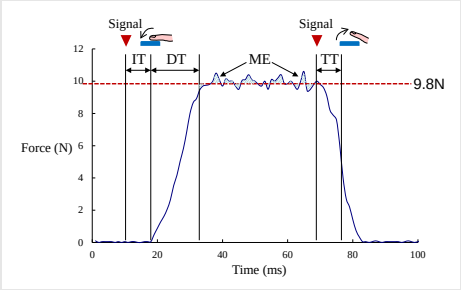
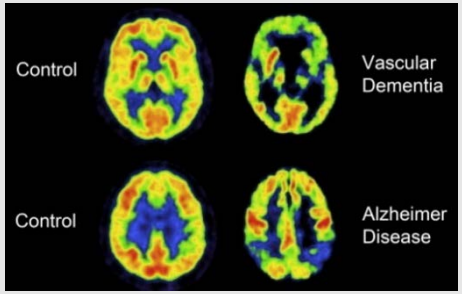
뇌 손상 환자 조기 선별을 위한 정상인 운동 능력 분석

*Analysis of **Motor Performance in Healthy Adults***
for the Early Screening of Patients with Brain Disorders





2013. 11. 15

박현지, 유희천

포항공과대학교 산업경영공학과
인간공학설계기술연구실(EDT)

AGENDA

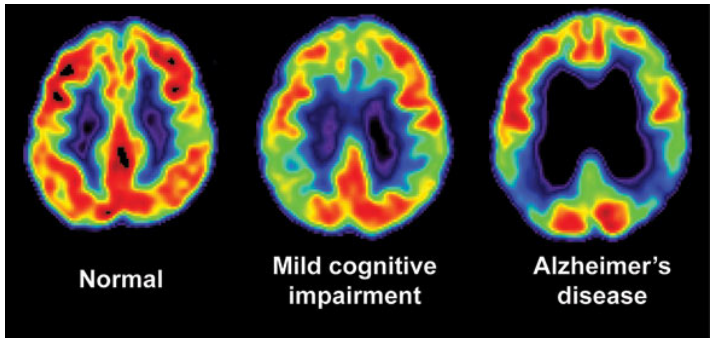
- **Introduction**
  - ✓ 연구 배경
  - ✓ 연구 목적
- **Evaluations of Motor Performance**
  - ✓ 운동국면별 힘 통제 능력
  - ✓ 힘 추적 능력
- **Results**
  1) 정상인 운동능력 특성
  2) 정상인과 환자의 운동능력 비교
  3) 뇌 손상 환자 판별 모형 개발
- **Discussion**

운동능력 저하

- 운동능력 저하의 주요 원인
  - ✓ 연령 (Holvia et al., 2012; Ward et al., 2003)
  - ✓ 뇌 손상으로 인한 motor impairments (Lindberg et al., 2012; Naik et al., 2011; Lodha et al., 2010;)
- 뇌 손상 환자(예: 뇌졸중, 혈관성 치매)는 발병 초기부터 운동능력 ↓(Hong, 2010; Weintraub, 2008)

⇒ 운동능력이 저하되면 정확한 힘 조절이 어렵고 움직임의 속도가 저하되므로, 운동능력을 조기에 정확하게 평가하는 것이 중요함

Aging



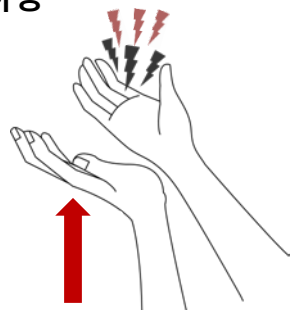
정상, 경도인지장애, 알츠하이머의 뇌 PET

기존 운동능력 평가의 한계점

- 임상가에 의한 환자의 행동 관찰과 병력 청취 등을 통해 motor impairment 유무 진단(Crucian et al., 2007; Heilman, 2004) ➔ 정성적 & 주관적

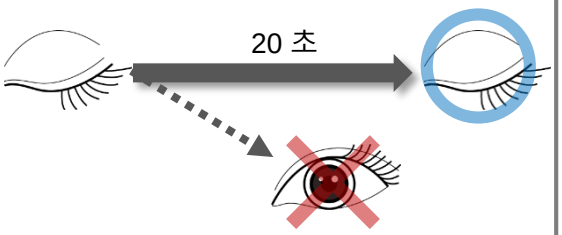
⇒ **환자의 정확한 조기 선별을 위해서는 정상인의 운동능력 특성에 대한 정량적 분석과 심층적 이해가 필요함**

