

European NPH study:

*NPH outcome scale
and
predictors of outcome*

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Data on 142 patients

The neuropsychology of iNPH: findings and evaluation of tests in the European multicentre study.

Hellström P, Klinge P, Tans J, Wikkelsø C.

Clin Neurol Neurosurg. 2012 Feb;114(2):130-4. Epub 2011 Oct 22.

One year outcome in the European Multicentre Study on iNPH

Klinge, P.1, Hellström, P.2, Tans, J.3 and Wikkelsø, C.2

Accepted for publication Acta Neurologica Scan 2012

A new scale for assessment of severity and outcome in iNPH.

Hellström, P. 1, Klinge, P.2, Tans, J.3 and Wikkelsø, C.1

Accepted for publication Acta Neurologica Scan 2012

*Participants in the European multi-centre
study on the Predictive value of Rout and CSF*

TT.

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Study protocol consistent with INPH Guidelines Recommendations



Entry based on clinical and radiological criteria (“typical” and “questionable” iNPH)

Exclusion criteria (Secondary NPH, non-communicating H., ICP at baseline > 18mmHg)

Tap test response after 3 hours, Resistance to CSF outflow, Compliance and CSF biomarker

**VP shunt (Codman programmable valve - 120mmH2O)
Shunt function assessment at one months**

**Outcome after 1, 3,12 m
(MMSE, Rankin-Scale/ Psychometric and motor test battery
=composite NPH scale)**

NPH Classification

Typical INPH

Clinical:

- o Gait disturbance unexplained by other conditions with disturbed tandem walking, multistep turning, small steps, wide base
- o Mild to moderate cognitive deficit, MMSE 21-29

Radiological:

- o no cortical infarcts or other relevant parenchymal lesions, lacunar infarcts < 1 cc allowed
- o temporal horns and 3rd ventricle relatively enlarged
- o mild cortical atrophy and Leuco- araiosis may be present

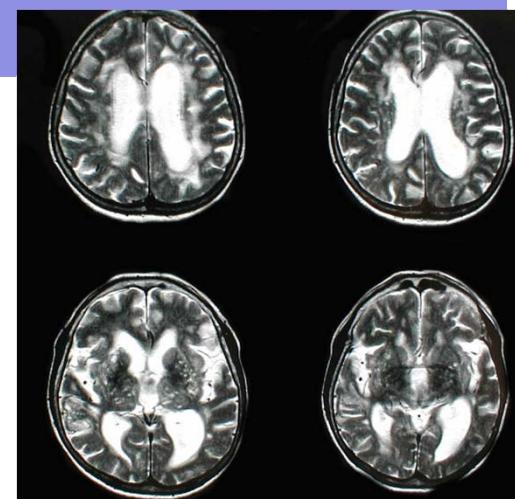
Questionable INPH

Clinical:

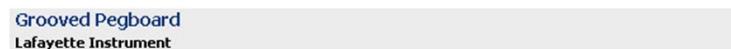
- o Any gait disturbance of both legs, not typical and entirely explained for but compatible with INPH
- o Any cognitive deficit not typical for INPH or MMSE <= 21 or no cognitive deficit (MMSE 30)

Radiological:

- o no major parenchymal lesions, cortical and lacunar infarcts >1cc are allowed
- o Cortical atrophy and moderate to severe leuco- araiosis may be present

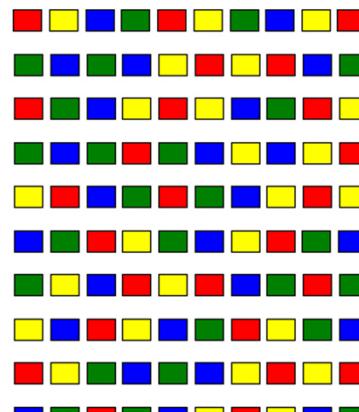


Cognitive test battery and outcome



Evaluates lateralized brain damage in adults, adolescents, and children.

Purpose:	Evaluates lateralized brain damage whenever manual dexterity is at issue
Age Range:	Child Adolescent Adult
Admin:	Individual
Time:	Varies
Qualification:	<u>B</u>
Sample Reports:	N/A



green blue red yellow green red blue green blue yellow
red yellow blue green blue yellow green blue yellow red
green yellow red green yellow blue red yellow green blue
red green blue green blue yellow blue green red yellow
red blue yellow red green yellow red green blue red
green yellow green red blue green blue yellow red yellow
blue red green yellow green blue yellow red blue yellow
blue red yellow blue red yellow green red blue red
blue green red yellow blue green red yellow green blue
yellow red green yellow red green blue green red yellow

