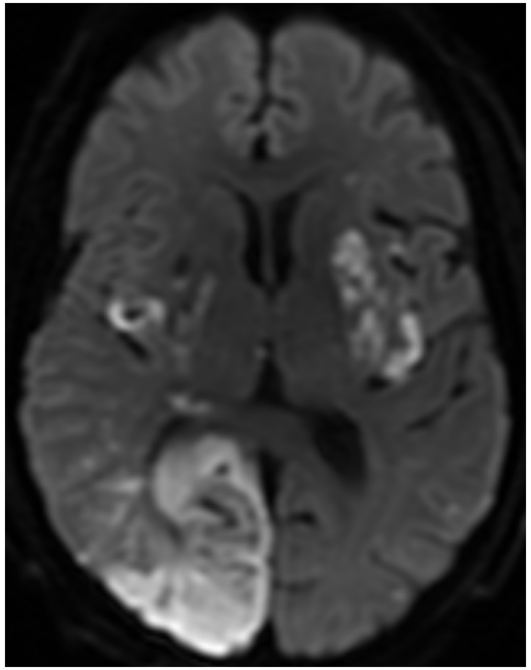
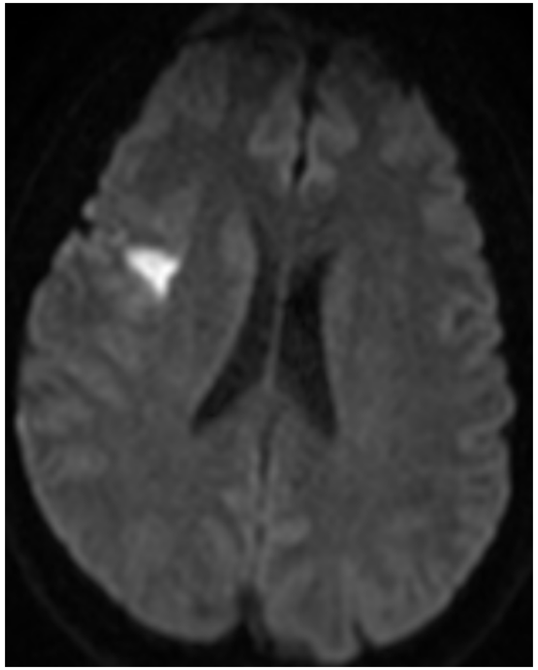
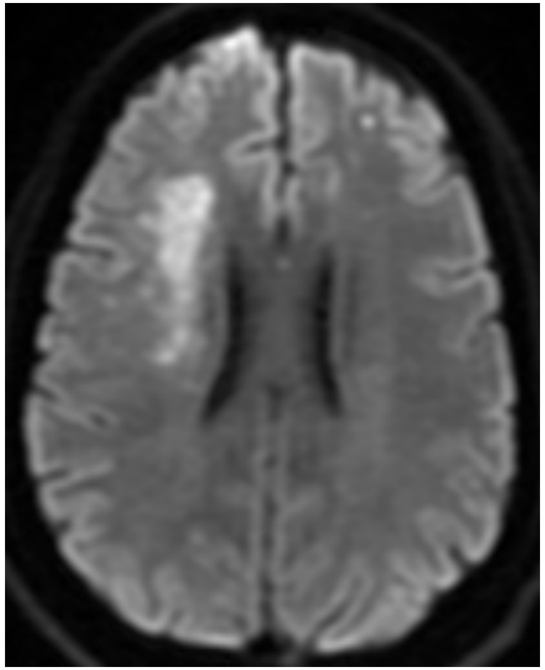
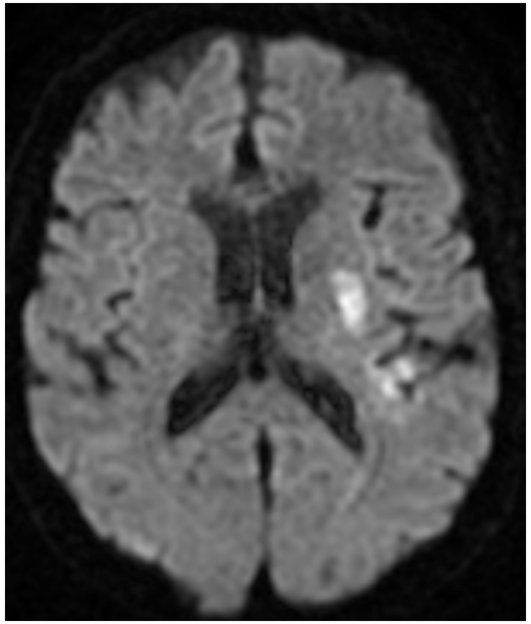
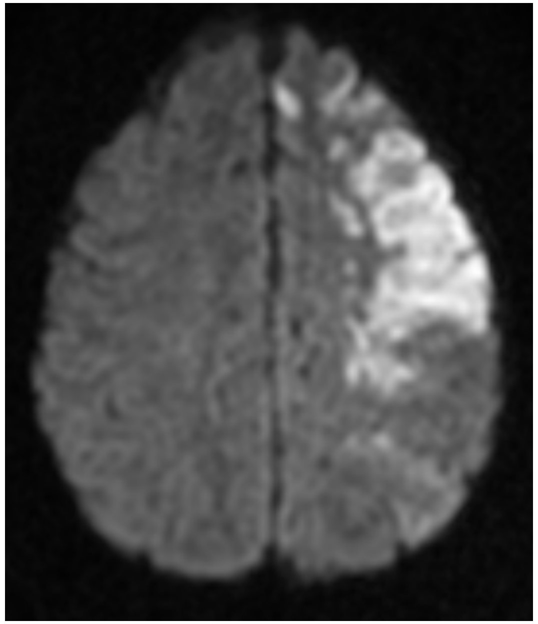
How do I get better after stroke?
An Inpatient Perspective

