepping Threshold



Significant group differences all directions (p<.01)

Falls after stroke: 3 statements

Huge clinical and societal problem



Dynamic balance deficits are important underlying factor

Little proof of effective interventions

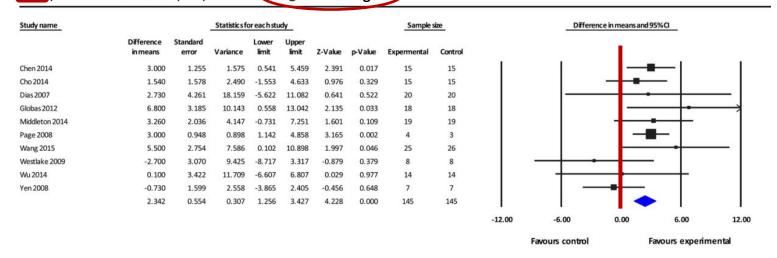
BBS post intervention | experimenta : balance training

| Study name | | 2 | Statistics fo | r each s | tudy | | | Sample : | size | | Difference | in means a | and 95% CI | |
|---------------|---------------------|-------------------|---------------|----------------|----------------|---------|---------|-------------|---------|--------|-----------------|------------|-----------------|---------------|
| | Difference in means | Standard error | Variance | Lower limit | Upper limit | Z-Value | p-Value | Expermental | Control | | | | | |
| Cho KH 2012 | -0.810 | 1.896 | 3.593 | -4.525 | 2.905 | -0.427 | 0.669 | 11 | 11 | Ĩ | <u> </u> | - | - [| 1 |
| Farqalit 2013 | 6.600 | 1.906 | 3.633 | 2.864 | 10.336 | 3.463 | 0.001 | 20 | 20 | | | | | - |
| Kim 2009 | 2.920 | 1.682 | 2.831 | -0.378 | 6.218 | 1.736 | 0.083 | 12 | 12 | | | - | ■ | |
| Lee 2014 | 7.500 | 2.691 | 7.243 | 2.225 | 12.775 | 2.787 | 0.005 | 10 | 11 | | | 1 | | \rightarrow |
| Lee 2012 | 4.000 | 2.329 | 5.423 | -0.564 | 8.564 | 1.718 | 0.086 | 20 | 20 | | | - | - | |
| Llorens 2014 | 4.800 | 2.316 | 5.365 | 0.260 | 9.340 | 2.072 | 0.038 | 10 | 10 | | | _ | - | - |
| Marigold 2005 | 1.000 | 1.562 | 2.439 | -2.061 | 4.061 | 0.640 | 0.522 | 22 | 26 | | | — | | |
| Noh 2008 | 6.400 | 2.296 | 5.273 | 1.899 | 10.901 | 2.787 | 0.005 | 10 | 10 | | | 1 | | |
| | 3.747 | 1.039 | 1.080 | 1.710 | 5.784 | 3.605 | 0.000 | 115 | 120 | | ı | 15 | | |
| | | | | | | | | | | -12.00 | -6.00 | 0.00 | 6.00 | 12.00 |
| | | | | | | | | | | | Favours control | | Favours experim | nental |

BBS post intervention | experimental: balance training

| Study name | | | Statistics fo | or each s | tudy | | | Sample | size | | Difference | in means a | and 95% CI | |
|---------------|---------------------|-------------------|---------------|----------------|----------------|---------|---------|-------------|---------|--------|-----------------|------------|------------------|---------------|
| | Difference in means | Standard error | Variance | Lower limit | Upper limit | Z-Value | p-Value | Expermental | Control | | | | | |
| Cho KH 2012 | -0.810 | 1.896 | 3.593 | -4.525 | 2.905 | -0.427 | 0.669 | 11 | 11 | | | - | - 1 | - 1 |
| Farqalit 2013 | 6.600 | 1.906 | 3.633 | 2.864 | 10.336 | 3.463 | 0.001 | 20 | 20 | | | | | _ |
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| Lee 2012 | 4.000 | 2.329 | 5.423 | -0.564 | 8.564 | 1.718 | 0.086 | 20 | 20 | | | | - | |
| Llorens 2014 | 4.800 | 2.316 | 5.365 | 0.260 | 9.340 | 2.072 | 0.038 | 10 | 10 | | | _ | - | - |
| Marigold 2005 | 1.000 | 1.562 | 2.439 | -2.061 | 4.061 | 0.640 | 0.522 | 22 | 26 | | | | | |
| Noh 2008 | 6.400 | 2.296 | 5.273 | 1.899 | 10.901 | 2.787 | 0.005 | 10 | 10 | | | | | |
| | 3.747 | 1.039 | 1.080 | 1.710 | 5.784 | 3.605 | 0.000 | 115 | 120 | | | 15 | | |
| | | | | | | | | | | -12.00 | -6.00 | 0.00 | 6.00 | 12.00 |
| | | | | | | | | | | | Favours control | | Favours experin | nental |