Demographics

	10 ms walk at free pace (n= 163)	Neuropsychologic al assessment (n=122)	Ordinal ratings of gait, balance and continence (n=81)
Demography			
Age, mean (SD)	70 (10)	69 (9.5)	70 (8.7)
Sex (m/f)	92/71	75/47	49/34
Education, mean(SD)	11 (3.9)	11 (3.8)	11 (4.0)
MMSE, mean (SD)	24.4 (4.9)	24.1 (5.1)	23.8 (5.7)
Comorbidity			
Hypertension	42%	43%	44%
Cardiovasc. disease	18%	18%	18%
Diabetes	12%	12%	12%
Vascular disease	16%	15%	15%
Previous stroke	5%	6%	6%

Domain Scores

Gait domain score

(Gait rating + walking 10 m, steps + walking 10 m, time)/ 3 (or number of available values, all converted units, see appendix 2)

Neuropsychological score

(Grooved pegboard (best hand) + Rey Auditory + Stroop Color naming + Stroop Response selection)/ 4 (or number of available values, all in converted units)

Balance score

(Balance rating in converted units)

Continence score

(Continence rating in converted units)

Total iNPH scale score

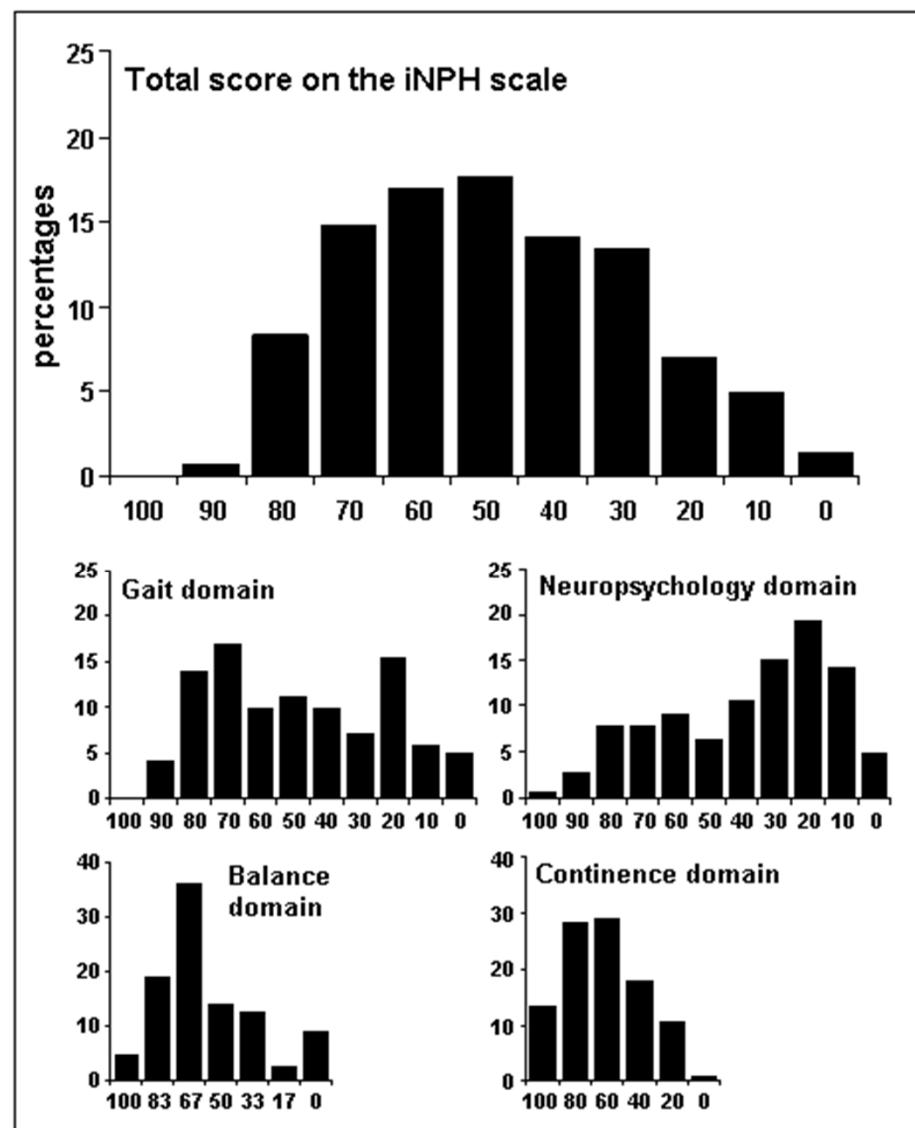
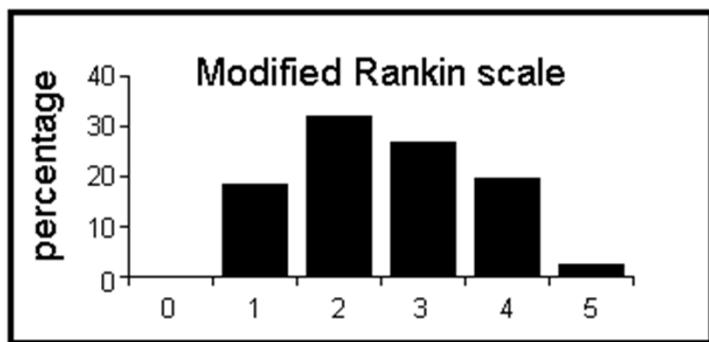
(2 x gait domain score + neuropsychological score + balance score + continence score)/ 5
(or number of available values).