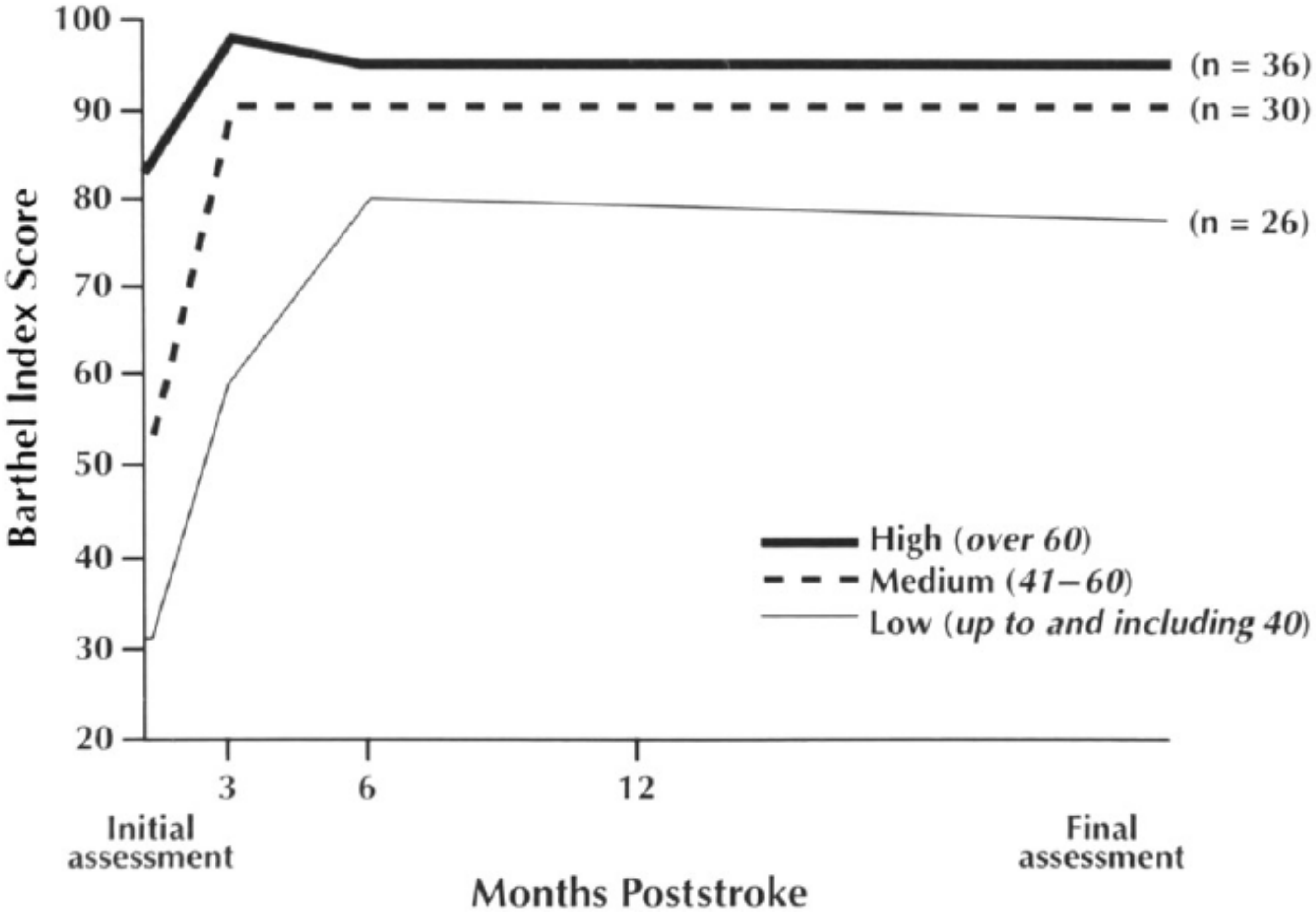
Kunal Agrawal, MD

Assistant Professor

University of California, San Diego

Pattern of recovery based on degree of disability



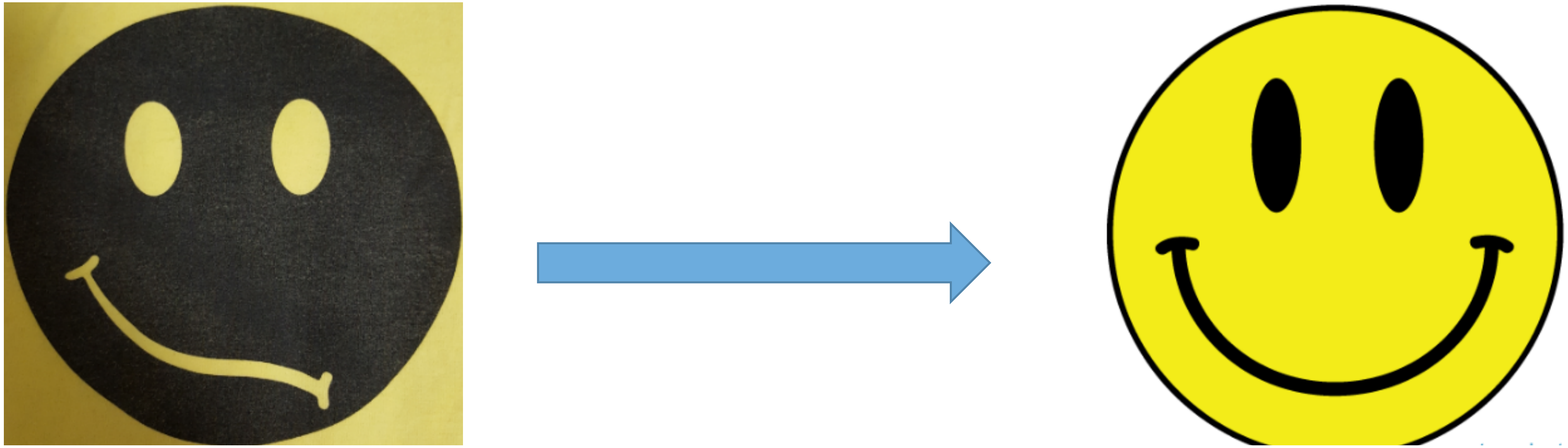
Wade DT, et al. *Arch Phys Med Rehabil.* 1983;64(1):24-28

Neuroplasticity

- The ability of the brain to change its structure/function as a result of internal and/or external constraints and goals
- Upregulation of genes and growth-promoting molecules within the first few days after stroke:
  - Dendritic branching and axonal sprouting
  - Synaptogenesis
  - Cell-cycle regulatory genes
- Also upregulation of growth inhibiting genes and molecules
- Spontaneous versus therapeutic-induced mechanisms after stroke

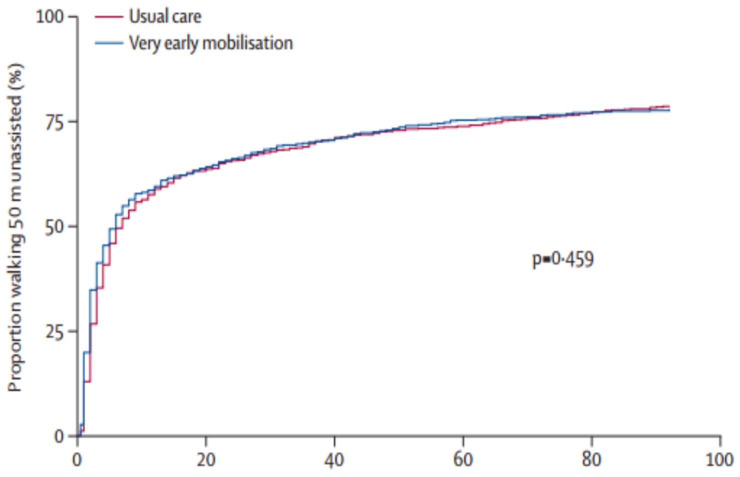
How do I get better in the hospital?
Three Components

1. Appropriate rehabilitation timing
2. Patient surveillance during hospital admission (i.e. preventing backward steps in rehabilitation)
3. Get out of the hospital as soon as possible!



First Component
Rehabilitation timing: When is the best time to start?

	Very early mobilisation (n=1038*)	Usual care (n=1045*)	Adjusted analysis		Unadjusted analysis	
			OR, generalised OR, or HR† (95% CI)	p value	OR generalised OR, or HR† (95% CI)	p value
Primary						
Favourable outcome‡	480 (46%)	525 (50%)	0·73 (0·59–0·90)	0·004	0·85 (0·72–1·0)	0·068
Secondary						
mRS category	..	..	0·94 (0·85–1·03)	0·193	0·94 (0·85–1·03)	0·202
0	90 (9%)	96 (9%)	..	..	..	..
1	200 (19%)	204 (19%)	..	..	..	..
2	190 (18%)	225 (22%)	..	..	..	..
3	238 (23%)	218 (21%)	..	..	..	..
4	140 (14%)	127 (12%)	..	..	..	..
5	92 (9%)	103 (10%)	..	..	..	..
6	88 (8%)	72 (7%)	..	..	..	..
Walking 50 m unassisted§	6 (5–7; n=1051)	7 (6–8; n=1049)	1·04 (0·94–1·15)	0·459	1·05 (0·95–1·16)	0·331



Number at risk*						
Usual care	1049	359	276	231	200	0
Very early mobilisation	1051	342	263	215	198	0

Figure 3: **Time to walking unassisted 50 m by 3 months**
*Number of patients who had not achieved walking.

Bernhardt, et al. *Lancet*. 2015;386:46–55

	Very early mobilisation (n=1054)	Usual care (n=1050)	p value	Median shift (95% CI)
Time to first mobilisation (h)	18·5 (12·8–22·3; n=1042*)	22·4 (16·5–29·3; n=1036*)	<0·0001	4·8 (4·1–5·7)
Frequency per person†	6·5 (4·0–9·5)	3 (2·0–4·5)	<0·0001	3 (3–3·5)
Daily amount per person (min)‡	31 (16·5–50·5)	10 (0–18)	<0·0001	21·0 (20–22·5)
Total amount per person (min)§	201·5 (108–340)	70 (32–130)	<0·0001	117 (107–128)

	Very early mobilisation (n=1054)	Usual care (n=1050)	OR or IRR* (95% CI)	p value
Death	88/1048 (8%)†	72 (7%)	1·34 (0·93–1·93)	0·113
Non-fatal serious adverse events			0·88 (0·72–1·07)	0·194
0	853 (81%)	842 (80%)	..	..
1	157 (15%)	146 (14%)	..	..
2	32 (3%)	41 (4%)	..	..
3	10 (1%)	16 (2%)	..	..
4	2 (<1%)	4 (<1%)	..	..
5	0	1 (<1%)	..	..
Immobility serious adverse events‡			0·92 (0·62–1·35)	0·665
0	1000 (95%)	997 (95%)	..	..
1	50 (5%)	46 (4%)	..	..
2	4 (<1%)	5 (1%)	..	..
3	0	2 (<1%)	..	..
4	0	0	..	..
5	0	0	..	..
Neurological serious adverse events‡			1·26 (0·95–1·66)	0·108
0	947 (90%)	967 (92%)	..	..
1	104 (10%)	78 (7%)	..	..
2	3 (<1%)	4 (<1%)	..	..
3	0	1 (<1%)	..	..
4	0	0	..	..

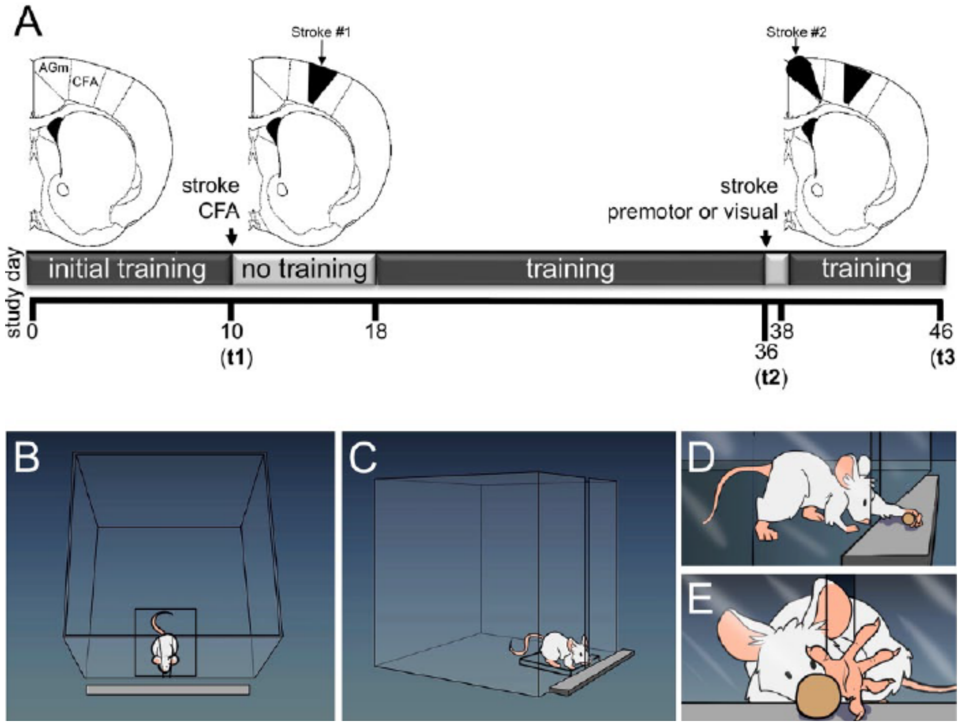
How do we explain these results?