BBS post intervention | experimental: gait training



BBS post intervention | experimental multisensory training

| Study name | | | Statistics fo | or each s | tudy | | | Sample | size | | Differenc | e in means | and 95% CI | |
|---------------|------------------------|-------------------|---------------|----------------|----------------|---------|---------|-------------|---------|--------|-----------------|------------|-----------------|--------|
| | Difference in means | Standard error | Variance | Lower limit | Upper limit | Z-Value | p-Value | Expermental | Control | | | | | |
| Brogardh 2012 | -0.200 | 0.773 | 0.597 | -1.715 | 1.315 | -0.259 | 0.796 | 16 | 15 | 1 | 1 | - | 1 | 1 |
| Cha 2014 | 5.000 | 3.291 | 10.829 | -1.450 | 11.450 | 1.519 | 0.129 | 10 | 10 | | | | | —I |
| Lau 2012 | -0.300 | 1.318 | 1.738 | -2.884 | 2.284 | -0.228 | 0.820 | 41 | 41 | | 8 | - | - | |
| Marin 2013 | 4.000 | 3.324 | 11.048 | -2.515 | 10.515 | 1.203 | 0.229 | 11 | 9 | | | _ | | —: |
| | 0.130 | 0.641 | 0.411 | -1.127 | 1.386 | 0.203 | 0.839 | 78 | 75 | ı | | - | | L |
| | | | | | | | | | | -12.00 | -6.00 | 0.00 | 6.00 | 12.00 |
| | | | | | | | | | | | Favours control | | Favours experir | nental |

BBS post intervention | experimental multisensory training

| Study name | | | Statistics fo | or each s | tudy | | | Sample : | size | | Difference | in means | and 95% CI | |
|---------------|------------------------|-------------------|---------------|----------------|----------------|---------|---------|-------------|---------|--------|-----------------|----------|-----------------|--------|
| | Difference in means | Standard error | Variance | Lower limit | Upper limit | Z-Value | p-Value | Expermental | Control | | | | | |
| Brogardh 2012 | -0.200 | 0.773 | 0.597 | -1.715 | 1.315 | -0.259 | 0.796 | 16 | 15 | 1 | ľ | - | 1 | 1 |
| Cha 2014 | 5.000 | 3.291 | 10.829 | -1.450 | 11.450 | 1.519 | 0.129 | 10 | 10 | | | _ | | —1 |
| Lau 2012 | -0.300 | 1.318 | 1.738 | -2.884 | 2.284 | -0.228 | 0.820 | 41 | 41 | | - | - | - | |
| Marin 2013 | 4.000 | 3.324 | 11.048 | -2.515 | 10.515 | 1.203 | 0.229 | 11 | 9 | | | _ | | |
| | 0.130 | 0.641 | 0.411 | -1.127 | 1.386 | 0.203 | 0.839 | 78 | 75 | I | I | - | I | - 1 |
| | | | | | | | | | | -12.00 | -6.00 | 0.00 | 6.00 | 12.00 |
| | | | | | | | | | | | Favours control | | Favours experin | nental |