Converted scores

Ordinal rating of gait	Walk 10 meters, free pace, number of steps	Walk 10 meters, free pace seconds	Balance domain
1 = 100	<15.50 = 100	<8.75 = 100	1=100
2 = 86	15.50-16.50 = 90	8.75-9.25 = 90	2=83
3 = 71	16.75-17.25 = 80	9.50-9.75 = 80	3=67
4 = 57	17.50-18.00 = 70	10.00-10.25 = 70	4=50
5 = 43	18.25-19.25 = 60	10.50-10.75 = 60	5=33
6 = 29	19.50-20.25 = 50	11.00-11.50 = 50	6=17
7 = 14	20.50-21.25 = 40	11.75-13.00 = 40	7=0
8 = 0	21.50-23.75 = 30 24.00-27.25 = 20 27.50-40.00 = 10 >40 or fail = 0	13.25-16.00 = 30 16.25-19.25 = 20 19.50-27.00 = 10 >27 or fail = 0	

Continence domain	Gr. pegboard, fastest trial	Rey, sum	Stroop, colour naming	Stroop, interference
1 = 100	<79 = 100	>44 = 100	<68 = 100	<132 = 100
2 = 80	79-87 = 90	38-44 = 90	68-77 = 90	132-160 = 90
3 = 60	88-96 = 80	32-37 = 80	78-81 = 80	161-188 = 80
4 = 40	97-105 = 70	30-31 = 70	82-87 = 70	189-210 = 70
5 = 20	106-114 = 60	28-29 = 60	88-96 = 60	211-239 = 60
6 = 0	115-128 = 50	26-27 = 50	97-106 = 50	240-298 = 50
	129-144 = 40	22-25 = 40	107-121 = 40	299-385 = 40
	145-173 = 30	19-21 = 30	122-134 = 30	386-600 = 30
	174-245 = 20	15-18 = 20	135-171 = 20	> 600 = 20
	246-600 = 10	11-14 = 10	172-300 = 10	fail = 10
	>600 or fail = 0	<11 or fail = 0	>300 or fail = 0	