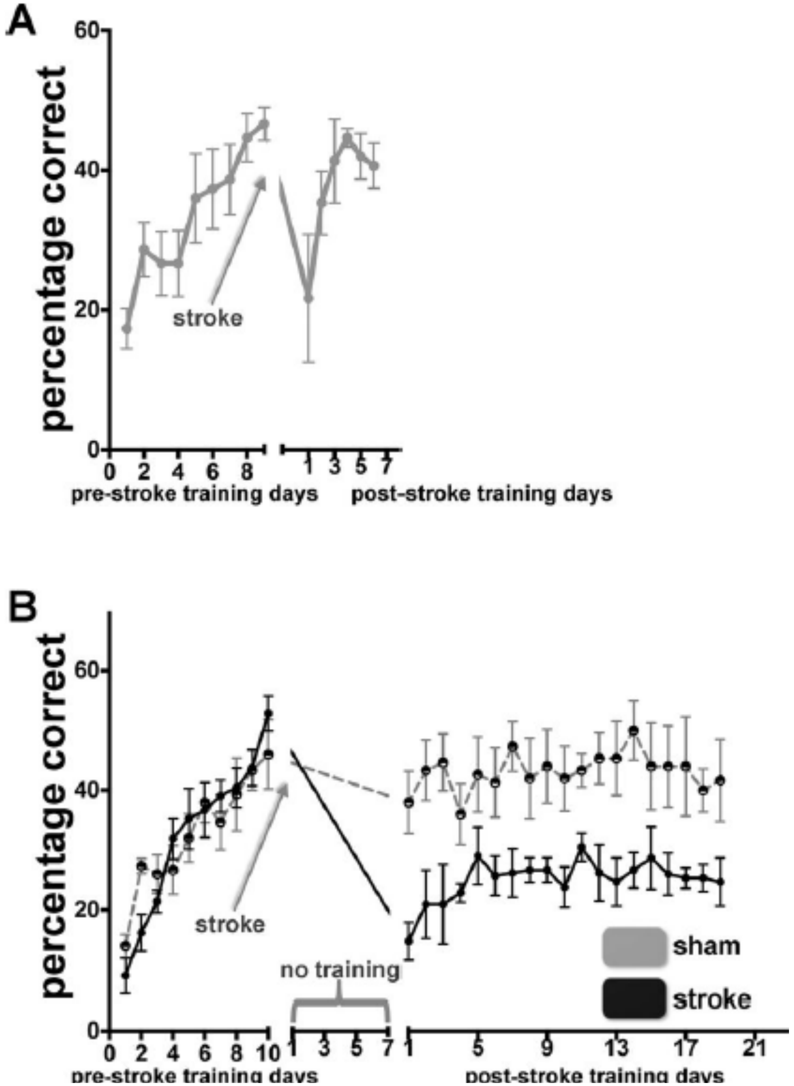
- Physiological?
- Intensity?
- Is early rehab bad?

Bernhardt, et al. *Lancet.* 2015;386:46–55

Something to think about:

Rodents do weird things…..





….But researchers are weirder.

Ng, et al. *Stroke*. 2015 Oct; 46(10):2951-60

Second Component
Patient Surveillance (preventing backward steps)

- Fear of falling
- Poststroke depression
- Contractures prevention and spasticity treatment
- Prevention of stroke medical complications

Rehab and the Fear of Falling

Up to 70% stroke patients fall during the first 6 months after hospital or rehab facility discharge

30-80% of stroke patients report various levels of fear associated with falling and mobility

Table 1 OR (95% CI) for demographic and functional characteristics when comparing patients with low and high fall-related self-efficacy ($n = 140$)

Explanatory variables	Low self-efficacy ($n = 70$)	High self-efficacy ($n = 70$)	Univariate analysis OR (95% CI)	Multivariate analysis OR (95% CI)
Aged 75 years or older, *n* (%)	43 (61)	28 (40)	2.4 (1.2–4.7)	1.5 (0.5–4.4)
Female sex, *n* (%)	38 (54)	24 (34)	2.3 (1.2–4.5)	1.8 (0.6–5.3)
Fallers, *n* (%)	42 (60)	16 (23)	5.1 (2.4–10.6)	5.0 (1.6–15.7)
Visual impairment, *n* (%)	39 (56)	17 (24)	3.9 (1.9–8.1)	2.3 (0.7–7.1)
Cognitive impairment, MMSE ≤ 23, *n* (%)	26 (37)	11 (16)	3.2 (1.4–7.1)	1.5 (0.4–5.9)
Low mood, GDS ≥ 6, *n* (%)	40 (57)	19 (27)	3.6 (1.8–7.3)	2.0 (0.7–6.3)
Motor impairment upper extremity, BL ≤ 56, *n* (%)	50 (71)	18 (26)	7.2 (3.4–15.2)	4.1 (1.4–11.9)
Motor impairment lower extremity, BL ≤ 35, *n* (%)	46 (67)	13 (19)	8.8 (4.0–19.2)	3.2 (1.0–10.2)
Impaired functional mobility, TUG > 14 s, *n* (%)	41 (63)	4 (6)	28.2 (9.1–87.1)	12.9 (2.5–66.3)
Impaired balance, BBS < 45 *n* (%)	39 (56)	5 (7)	16.4 (5.9–45.6)	0.5 (0.1–3.0)

Anderson, et al. *Int J Rehabil Res*. 2008;31:261-264

Nonnfallers with low self-efficacy had significant motor impairment and impaired functional ability. What does this mean in the setting of hospital rehab?

What about nonfallers with low self-efficacy who have good physical condition?

We need to correct the fear of falling perception and encourage therapy participation no matter the degree of impairment

Table 2 Patients with a history of falls: comparing patients with low and high fall-related self-efficacy (*n*=58)

	Low self-efficacy (*n*=42)	High self-efficacy (*n*=16)	χ^2	*P* value
Aged 75 years or older, *n* (%)	23 (55)	7 (44)	0.6	0.453
Female sex, *n* (%)	18 (43)	6 (37)	0.1	0.711
Visual impairment, *n* (%)	23 (55)	3 (19)	6.1	0.014
Cognitive impairment, MMSE ≤ 23, *n* (%)	19 (45)	2 (12)	5.4	0.020
Low mood, GDS ≥ 6, *n* (%)	26 (62)	5 (31)	4.4	0.036
Motor impairment upper extremity, BL ≤ 56, *n* (%)	29 (69)	3 (19)	11.9	0.001
Motor impairment lower extremity, BL ≤ 35, *n* (%)	30 (73)	1 (6)	20.8	<0.001
Impaired functional mobility, TUG >14 s, *n* (%)	28 (70)	1 (6)	18.6	<0.001
Impaired balance, BBS <45, *n* (%)	27 (64)	2 (12)	12.4	<0.001

Low fall-related self-efficacy=FES-S values below or at median.
High fall-related self-efficacy=FES-S values above median.
BBS, Berg Balance Scale; BL, Birgitta Lindmark motor assessment scale; GDS, Swedish version of the Geriatric Depression Scale; MMSE, Mini-Mental State Examination; TUG, Timed Up and Go test.