운동저하증



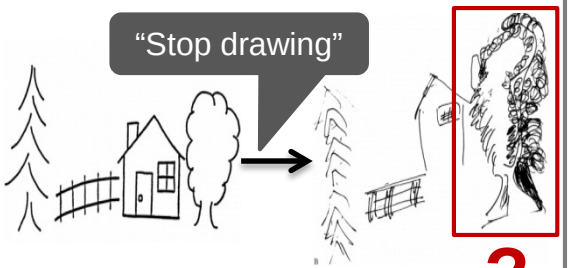
Crossed response inhibition (CRI) task

운동지속불능증



Eye closure task

운동보속증

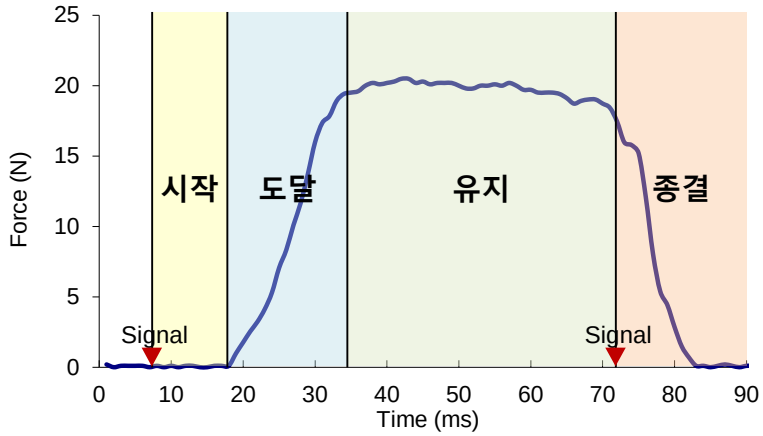


Drawing luria loop

운동능력 평가 연구: State-of-the-Art

운동국면별 힘 통제 능력 평가

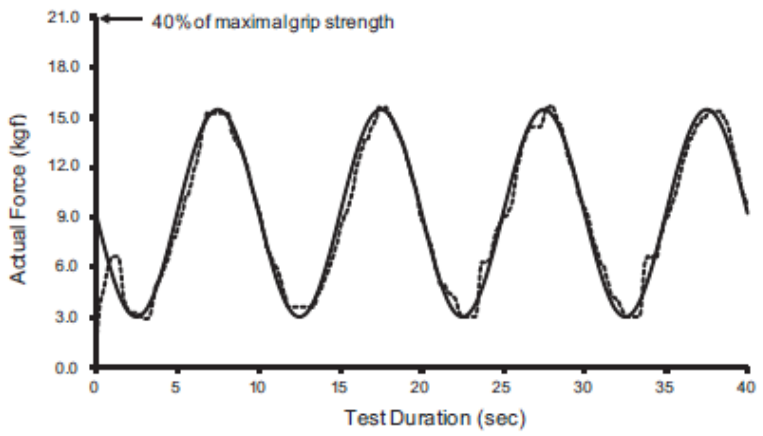
- 힘 통제(force control) 특성에 따라 시작, 도달, 유지, 종결의 네 가지 운동국면별로 운동능력 특성 평가



(Jimenez et al., 2011; Seo et al., 2009; Sosnoff et al., 2006; Der and Deary, 2006; Vinoth et al., 2001; Heilman, 2004)

힘 추적 능력 평가

- 힘을 조절(force modulation)하여 주어진 파형을 최대한 정확하게 추적함으로써 운동 능력 평가



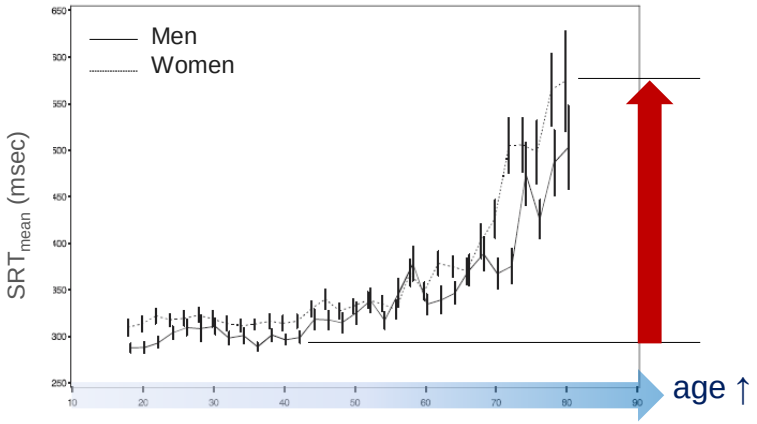
(Vieluf et al., 2013; Nagasawa et al., 2013; Lindberg et al., 2012; Naik et al., 2011; Voelcker-Rehage and Alberts, 2005)