Pre op



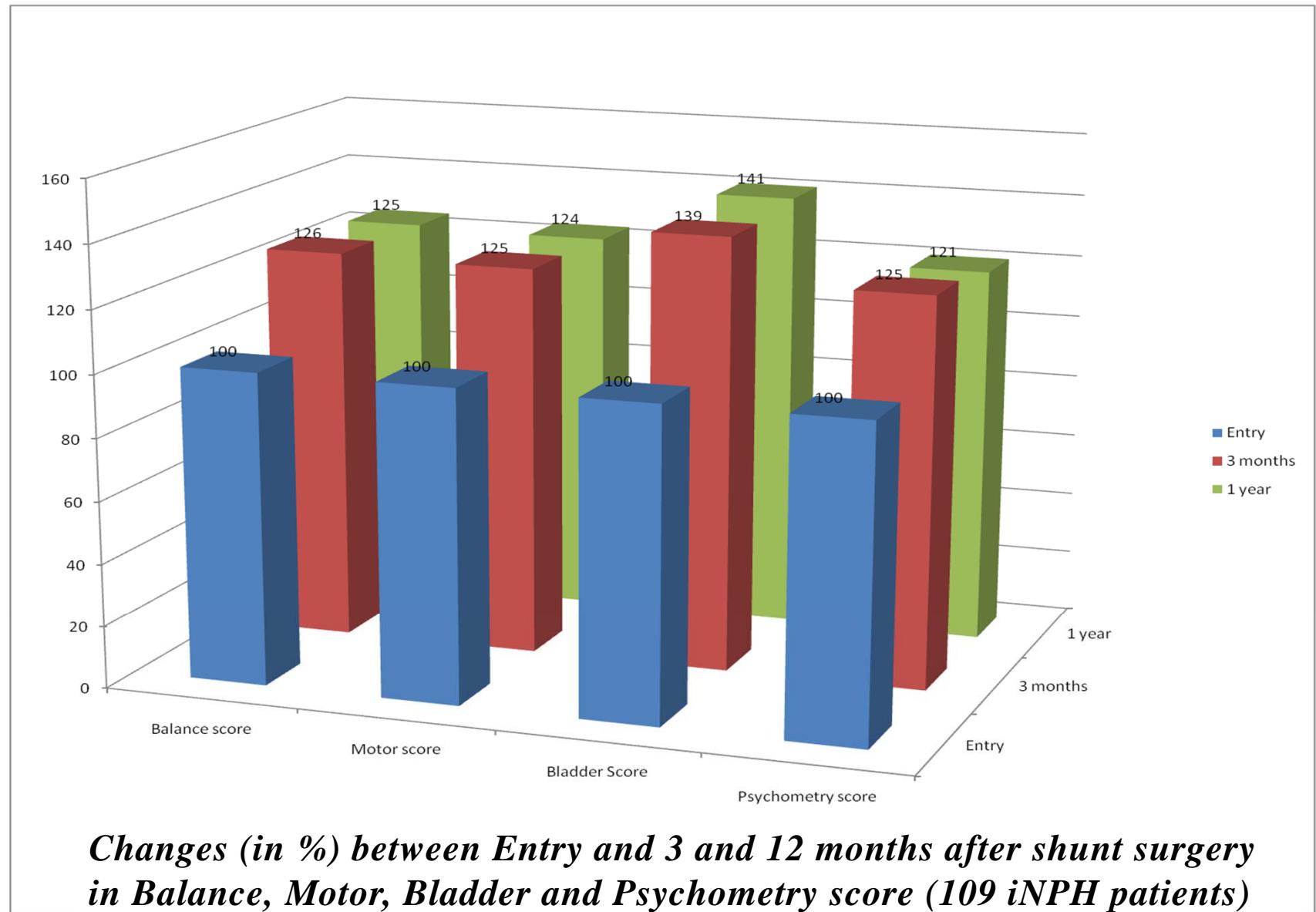
One year outcome in 142 iNPH patients included in the European Multicentre Study.

The patients were and classified as typical or questionable iNPH. Re-examinations 12 months after shunt insertion could be performed in 115 patients and outcome was assessed by the modified Rankin scale (mRs) and a new age normed iNPH grading scale. Improvement was defined as 1 or more steps on the mRs and 5 or more points on the iNPH scale.

69 % of the patients were improved one year after shunt treatment according to the mRs and 84% according to the new iNPH scale. The proportion of patients able to live independently (scores 0-2 on the mRs) was increased from 53 % before to 82 % 12 months after surgery.

Neither classification (typical or questionable iNPH) nor comorbidity (absence or presence of vascular risk factors) affected the level of improvement.

The TRIAD outcome after shunt



Cognitive outcome (Per Hellström et al.)

	Entry	3 months	1 year
<i>Neuropsychological test</i>			
	Performing normally	>1sd Imp/ Performing normally	1sd Imp/ Performing normally
Grooved Pegboard			
Dominant hand	12 %	61 % / 22 %	56 % / 19 %
Non-dominant hand	16 %	62 % / 30 %	54 % / 28 %
Sum of both hands	15 %	59 % / 26 %	56 % / 21 %
Rey AVLT			
Sum of trials 1-5	23 %	16 % / 41 %	23 % / 44 %
Delayed Recall	45 %	20 % / 66 %	16 % / 68 %
Stroop test			
Color Naming	18 %	48 % / 25 %	41 % / 27 %
Response Selection	17 %	47 % / 34 %	43 % / 35 %
Increment	27 %	48 % / 39 %	49 % / 46 %