Table 3 Patients without a history of falls: comparing patients with low and high fall-related self-efficacy (*n*=82)

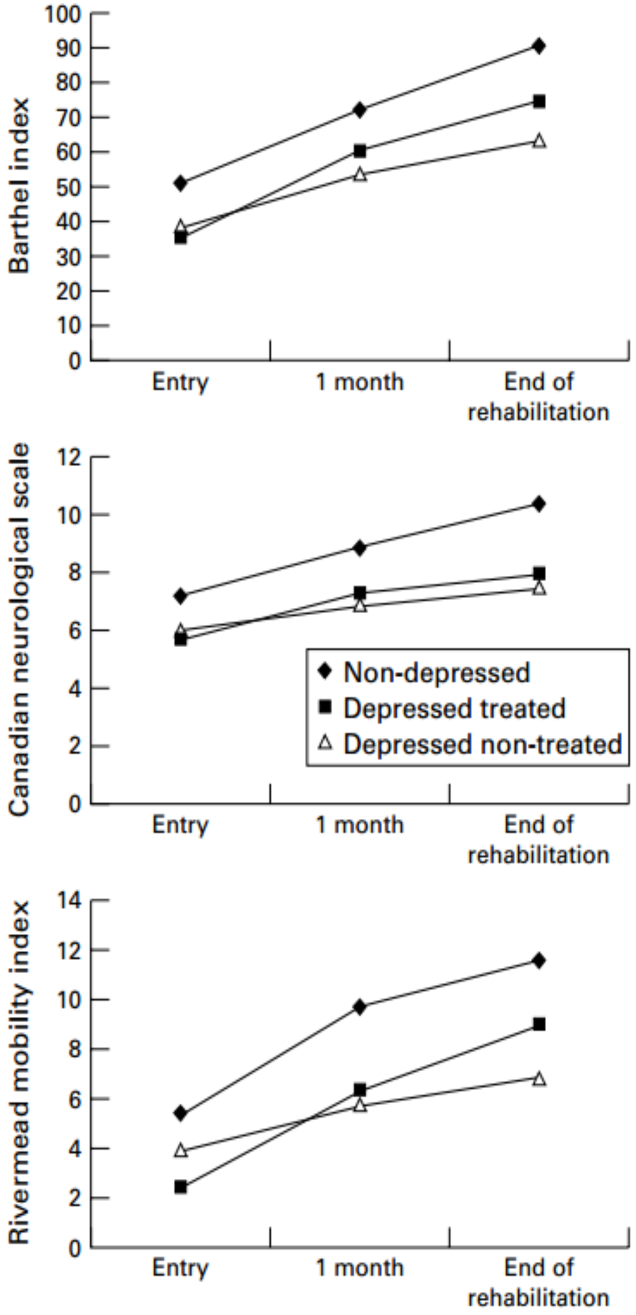
	Low self-efficacy (*n*=28)	High self-efficacy (*n*=54)	χ^2	*P* value
Aged 75 years or older, *n* (%)	20 (71)	21 (39)	7.8	0.005
Female sex, *n* (%)	20 (71)	18 (33)	10.8	0.001
Visual impairment, *n* (%)	16 (57)	14 (26)	7.7	0.005
Cognitive impairment, MMSE ≤ 23, *n* (%)	7 (25)	9 (17)	0.8	0.367
Low mood, GDS ≥ 6, *n* (%)	14 (50)	14 (26)	4.8	0.029
Motor impairment upper extremity, BL ≤ 56, *n* (%)	21 (75)	15 (28)	16.7	<0.001
Motor impairment lower extremity, BL ≤ 35, *n* (%)	16 (57)	12 (22)	10.0	0.002
Impaired functional mobility, TUG >14 s, *n* (%)	13 (52)	3 (6)	22.8	<0.001
Impaired balance, BBS <45, *n* (%)	12 (43)	3 (6)	17.2	<0.001

Anderson, et al. *Int J Rehabil Res*. 2008;31:261-264

Poststroke Depression

Depression reported in up to **33%** of stroke patients, compared to 13% of age- and sex-matched control subjects

Depression negatively affects a patient's ability to actively participate in rehabilitation therapies

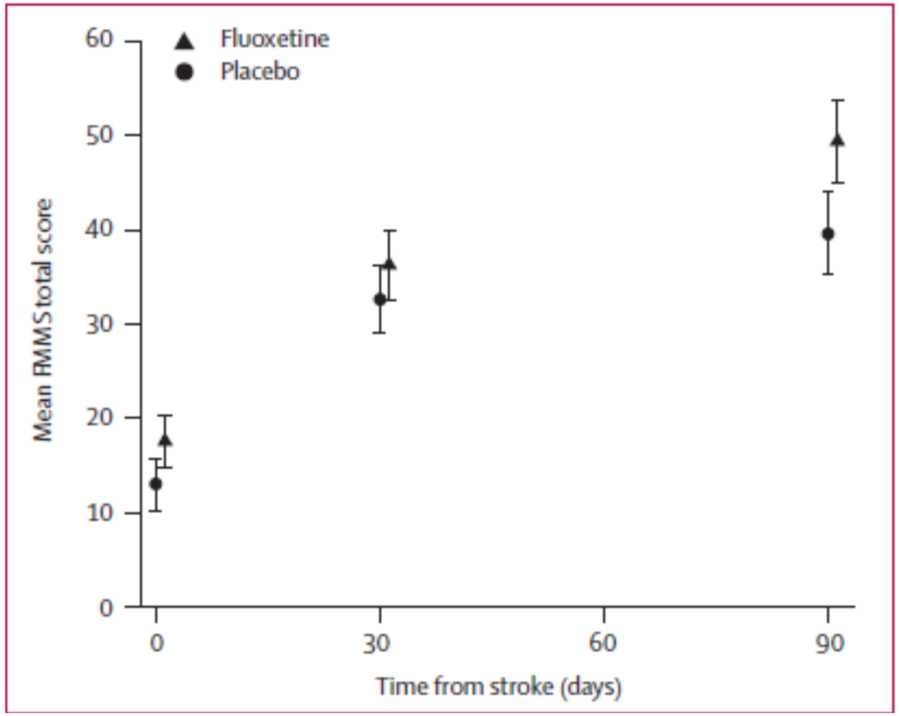


$p < 0.01$

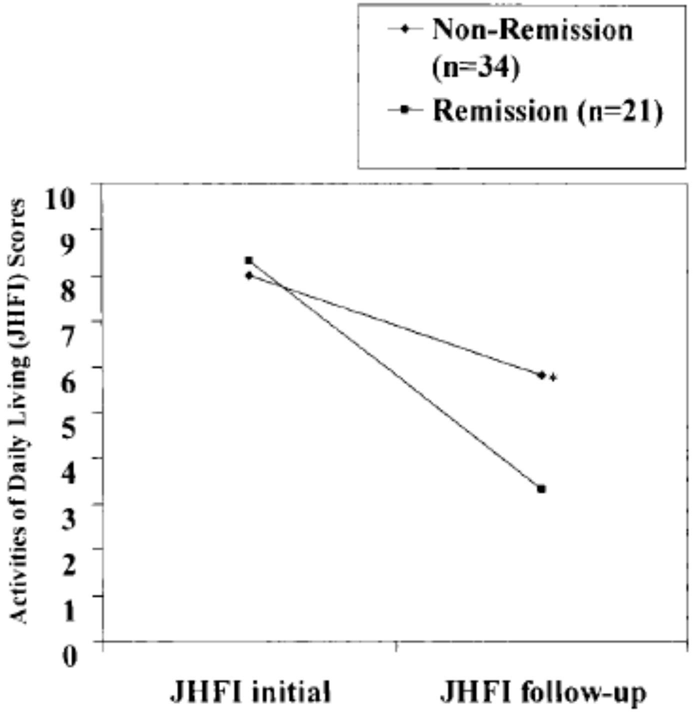
$p < 0.03$

$p < 0.0001$

Gainotti, et al. *J Neur Neurosurg Psych*. 2001;71:258–261



FLAME Trial: Fluoxetine versus Placebo
Treatment 5-10 after stroke
Outcome: change in FMMS



Effect of depression remission on activities of daily living
Longitudinal observ. Study
Eval for mood improvement

Early identification of depression during an inpatient hospitalization after stroke is CRITICAL, and provides opportunities for appropriate therapy with possible subsequent impact on stroke recovery

Chollet F, et al. *Lancet Neurol*. 2011 Feb;10(2):123-30
Chemerinski E, et al. *Stroke*. 2001 Jan;32(1):113-7

Third Component
Get our patients discharged!

Early Supported Discharge

Links inpatient care with community services and allows certain patients to be discharged home sooner with support of the rehabilitation team

Meta-Analysis: 11 trials (usu. care v. ESD)
Primary outcome: death/dependency

Overall, significant reduction in the odds of death or dependency among patients assigned ESD

Outcome	Trials	Patients randomised	Summary statistic	Summary result (95% CI)	p
Patients' outcomes					
Death or dependency	11	1597	OR	0·79 (0·64 to 0·97)	0·02
Death	11	1597	OR	0·90 (0·64 to 1·27)	0·56
Death or institution	9	1398	OR	0·74 (0·56 to 0·96)	0·02
ADL score	6	811	SMD	0·04 (−0·10 to 0·17)	0·60
Extended ADL score	9	1051	SMD	0·12 (0 to 0·25)	0·05
Subjective health status score	10	1154	SMD	−0·02 (−0·15 to 0·12)	0·87
Mood score	8	851	SMD	−0·06 (−0·19 to 0·07)	0·38
Satisfied with outpatient services	5	513	OR	1·60 (1·08 to 2·38)	0·02
Carers' outcomes					
Subjective health status score	6	613	SMD	0 (−0·25 to 0·24)	0·97
Mood score	2	58	SMD	−0·19 (−1·60 to 1·22)	0·79
Satisfied with outpatient services	4	279	OR	1·56 (0·87 to 2·81)	0·14
Resource outcomes					
Length of hospital stay	9	1015	WMD	−7·7 (−10·7 to −4·2)	<0·0001
Readmission to hospital	5	633	OR	1·14 (0·80 to 1·63)	0·48

OR=odds ratio; SMD=standardised mean difference; WMD=weighted mean difference. Results are presented as the pooled summary statistic for each outcome comparing ESD services with conventional care.