운동국면별 힘 특성 연구: 한계점

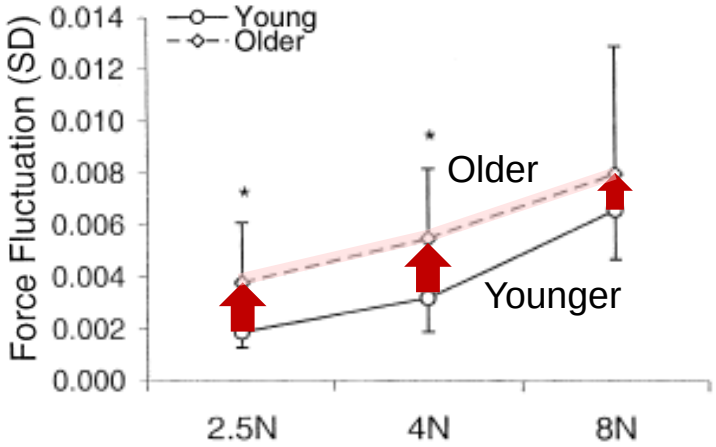
- 힘 시작과 유지에 따른 운동능력(예: reaction time, force variability) 평가가 주로 이루어짐
  - ➔ 도달, 종결 국면에 대한 motor performance 연구 미흡
- 일부 연령 집단(20 ~ 30대 vs. 60 ~ 70대)을 대상으로 평가, 표본 수 적음(n < 50)

⇒ 평가 대상의 연령과 성별을 체계적으로 고려한 운동국면별 운동능력 평가 필요

⇒ 뇌 손상 환자와의 정확한 판별을 위해 운동국면별 규준(normative database) 수립 필요



Age effect on reaction time
(Der and Deary, 2006)

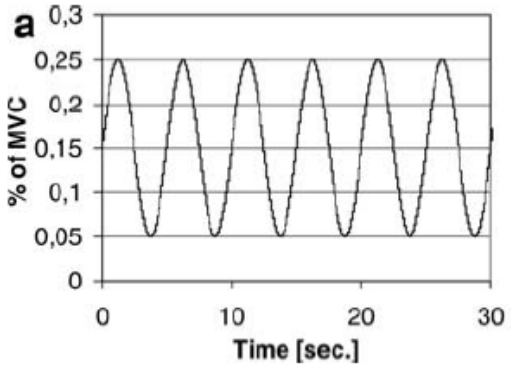


Age effect on force fluctuation
(Vinoth et al., 2001)

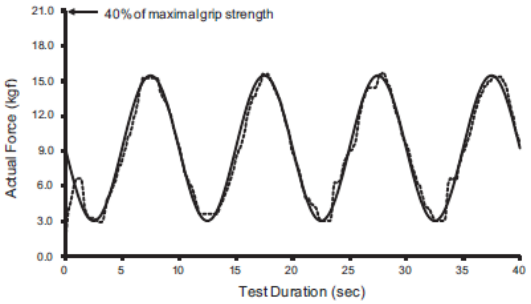
힘 추적 연구: 한계점

- 힘 추적 능력은 profile의 특성(예: 힘 수준, 진폭, 진동수)에 따라 상이하게 나타남 (Vieluf et al., 2013)
- 기존의 force profile은 주로 sinusoidal 곡선과 stair-stepping 형태의 단일 파형의 반복으로 구성되어 다양한 진폭과 진동수의 profile 특성을 복합적으로 고려하지 못함

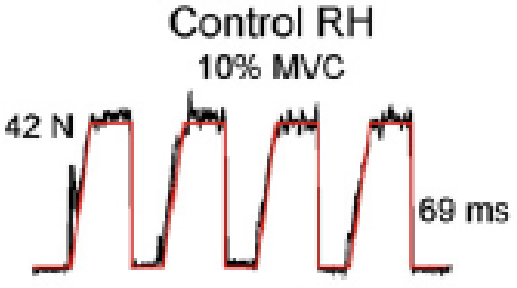
⇒ 다양한 진폭과 진동수의 profile이 복합적으로 고려된 새로운 파형 개발 필요



Voelcker-Rehage and Alberts (2005)



Nagasawa et al. (2013)



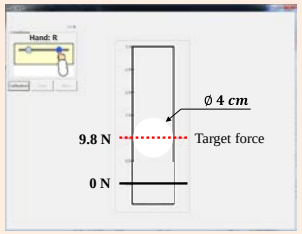
Lindberg et al. (2012)