Rankin Scale and NPH Scale

1 year post surgery

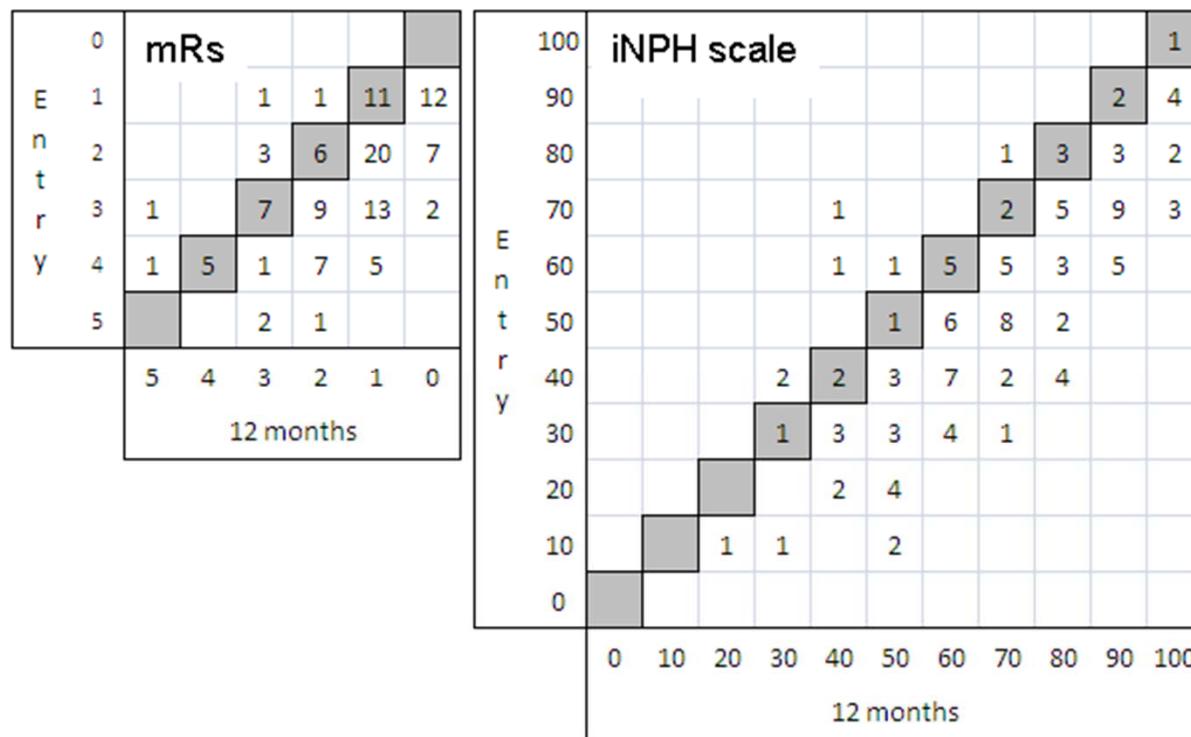
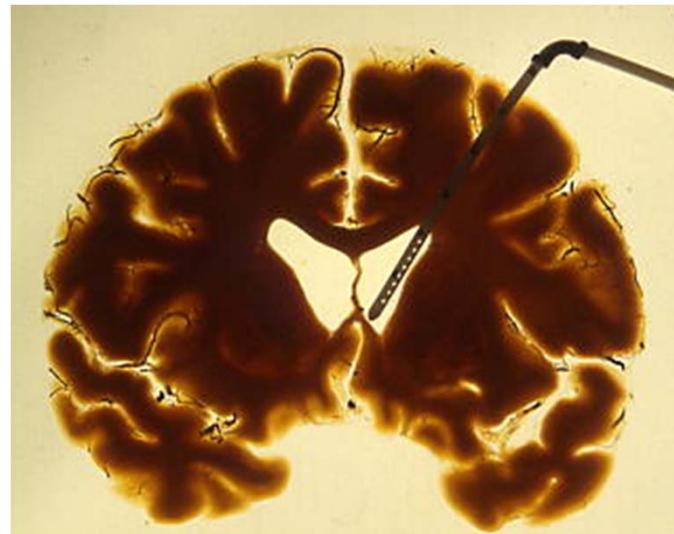
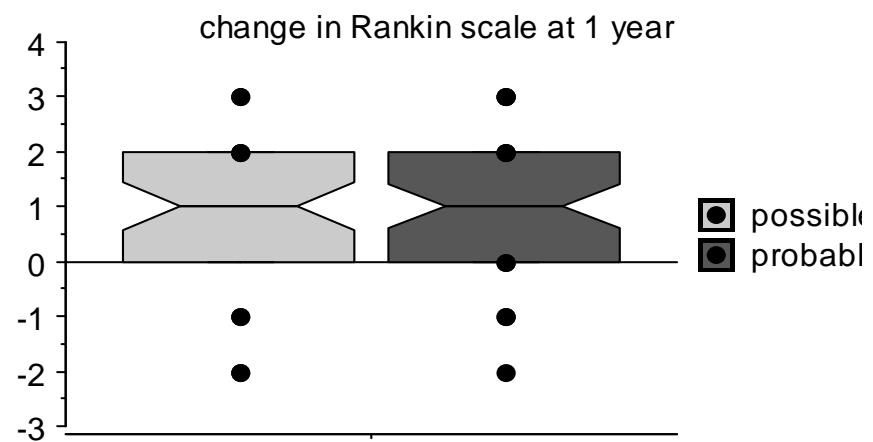
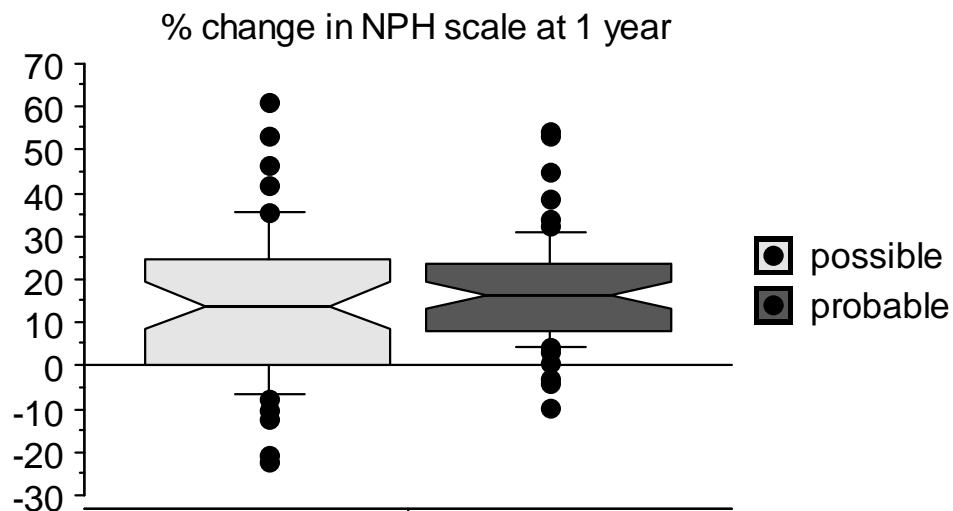