BBS post intervention | experimenta caerobic training

| Study name | | | Statistics fo | or each s | tudy | | | Sample | size | | Difference | in means | and 95% CI | |
|-------------|---------------------|-------------------|---------------|-----------|----------------|---------|---------|-------------|---------|--------|-----------------|----------|-----------------|--------|
| | Difference in means | Standard error | Variance | | Upper limit | Z-Value | p-Value | Expermental | Control | | | | | |
| Chu 2004 | -0.200 | 2.004 | 4.018 | -4.129 | 3.729 | -0.100 | 0.921 | 7 | 5 | - 1 | <u> </u> | -+- | - 1 | 1 |
| Jin 2012 | 0.300 | 0.594 | 0.353 | -0.865 | 1.465 | 0.505 | 0.614 | 68 | 65 | | | - | - 1 | |
| Pang 2005 | 0.400 | 1.294 | 1.676 | -2.137 | 2.937 | 0.309 | 0.757 | 32 | 31 | | | | - | |
| Quaney 2009 | 2.630 | 3.948 | 15.588 | -5.108 | 10.368 | 0.666 | 0.505 | 19 | 19 | | <u> </u> | | • | _ |
| | 0.323 | 0.517 | 0.267 | -0.690 | 1.336 | 0.624 | 0.533 | 126 | 120 | | | - | | 1 |
| | | | | | | | | | | -12.00 | -6.00 | 0.00 | 6.00 | 12.00 |
| | | | | | | | | | | | Favours control | | Favours experin | nental |

Updated Cochrane review



Cochrane Database of Systematic Reviews

Interventions for preventing falls in people after stroke (Review)

Denissen S, Staring W, Kunkel D, Pickering RM, Lennon S, Geurts ACH, Weerdesteyn V, Verheyden GSAF

Denissen et al. Cochrane Database of Systematic Reviews 2019, Issue 10. Art. No.: CD008728.

Updated Cochrane review

Analysis 1.1. Comparison 1 Exercise, Outcome 1 Rate of falls.

| Study or subgroup | Exercises | Control | log[Rate Ratio] | Rate Ratio | Weight | Rate Ratio |
|---|--------------------------------------|----------------------|--------------------|----------------------|------------|--------------------|
| | N | N | (SE) | IV, Random, 95% CI | | IV, Random, 95% CI |
| Ada 2013 | 59 | 27 | -0.5 (0.181) | -+- | 20.68% | 0.63[0.44,0.9] |
| Batchelor 2012 | 60 | 79 | 0.1 (0.284) | | 13.78% | 1.1[0.63,1.92] |
| Dean 2010 | 46 | 49 | -0.1 (0.367) | | 10.03% | 0.92[0.45,1.9] |
| Dean 2012 | 76 | 75 | -0 (0.27) | | 14.56% | 0.96[0.57,1.63] |
| Lau 2012 | 41 | 41 | 0 (0.816) | | 2.73% | 1[0.2,4.95] |
| Mansfield 2018 | 41 | 42 | -0.2 (0.36) | + | 10.32% | 0.85[0.42,1.72] |
| Marigold 2005 | 19 | 21 | -1 (0.231) | | 17.02% | 0.38[0.24,0.6] |
| Taylor-Piliae 2014 | 61 | 28 | -0.5 (0.345) | | 10.88% | 0.58[0.3,1.14] |
| Total (95% CI) | | | | • | 100% | 0.72[0.54,0.94] |
| Heterogeneity: Tau ² =0.06; Chi ² = | =12.25, df=7(P=0.09); I ² | ² =42.87% | | | | |
| Test for overall effect: Z=2.37(P= | =0.02) | | | | ı | |
| | | Fav | vours exercises | 0.1 0.2 0.5 1 2 5 10 | Favours co | ntrol |

Significant reduction in rate of falls of 28%

8 studies: N=765 → RR=0.72 (95%CI: 0.54-0.94)

Updated Cochrane review

Analysis 1.2. Comparison 1 Exercise, Outcome 2 Number of fallers.