***Table 2:* Summary of all outcomes for ESD services versus conventional care**

Langhorne P, et al. *Lancet*. 2005 Feb;365(9458):501-6

Disposition depends on assessment of intensity level

Inpatient Rehab Facilities

Long-Term Care Hospital

Skilled Nursing Facilities

Home Health Care Agency

Outpatient Rehab

Nursing Homes

Summary

- Each healthcare professional contributes to the components of stroke recovery while in the hospital
  - Importance of a multidisciplinary team
- Therapists: Heterogeneous and involves broad array of techniques
  - Current rehabilitations programs emphasize repetition, gradually progressive task difficulty, and functional practice
  - Individually-tailored to the patient's deficits

Winstein CJ, et al. *Stroke*. 2016 Jun;47(6):e98-e169

Current Reality of Stroke Rehab

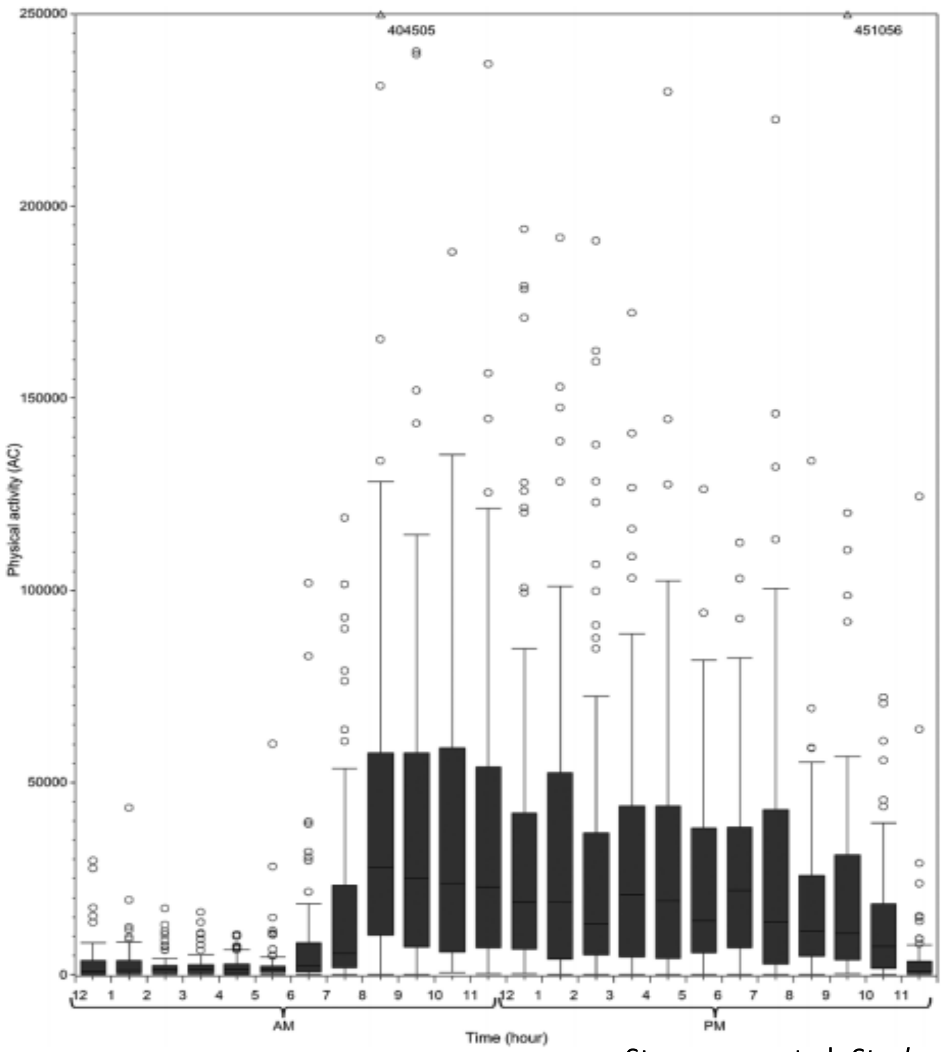
- Inactivity in the hospital setting
- Compensatory as opposed to restorative techniques
- Decreased available time to conduct therapy
- Decreased access to post-hospital rehab

Reality: Inpatient activity throughout the day

Within the first few weeks of stroke, patients generally have low level of physical activity

44-98% of daytime observations are spent inactive in bed

Comprehensive stroke units, **30-46%** of daytime observations are inactive



Strommen, et al. *Stroke*. 2014 Dec; 45(12):3649-55

Reality: PAC Utilization and Readmissions (2006)

Table 3-7. First Site of PAC, by Acute Index Admission DRG, Top 20 DRGs by Volume for PAC Users, 2006

Acute Index DRG[1]	Total Hospital Discharges for PAC Users	Percent Using PAC[2]	Percent of Beneficiaries Discharged to Each Setting[3]				
			LTCH	IRF	SNF	HHA	Outpatient
014: Specific Cerebrovascular Disorders Except TIA	4,882	58.1	1.8	34.4	35.6	19.7	8.5

Figure 3-1. Distribution of Freestanding versus Hospital-Based SNFs, IRFs, and Freestanding and HWH LTCHs in 2007

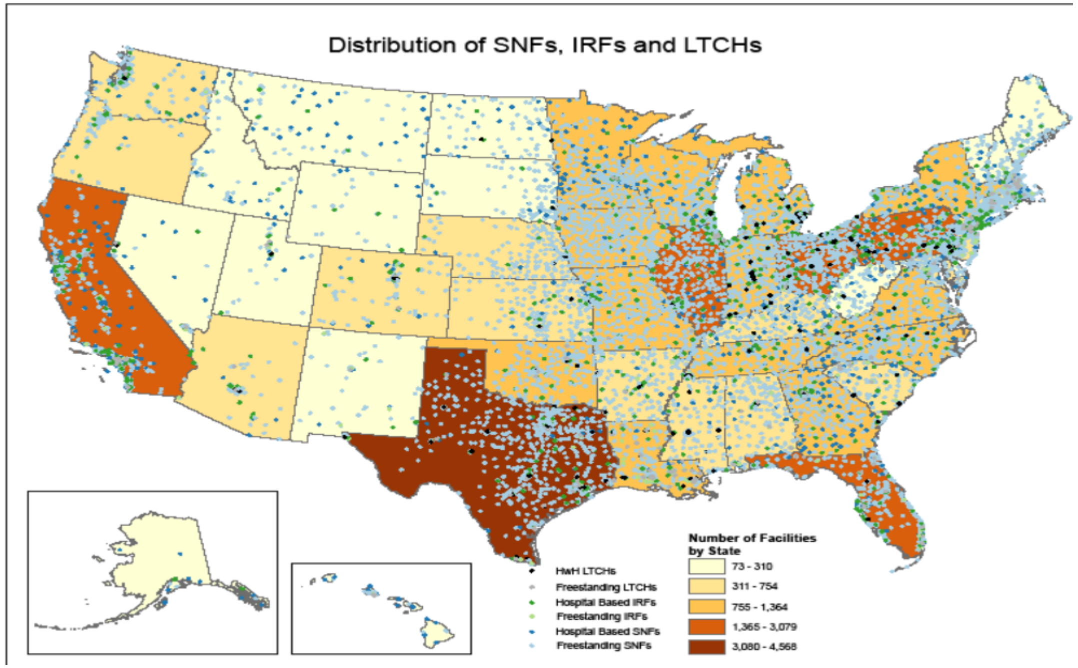


Table 3-10. Readmissions During Episodes of Post Acute Care, Overall, and for Top 10 DRGs by Volume, 2006

	N PAC Users	Mean Episode Payments	Percent with Readmission	Mean Readmission Payments
Overall Sample of PAC Users	109,236	$30,028	30.5	$15,636
Index Acute Admission DRG[1] (Top 10 DRGs for PAC Users)				
544 Major Joint Replacement or Reattachment of Lower Extremity	15,261	$23,985	14.3	$12,952
014 Specific Cerebrovascular Disorders Except TIA	4,882	$33,484	32.6	$13,409
089 Simple Pneumonia & Pleurisy Age >17 w CC	4,675	$20,476	31.6	$13,023
127 Heart Failure & Shock	4,096	$26,076	43.1	$17,449
210 Hip & Femur Procedures except Major Joint Age >17 w CC	3,552	$36,882	30.6	$12,919
088 Chronic Obstructive Pulmonary Disease	2,439	$21,118	36.3	$14,888
320 Kidney & Urinary Tract Infections Age >17 w CC	2,396	$22,039	31.8	$12,994
416 Septicemia Age >17	1,996	$30,627	33.1	$16,956
316 Renal Failure	1,848	$28,729	38.4	$16,999
296 Nutritional & Misc Metabolic Disorders Age >17 w CC	1,757	$22,852	33.1	$15,078

American Heart Association | American Stroke Association. MEDPAGE TODAY

Cardiovascular Daily

Latest Breaking Cardiology News from
The American Heart Association and MedPage Today.

Cardiovascular Daily

Latest Breaking Cardiology News from
The American Heart Association and
MedPage Today.

MEDPAGE TODAY American Heart Association | American Stroke Association.