Figure 5. Distribution of changes in the modified Rankin scale and the iNPH scale (scores from entry to 12 months). The shaded cells represent no changes; cells to the right of this diagonal represent improvement.

Predictors ?



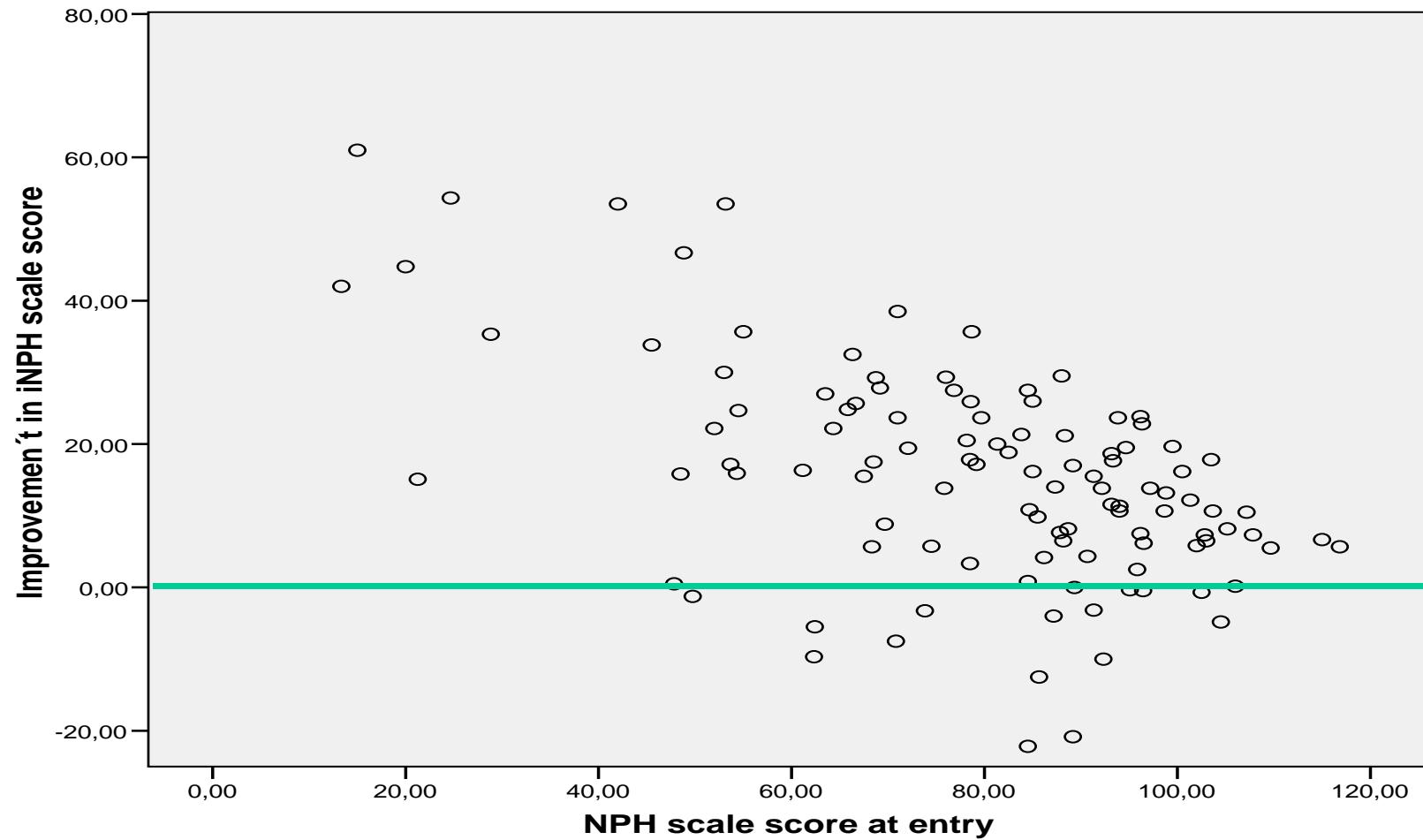
Typical vs. Questionable INPH



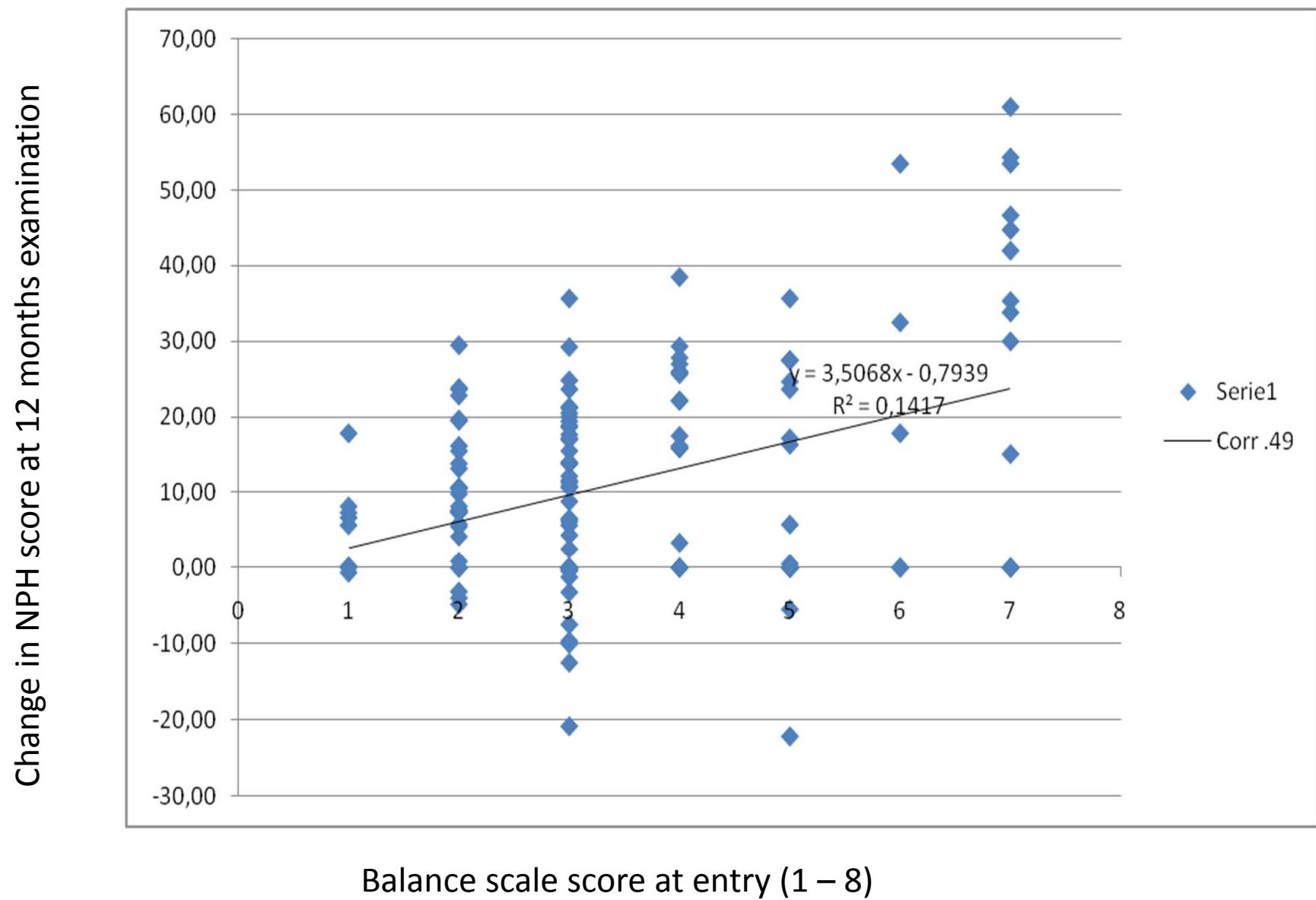
Demographics

	Responders (n=96)	Non-responders (n=19)
<i>Demography</i>		
Age (mean and range), years	70 (30 - 87)	72 (40 - 85)
Sex (Female/ male)	52 / 44	5 / 14*
Education (mean and range), years	10 (3 - 20)	10 (3 - 14)
MMSE (mean and range)	25 (14 - 30)	24 (18 - 30)
<i>Duration of symptoms (months)</i>		
Gait disturbance (median, IQR)	18 (12 - 30)	24 (12 – 24)
Cognitive impairment (median, IQR)	12 (6 - 24)	12 (12 - 36)
Urgency/incontinence (median, IQR)	11 (2 - 17)	8 (0 - 24)
<i>Co-morbidity and risk factors</i>		
Hypertension	53 (55 %)	6 (32 %) (T)
Smoking	29 (30 %)	5 (26 %)
Diabetes	20 (21 %)	5 (26 %)
Cardiac disease	18 (19 %)	1 (5 %)
Previous stroke	6 (6 %)	3 (16 %)
Peripheral vascular disease	7 (7 %)	2 (10 %)
<i>Typical neurological findings</i>	55 (58 %)	9 (47 %)
<i>Evans' Index</i> (mean, range)	.42 (.31 - .66)	.40 (.31 - .51)

Patients with pronounced symptoms improve more than those with less symptoms