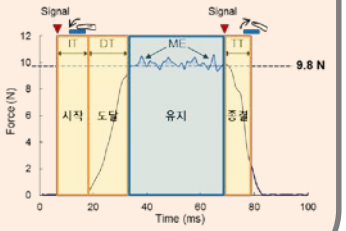
연구 목표

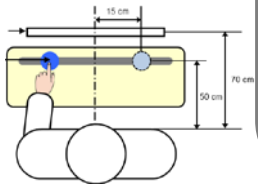
뇌 손상 환자 조기 선별을 위한 정상인 운동능력 분석

1. 운동국면별 정상인 힘 통제 특성 평가 및 규준 수립
2. 운동국면별 힘 통제 능력 비교: 정상인 vs. 환자
3. 정상인 힘 추적 특성 평가

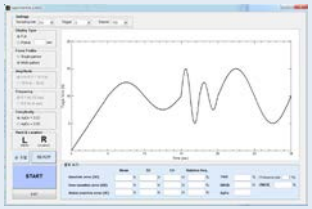
운동국면 별 힘 통제 능력 평가

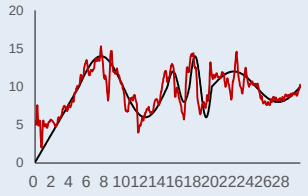






힘 추적 능력 평가



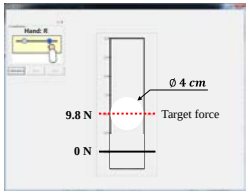


운동국면별 힘 통제 능력 평가

운동국면별 힘 통제 능력 평가: 연구 절차

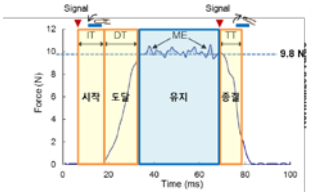
S1. 정상인 힘 통제 능력 평가 실험

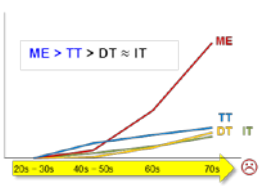
- 실험대상: 정상인 360명(20 ~ 70대)
- 운동국면별 손가락 힘 측정



S2. 정상인 힘 통제 특성 분석

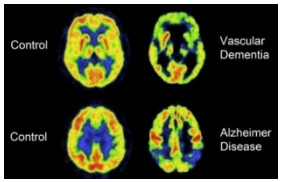
- 연령, 성별, 손 효과 영향 분석
- 정상인 규준 수립

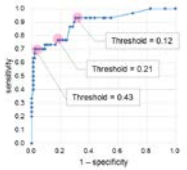




S3. 정상인과 환자의 운동능력 비교

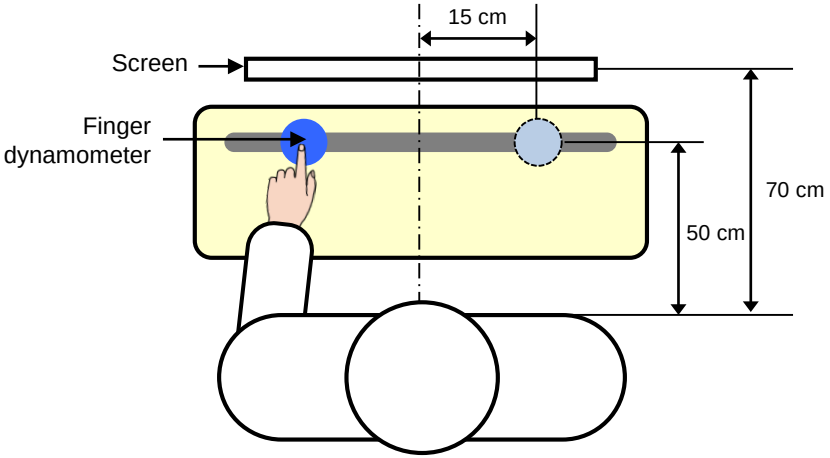
- 뇌 손상 환자(aMCI, svMCI, SVaD)의 유형별 힘 통제 특성 비교
- Logistic regression 적용