Wednesday: Focus on Stroke

May 04, 2016

In-Patient Facilities Better for Stroke Rehab

AHA/ASA release first adult stroke rehab and recovery guidelines Read more

Stroke Care Transition Program Cut Readmission

Calling patients is no substitute for clinic visits, researchers say

Read more

RESOURCE CENTER

Treatable Causes of Fatigue in Patients with MS

AHA/ASA Guideline

Guidelines for Adult Stroke Rehabilitation and Recovery

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

Endorsed by the American Academy of Physical Medicine and Rehabilitation and the American Society of Neurorehabilitation

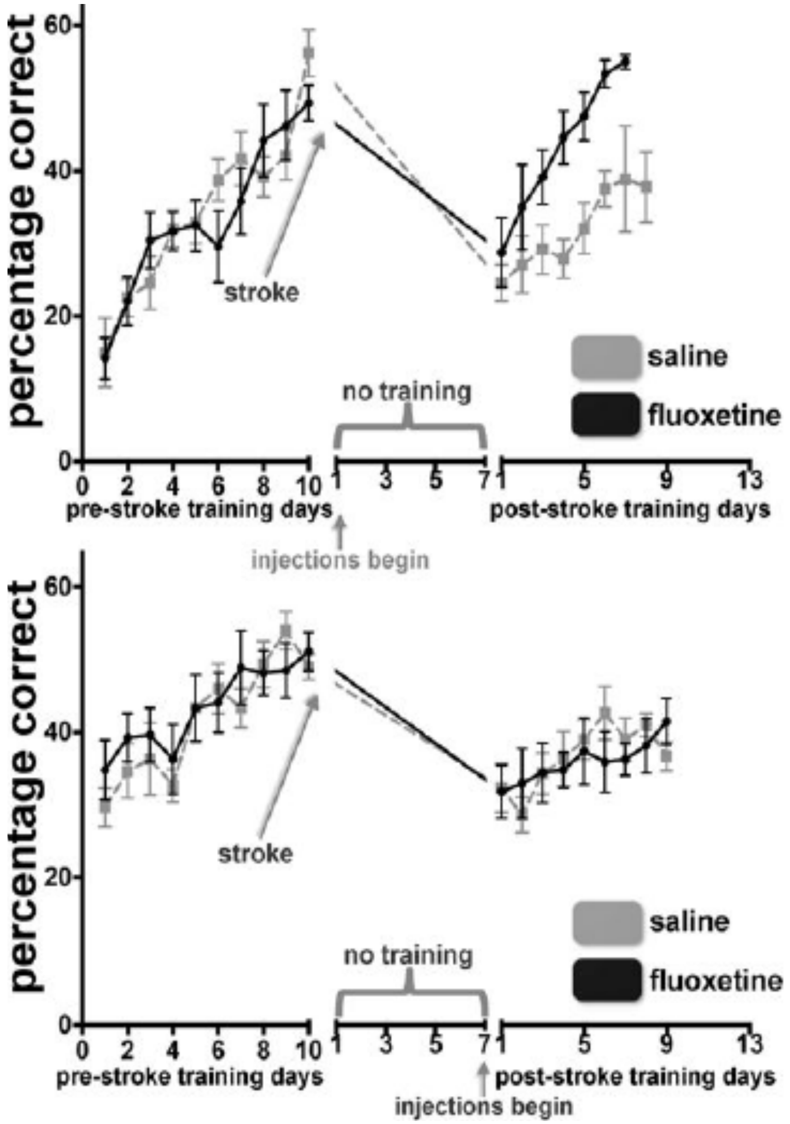
The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists and the American Congress of Rehabilitation Medicine also affirms the educational value of these guidelines for its members

Carolee J. Winstein, PhD, PT, Chair; Joel Stein, MD, Vice Chair;
Ross Arena, PhD, PT, FAHA; Barbara Bates, MD, MBA; Leora R. Cherney, PhD;
Steven C. Cramer, MD; Frank Deruyter, PhD; Janice J. Eng, PhD, BSc; Beth Fisher, PhD, PT;
Richard L. Harvey, MD; Catherine E. Lang, PhD, PT; Marilyn MacKay-Lyons, BSc, MScPT, PhD;
Kenneth J. Ottenbacher, PhD, OTR; Sue Pugh, MSN, RN, CNS-BC, CRRN, CNRN, FAHA;
Mathew J. Reeves, PhD, DVM, FAHA; Lorie G. Richards, PhD, OTR/L; William Stiers, PhD, ABPP (RP);
Richard D. Zorowitz, MD; on behalf of the American Heart Association Stroke Council, Council
on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on
Quality of Care and Outcomes Research

Stroke rehabilitation in development

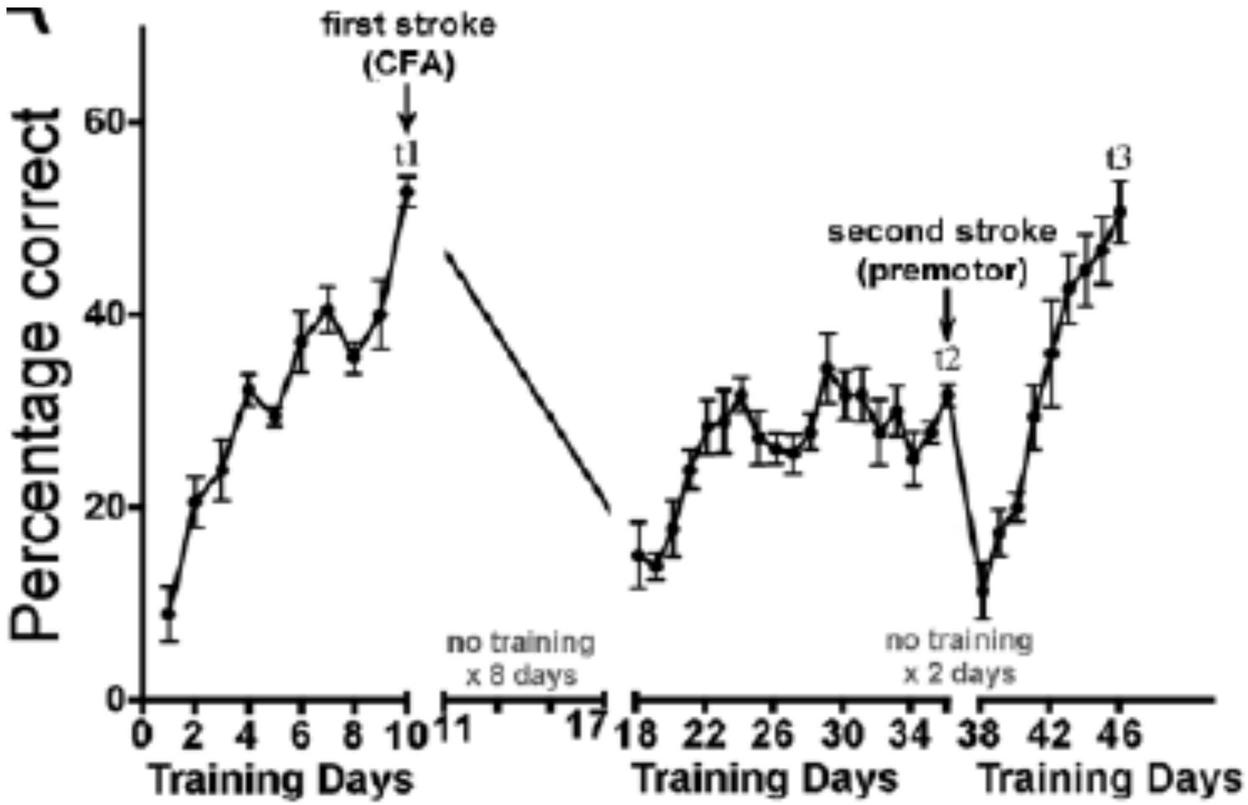
- Combining rehabilitation concepts with medical therapeutics
- Stem cells and recovery
- Combining rehabilitation with technology to improve access
- Utilizing an enriched environment to provide a more novel approach to stroke rehab