The NPH score before surgery correlates with improvement ($r = - ,472 **$)



**Balance score before surgery was sign. related to improvement
(not motor, psych or continence) in a stepwise mult. Reg. ana.**



The European iNPH Multicenter study on the predictive values of Resistance to CSF outflow and the CSF Tap Test in patients with idiopathic Normal Pressure Hydrocephalus

Rout and effect of CSF TT showed no correlation with outcome measured by either domain or total iNPH score or modified Rankin Scale score. Only increase in the gait task (10 m of walking at free speed) of the CSF TT correlated significantly ($r = .22$, $p = .02$) with improvement in iNPH score. The positive predictive value of both tests was $> 90\%$, the negative predictive value $< 20\%$. Combining both tests did not improve their predictive power. No correlation was found between Rout and effect of CSF TT.

Predictive values TT (Jos Tans)

10% Y			
	Imp	Not imp	
Taptest \geq 10	29	10	39
Taptest<10	42	25	67
	71	35	106

Sens 41
 Spec 71
 PPV 74 PLR 1,43
 NPV 37 NLR 0,83
 TotPow 51

15% Y			
	Imp	Not imp	
Taptest \geq 10	25	14	39
Taptest<10	35	32	67
	60	46	106

Sens 42
 Spec 70
 PPV 64 PLR 1,37
 NPV 48 NLR 0,84
 TotPow 54

20% Y			
	Imp	Not imp	
Taptest \geq 10	21	18	39