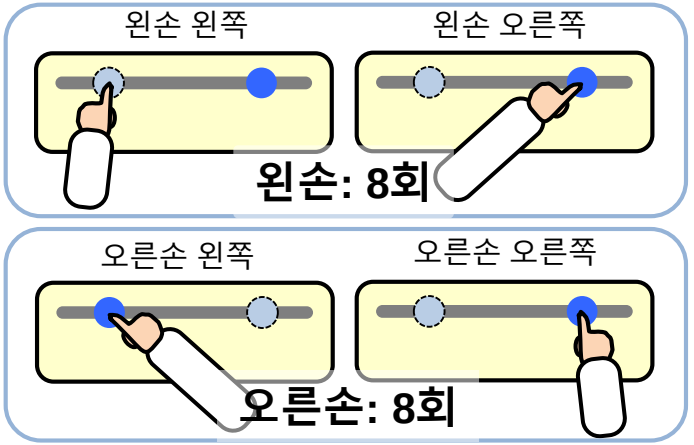


S1. 힘 통제 능력 평가 실험: 설계

- 실험 참여자: 정상인 360명 (20대 ~ 70대, 남녀 각 30명)
- 실험 방법: 검지손가락으로 운동국면에 따른 네 가지 task 수행(각 손에 대해 8회 반복)
- 분석 방법: three-factor mixed-subjects ANOVA
  - ✓ Between-subjects factors (b-s-f): 연령(20대 ~ 70대), 성별(남, 여)
  - ✓ Within-subjects factors (w-s-f): 손(왼손, 오른손)



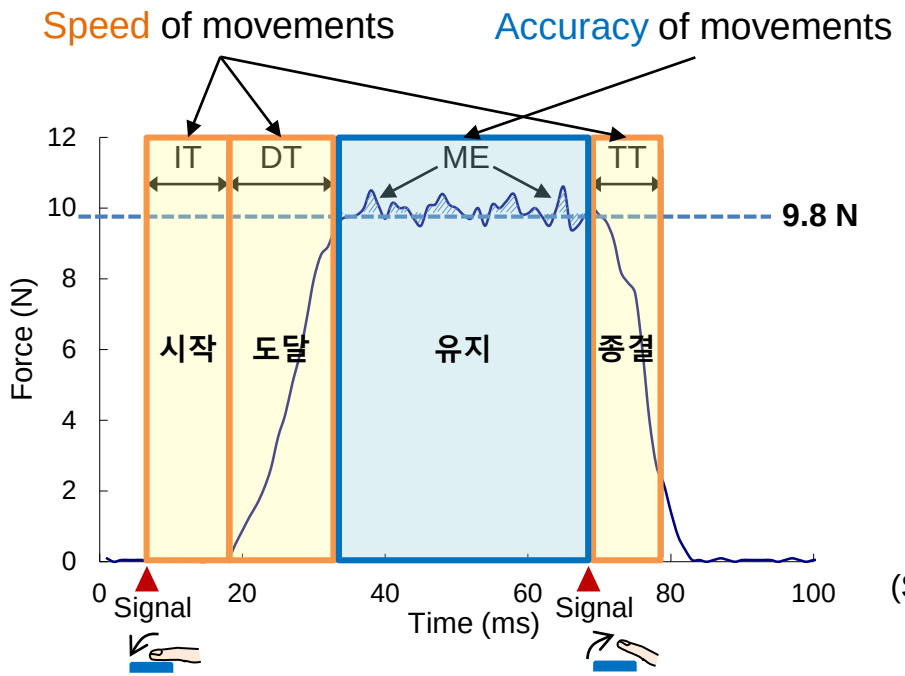
시스템 구성(검사 조건 예: 왼손 왼쪽)