| Study or subgroup | Exercises | Control | Risk Ratio | Weight | Risk Ratio |
|--|---------------------------------------|-----------------------|--------------------|--------------------|--------------------|
| | n/N | n/N | IV, Random, 95% CI | | IV, Random, 95% CI |
| Ada 2013 | 24/59 | 8/27 | | 4.62% | 1.37[0.71,2.65] |
| Batchelor 2012 | 29/60 | 46/79 | -+ | 19.36% | 0.83[0.6,1.14] |
| Dean 2010 | 28/46 | 25/49 | - | 15.52% | 1.19[0.83,1.71] |
| Dean 2012 | 47/76 | 38/75 | • - | 24.68% | 1.22[0.92,1.62] |
| Green 2002 | 30/85 | 23/85 | • - | 9.77% | 1.3[0.83,2.05] |
| Holmgren 2010 | 5/15 | 6/19 | | 2.11% | 1.06[0.4,2.8] |
| Lau 2012 | 3/41 | 3/41 | | 0.84% | 1[0.21,4.67] |
| Mansfield 2018 | 19/41 | 23/42 | -+ - | 10.87% | 0.85[0.55,1.3] |
| Marigold 2005 | 11/19 | 16/21 | | 9.8% | 0.76[0.48,1.19] |
| Taylor-Piliae 2014 | 10/61 | 6/28 | | 2.43% | 0.77[0.31,1.9] |
| Total (95% CI) | 503 | 466 | • | 100% | 1.03[0.9,1.19] |
| Total events: 206 (Exercises), 1 | .94 (Control) | | | | |
| Heterogeneity: Tau ² =0; Chi ² =8. | .48, df=9(P=0.49); I ² =0% | | | | |
| Test for overall effect: Z=0.43(P | P=0.67) | | | | |
| | | Favours exercises 0.1 | 0.2 0.5 1 2 5 1 | .0 Favours control | |

No significant reduction in number of fallers

10 studies: N=969 → RR=1.03 (95%CI: 0.9-1.19)

Anticipatory control:
maintaining balance
during activities

Reactive control:
recovering from loss of
balance

strategies

Anticipatory control: maintaining balance during activities

Reactive control: recovering from loss of balance

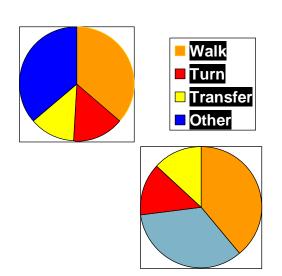
Damage control: impact reducing strategies



Overall program content:
Relatively few walking tasks



Fall circumstances: 39-90% of falls during walking





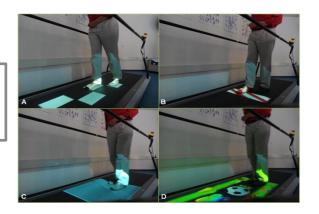




C-mill gait adaptability training



10 x 1 hour, 5 weeks

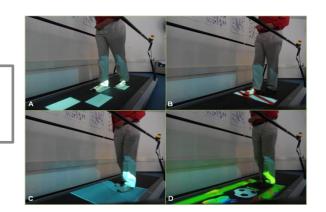


Pre-post design (n=16)

C-mill gait adaptability training



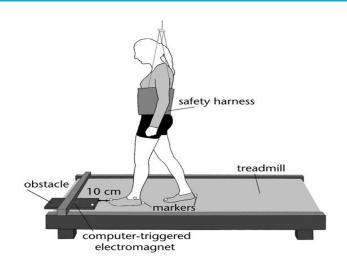
10 x 1 hour, 5 weeks

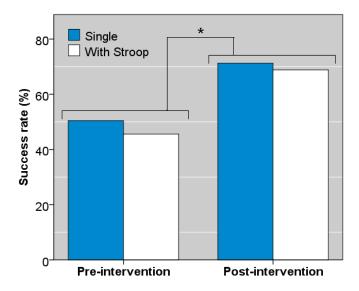


| Clinimetrics | T1 (n=15) | T2 (n=15) P | re-post design (n=16) |
|-----------------------------|---------------|---------------|-----------------------|
| 10MWT (seconds) | 9.54 ± 1.72 | 8.45 ± 1.36 | p=0.008 |
| EFAP (seconds) | 15.00 ± 3.19 | 13.10 ± 2.63* | <i>p</i> =0.016 |
| TUG (seconds) | 11.48 ± 1.6 | 9.8 ± 2.0** | p=0.006 |
| TIS Total (points) | 11.43 ± 3.1 | 11.93 ± 1.9 | p=0.45 |
| BBS (points) | 53.6 ± 2.77 | 55.0 ± 1.41* | <i>p</i> =0.017 |
| 6 item ABC (%) | 56.51 ± 24.39 | 63.08 ± 16.95 | p=0.29 |
| Pedometer (steps per day) ‡ | 5738 ± 1395 | 6864 ± 1645* | ρ=0.047 |