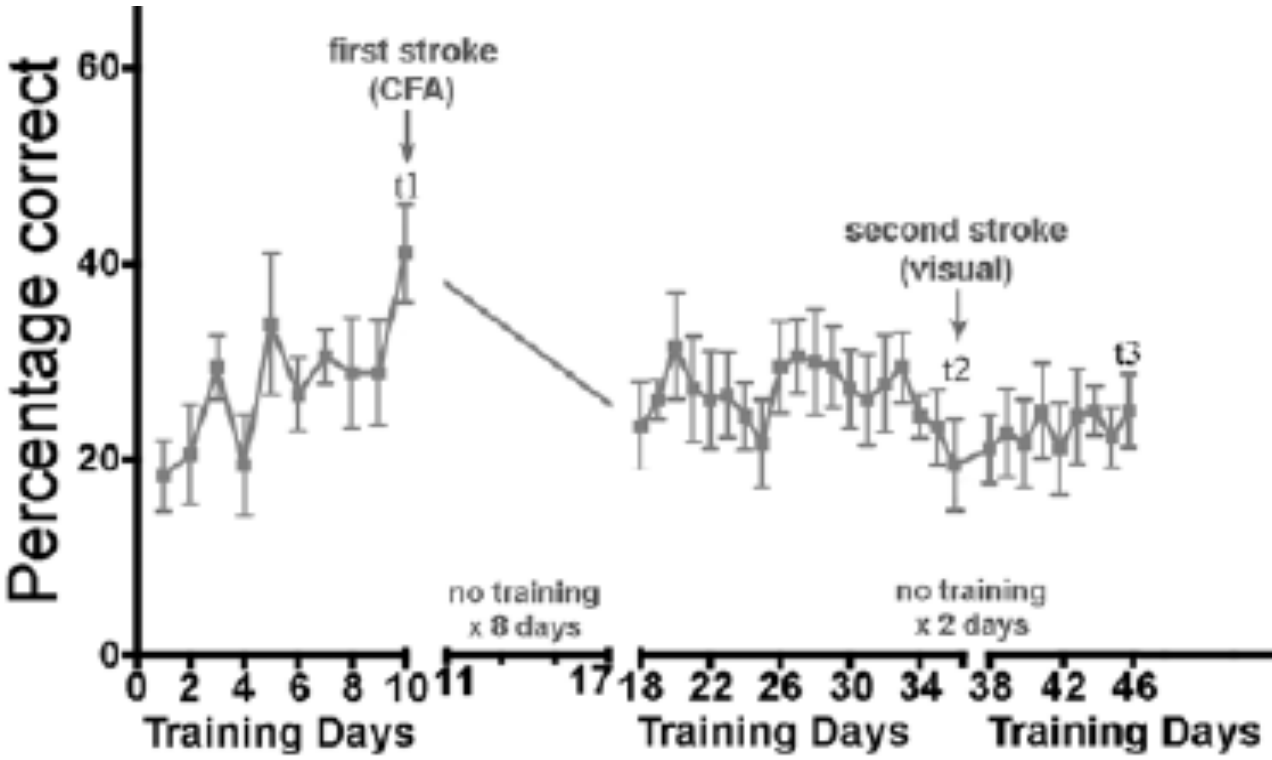
Rehabilitation, timing, and medication



Ng, et al. *Stroke*. 2015 Oct; 46(10):2951-60

Trying to further understand neuroplasticity

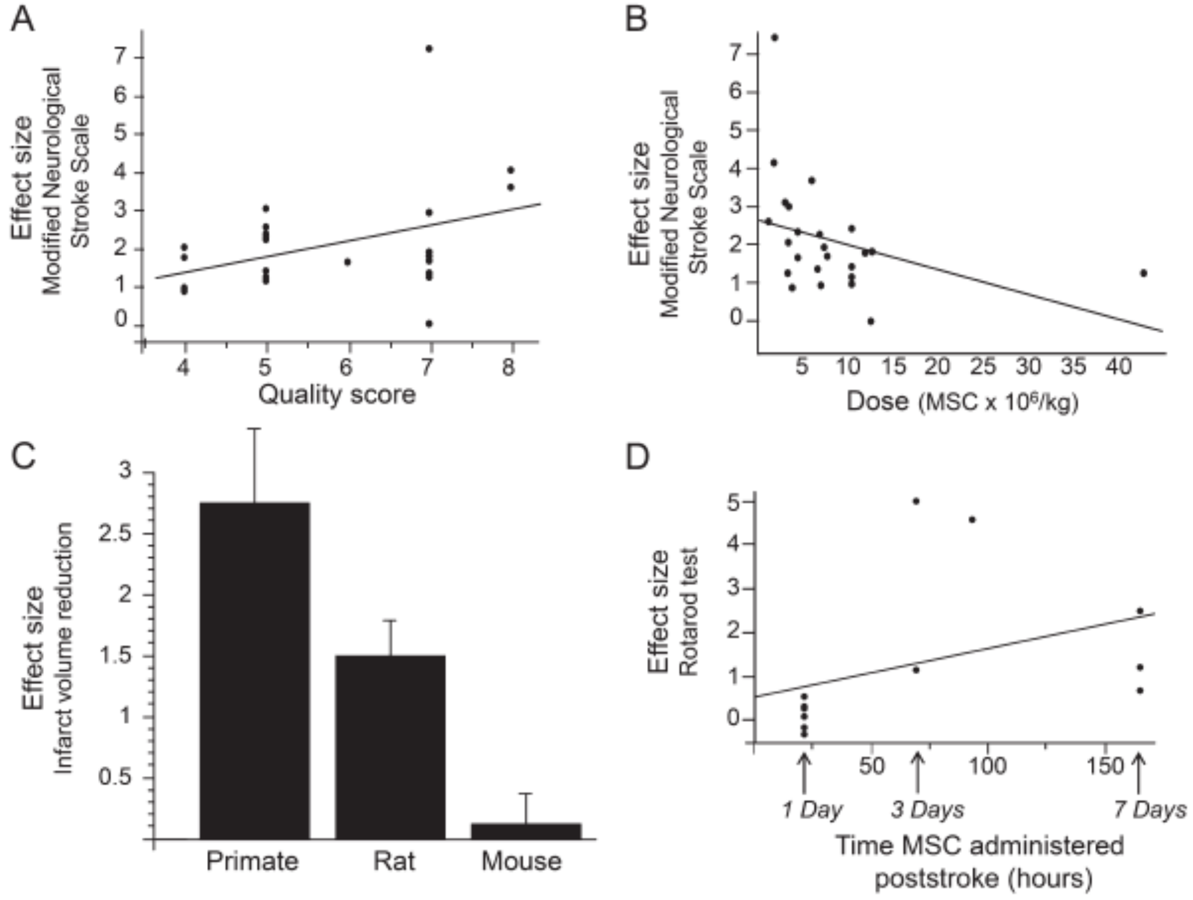




Zeiler SR, et al. *Neurorehabil Neural Repair*. 2016 Sep; 30(8): 794-800

Meta-analysis of stem cell administration: Promising future?

Figure 2 **Clinical correlates of effect size among studies introducing MSCs in the restorative therapy time window**



Wider treatment window for stroke patients

Compensatory versus restorative therapy

Understand repair mechanisms better (reduce injury early, promote repair later)