실험 조건

S1. 힘 통제 능력 평가 실험: 평가 척도

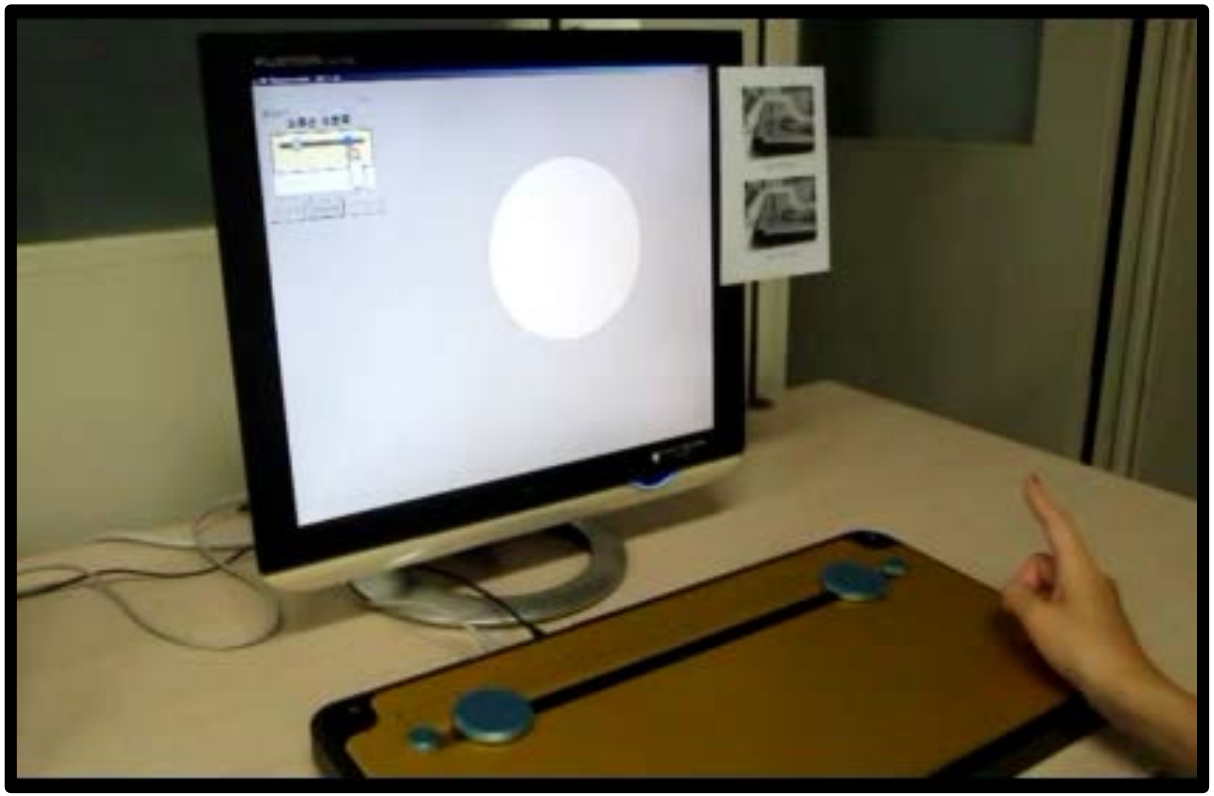
- **시작**: 얼마나 빠르게 반응하는가? ➔ initiation time (IT, 단위: msec)
- **도달**: 얼마나 빠르게 목표힘에 도달하는가? ➔ development time (DT, 단위: msec)
- **유지**: 목표힘을 일정하게 잘 유지하는가? ➔ maintenance error (ME, 단위: mN)
- **종결**: 얼마나 빠르게 힘을 종료하는가? ➔ termination time (TT, 단위: msec)

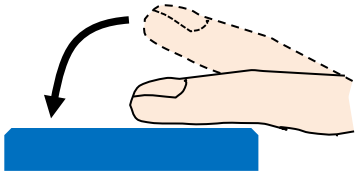


(Seo et al., 2009)