Radboudumc

C-mill gait adaptability training

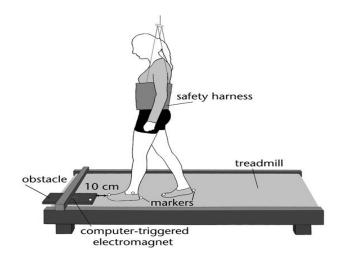




Obstacle avoidance performance

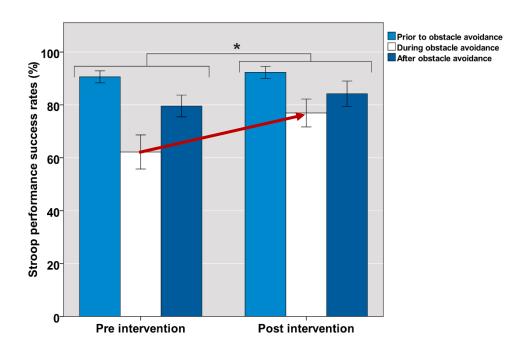
- Single task
- Dual task (concurrent auditory Stroop task)

Obstacle avoidance training



Obstacle avoidance performance

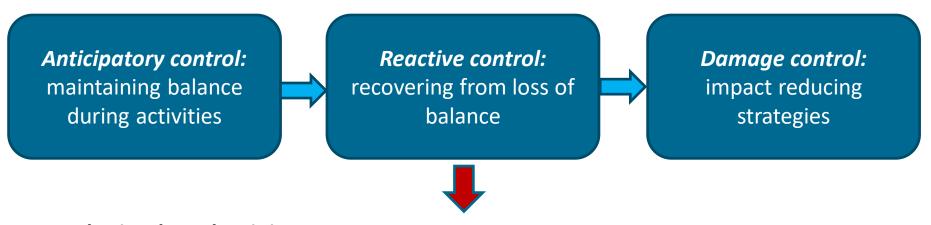
- Single task
- Dual task (concurrent auditory Stroop task)



Anticipatory control:
maintaining balance
during activities

Reactive control:
recovering from loss of
balance

Damage control:
impact reducing
strategies



Perturbation-based training:

- Meta analysis of studies in (mainly) elderly people: 46% reduction in fall rates
- Prospective cohort study after discharge from stroke rehab: 64% reduction in fall rates
- RCT in chronic phase after stroke: reduction in fall rates non significant

Perturbation-based balance training

10 x 45 min, 5 weeks





Lean-and-release perturbations



Strong indicator of step quality

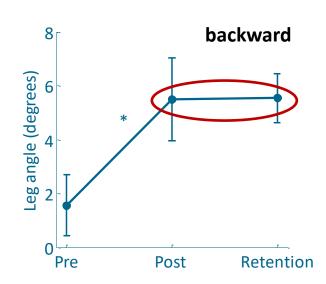
Perturbation-based balance training

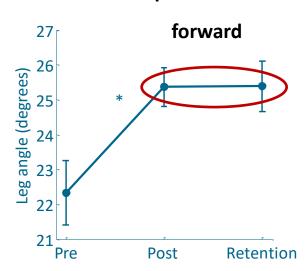
10 x 45 min, 5 weeks

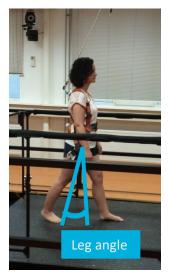




Lean-and-release perturbations







Strong indicator of step quality

Anticipatory control:
maintaining balance
during activities

Reactive control:
recovering from loss of
balance

Strategies

Anticipatory control: maintaining balance during activities

Reactive control: recovering from loss of balance

Damage control: impact reducing strategies



HEROES: Home-based ExeRgame fOr Enhancing resistance to falls after Stroke

- Exergaming at home (avatar & biofeedback → stepping responses based on action observation and imagery)
- One real RCT balance perturbation training (1 hour on GRAIL)
- RCT (n=60) (2022 2023)
- Two months daily exercises
- Control: WII training
- Primary: quality of stepping response