Vu Q, et al. *Neurology*. 2014 Apr;82(14):1277-86

Stroke rehab, technology, and the enriched environment

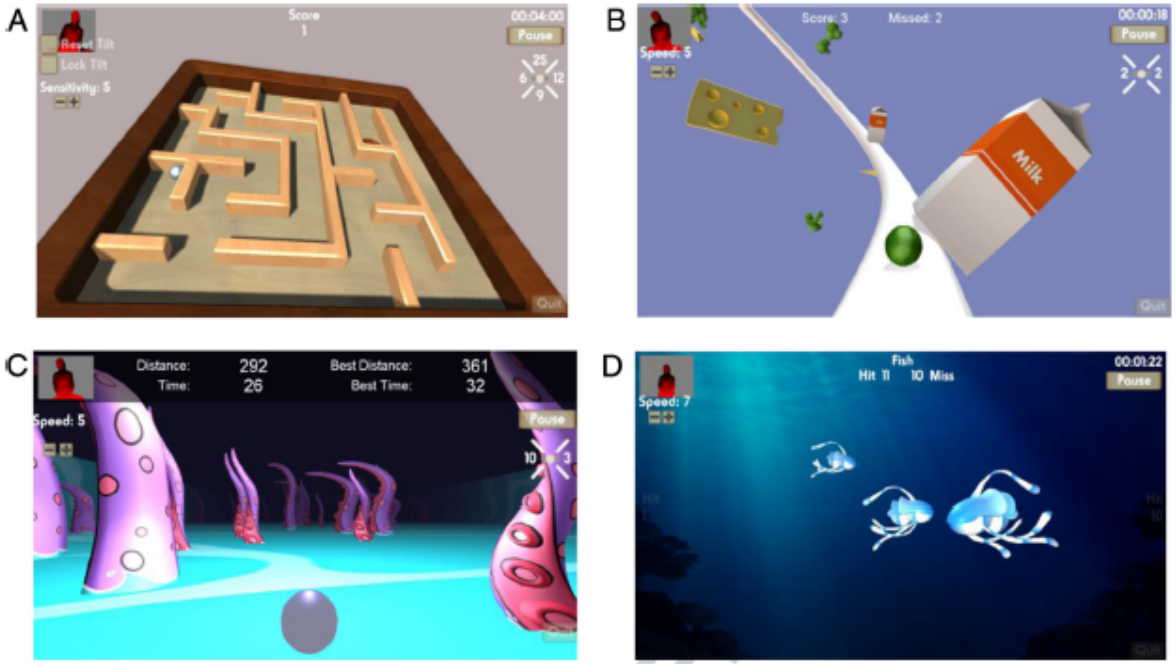
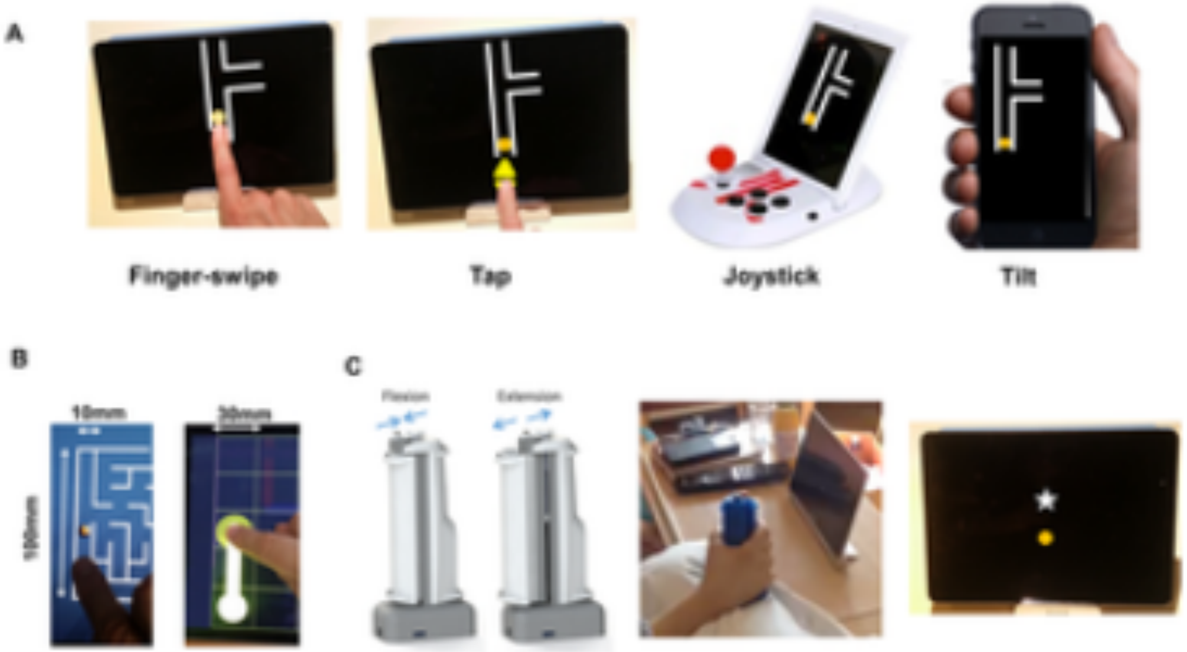
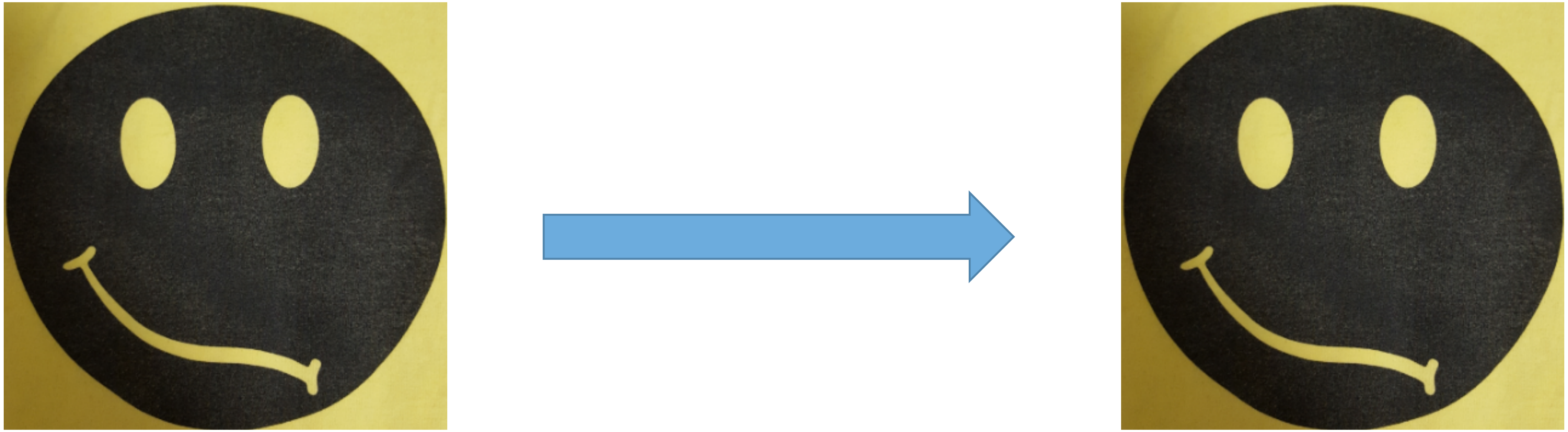


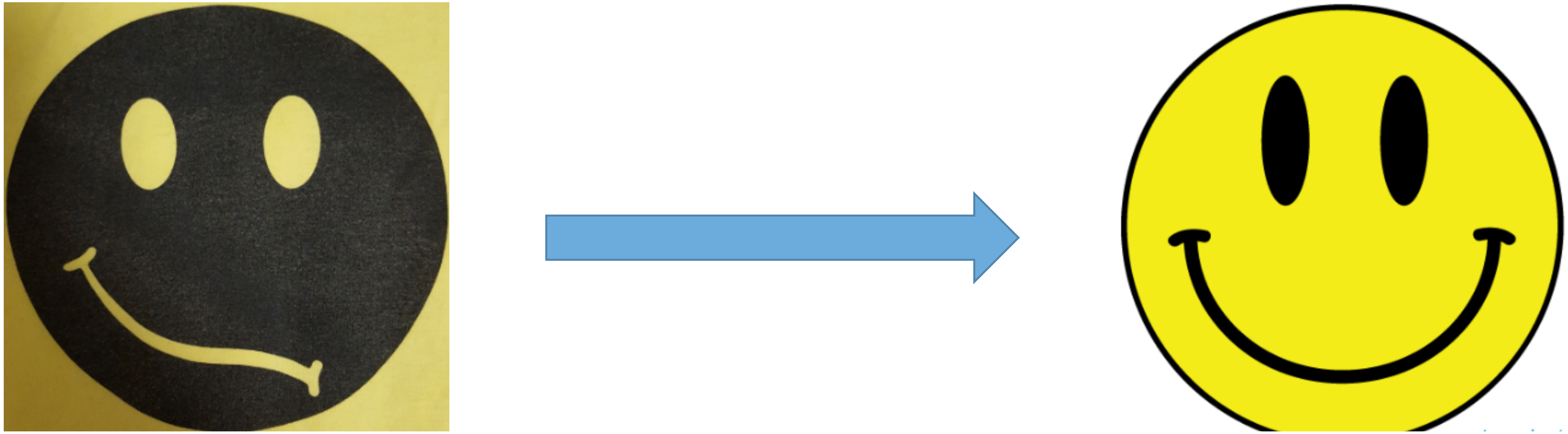
Fig. 1 Screen shots of the four game activities. *Legend*: **a**. Ball Maze **b**. Fridge Frenzy **c**. Tentacle Dash **d**. Bubble Fish



Take home message



Take home message



References

- Anderson AG, Kamwendo K, Appelros P. Fear of falling in stroke patients: relationship with previous falls and functional characteristics. Int J Rehabil Res. 2008;31:261-264.
- Bernhardt J, Langhorne P, Lindley RI, et al. Efficacy and safety of very early mobilisation within 24 h of stroke onset (AVERT): a randomised controlled trial. *Lancet*. 2015;386:46–55.
- Chemerinski E, Robinson RG, Kosier JT. Improved recovery in activities of daily living associated with remission of poststroke depression. Stroke. 2001 Jan;32(1):113-7.
- Chollet F, Tardy J, Albucher JF, et al. Fluoxetine for motor recovery after acute ischemic stroke (FLAME): a randomized placebo-control trial. Lancet Neurol. 2011 Feb;10(2):123-30.
- Gainotti G, Antonucci G, Marra C, Paolucci S. Relation between depression after stroke, antidepressant therapy, and functional recovery. *J Neurol Neurosurg Psychiatry*. 2001;71:258–261.
- Langhorne P, Taylor G, Murray G, et al. Early supported discharge services for stroke patients: a meta-analysis of individual patients' data. Lancet. 2005 Feb;365(9458):501-6.
- Ng KL, Gibson EM, Hubbard R, et al. Fluoxetine maintains a state of heightened responsiveness to motor training early after stroke in a mouse model. Stroke, 2015 Oct; 46(10):2951-60.

References (continued)

- Reding MJ, Potes E. Rehabilitation outcome following initial unilateral hemispheric stroke: life table analysis approach. Stroke. 1988; 19(11):1354-1358.
- Strommen AM, Christensen T, Jensen K. Quantitative measurement of physical activity in acute ischemic stroke and transient ischemic attack. Stroke. 2014 Dec; 45(12):3649-55.
- Vu Q, Xie K, Eckert M, et al. Meta-analysis of preclinical studies of mesenchymal stromal cells for ischemic stroke. Neurology. 2014 Apr;82(14):1277-86.
- Winstein CJ, Stein J, Arena R, et al. Guidelines for adult stroke rehabilitation and recovery: A guideline for healthcare professionals from the AHA/ASA. Stroke. 2016 Jun;47(6):e98-e169.
- Wade DT, Skilbeck CE, Hewer RL. Predicting Barthel ADL score at 6 months after an acute stroke. Arch Phys Med Rehabil 1983 Jan;64(1):24-28.
- Zeiler SR, Hubbard R, Gibson EM, et al. Paradoxical motor recovery from a first stroke after induction of a second stroke: reopening a postischemic sensitive period. Neurorehabil Neural Repair. 2016 Sep; 30(8): 794-800.