S1. 힘 통제 능력 평가 실험: Task – 시작

- **IT** (msec): 신호가 제시되면 최대한 신속하게 dynamometer 누름





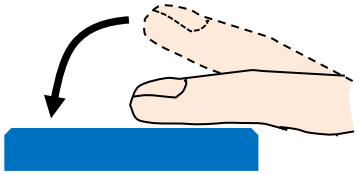
$$Initiation\ Time\ (IT) = t_i - t_j$$

i = time to press the sensor;
j = time to appear red signal

S1. 힘 통제 능력 평가 실험: Task – 도달

- **DT** (msec): dynamometer를 눌러 최대한 신속하게 목표 힘에 도달

※ Target force = 9.8N

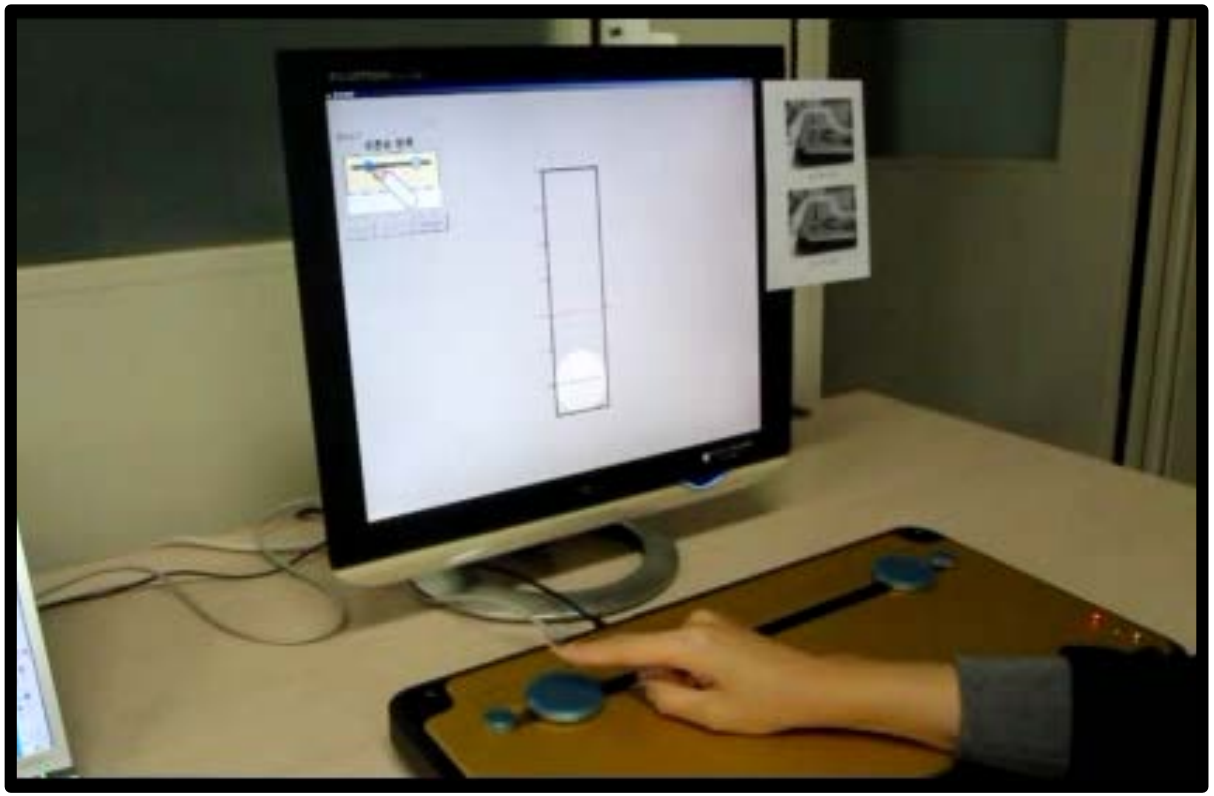


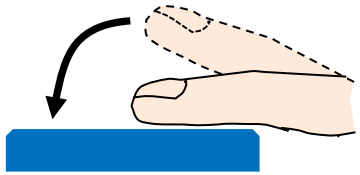
$$Development\ Time\ (DT) = t_i - t_j$$

i = time to reach 9.8N;
j = time to press the sensor

S1. 힘 통제 능력 평가 실험: Task – 유지

- **ME** (mN): 10초 동안 일정한 힘을 가하여 목표 힘을 최대한 유지



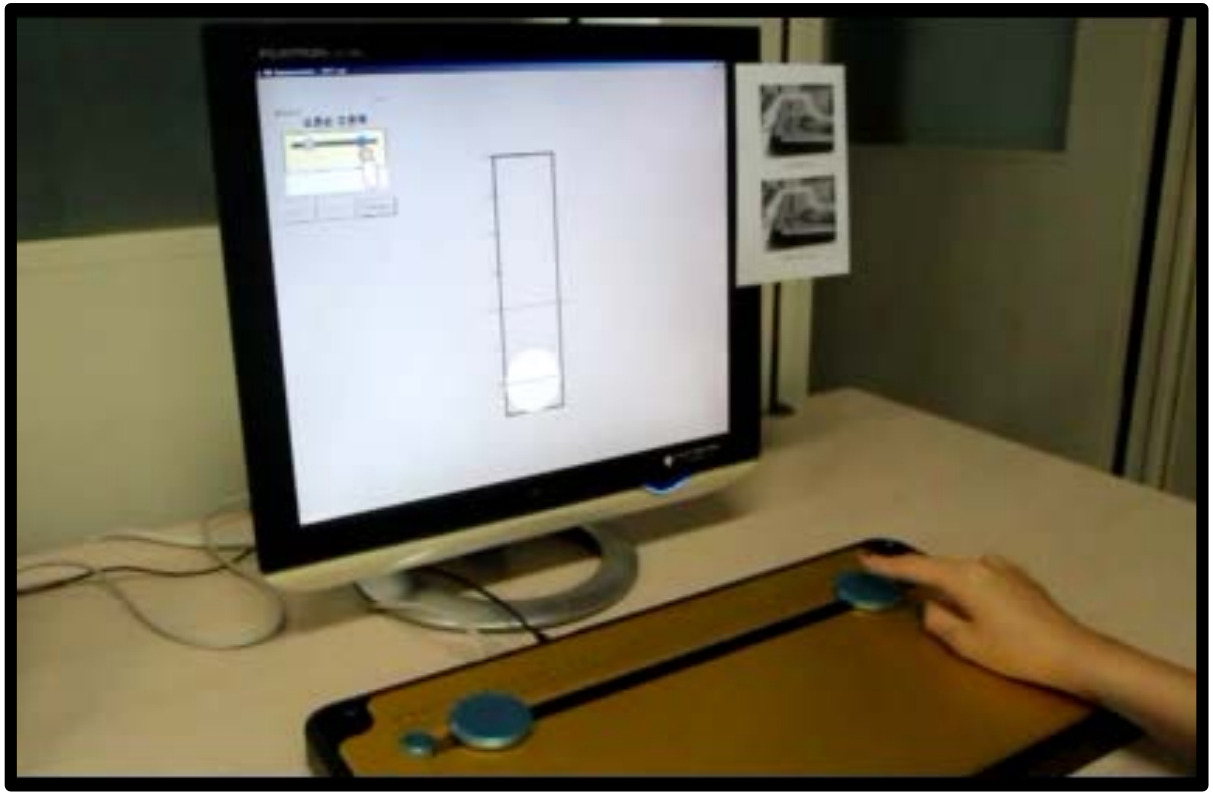