Anticipatory control: maintaining balance during activities

Reactive control: recovering from loss of balance

Damage control: impact reducing strategies



HEROES: Home-based ExeRgame fOr Enhancing resistance to falls after Stroke

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- One real RCT balance perturbation training (1 hour on GRAIL)
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- Two months daily exercises
- Control: WII training
- Primary: quality of stepping response



Academic participants: Radboudumc, VUMC, UT Clinical participants: Revant, Klimmendaal, Maartenskliniek,

MRC, Beatrixoord

Industrial partner: Motek Medical













Summary

Dynamic balance deficits are important determinants of falls after stroke

First evidence for efficacy of **exercise training** for falls prevention: balance training & gait training (Cochrane review 2019)

- Combination of feedforward and reactive balance training
- Great emphasis on gait adaptability training



Summary

Dynamic balance deficits are important determinants of falls after stroke

First evidence for efficacy of **exercise training** for falls prevention: balance training & gait training (Cochrane review 2019)

- Combination of feedforward and reactive balance training
- Great emphasis on gait adaptability training

Questions for future studies:

- Timing?
- Dosing?
- Tailoring?
- Working mechanisms?



Our team

















Funding sources

ZonMw











Poll 1

Wat is de belangrijkste oorzaak van valincidenten na CVA?

- 1. (Externe) omgevingsomstandigheden
- 2. (Intrinsieke) balansproblemen
- 3. Sleepvoet / struikelen
- 4. Spasticiteit

Poll 2

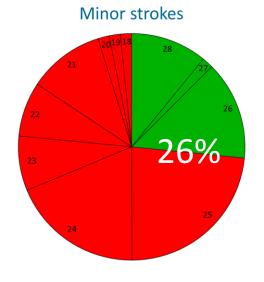
De volgende populaties tonen een verhoogde valincidentie t.o.v. gezonde controles:

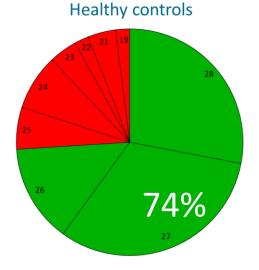
- 1. 'Major' stroke (evidente tekenen van motorisch hemibeeld)
- 2. 'Minor' stroke (hooguit subtiele tekenen van motorisch hemibeeld)
- 3. Beide groepen

People with minor stroke

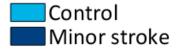
| Participant characteristics | Minor strokes (n=64) | Controls (n=50) |
|---|----------------------|-----------------|
| Age (years); mean (range) | 63.8 (40-85) | 63.6 (42-82) |
| Montreal Cognitive Assessment; median (range) | 27 (24-30) | 29 (24-30) |
| Fugl-Meyer Assessment – LE; median (range) | 28 (24-28) | |

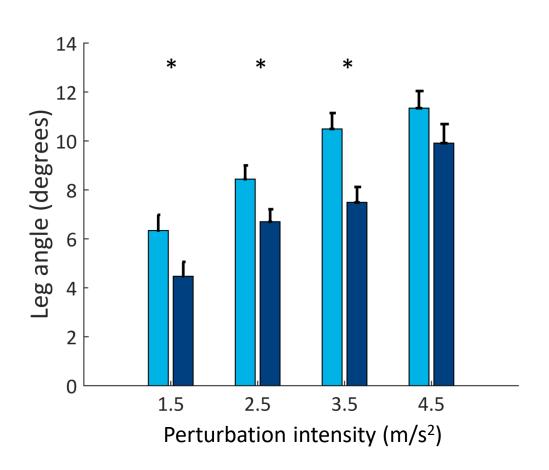
MiniBEST: Few people with minor stroke with (near-) maximum scores (≥26 pt)

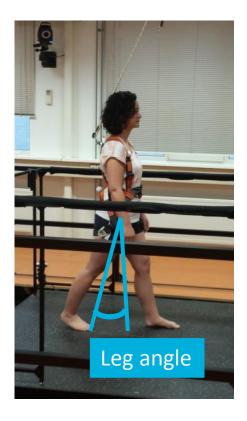




People with minor stroke







People with minor stroke

Minor strokes (n=62)





VS.



1.1 falls per person-year

0.52 falls per person-year