Taptest<10	29	38	67
	50	56	106

Sens 42
 Spec 68
 PPV 54 PLR 1,31
 NPV 57 NLR 0,85
 TotPow 56

25% Y			
	Imp	Not imp	
Taptest \geq 10	17	22	39
Taptest<10	21	46	67
	38	68	106

Sens 45
 Spec 68
 PPV 44 PLR 1,38
 NPV 69 NLR 0,82
 TotPow 59

2x2 tables created according to the dichotomizations with regard to percentage of improvement according to the NPH scale.

Predictive values Rout (Jos Tans)

10% Y				15% Y			
	Imp	Not imp		Imp	Not imp		
Rout>18	29	6	35	Rout>18	24	11	35
Rout<18	46	29	75	Rout<18	39	36	75
	75	35	110		63	47	110
Sens	39			Sens	38		
Spec	83			Spec	77		
PPV	83	PLR	2,26	PPV	69	PLR	1,63
NPV	39	NLR	0,74	NPV	48	NLR	0,81
TotPow	53			TotPow	55		
20% Y				25% Y			
	Imp	Not imp		Imp	Not imp		
Rout>18	23	12	35	Rout>18	18	17	35
Rout<18	31	44	75	Rout<18	24	51	75
	54	56	110		42	68	110
Sens	43			Sens	43		
Spec	79			Spec	75		
PPV	66	PLR	1,99	PPV	51	PLR	1,71
NPV	59	NLR	0,73	NPV	68	NLR	0,76
TotPow	61			TotPow	63		

2x2 tables created according to the dichotomizations with regard to percentage of improvement according to the NPH scale.

Highlights and Summary

- Cognitive Tests are discriminative
- Useful in 90% patients (RAVL)
- NPH scale predictive and sensitive to improvement
- No predictors in CSF dynamics

Role and Need for Neuro-imaging is clear!