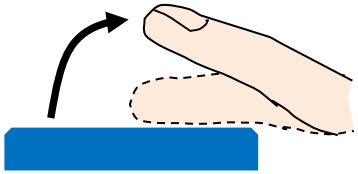
$$Maintenance\ Error\ (ME) = \frac{\sum_{i=0}^{10000} |f_i - 9.8\ N|}{10000}$$

f_i = finger force at time i

S1. 힘 통제 능력 평가 실험: Task – 종결

- **TT** (msec): 신호가 제시되면 최대한 신속하게 dynamometer에서 손가락을 뗌

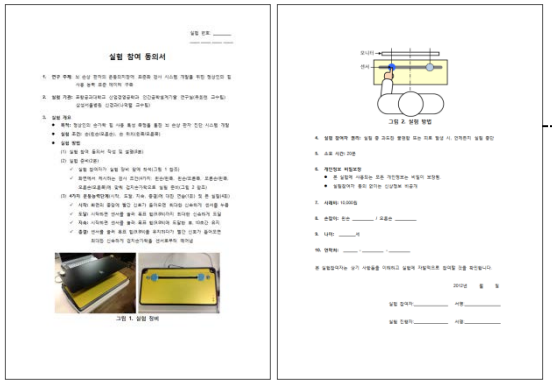


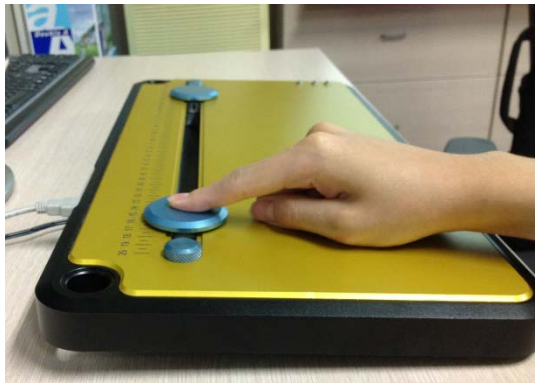


$$Termination\ Time\ (TT) = t_i - t_j$$

i = time to release the finger;
j = time to appear red signal

S1. 힘 통제 능력 평가 실험: 절차





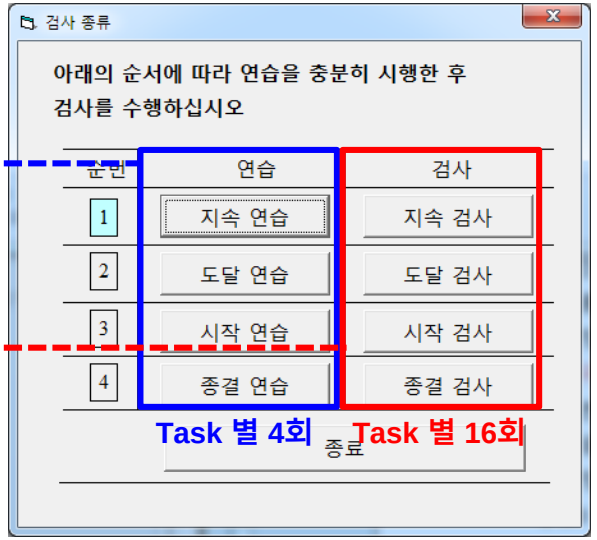
1인당 실험시간: 20분

S1. Preparation
(3 min)

S2. Practice
(5 min)

S3. Main experiment
(10 min)

S4. Debriefing
(2 min)



※ 검사 순서: random

S2. 정상인 힘 통제 특성: 분석 결과

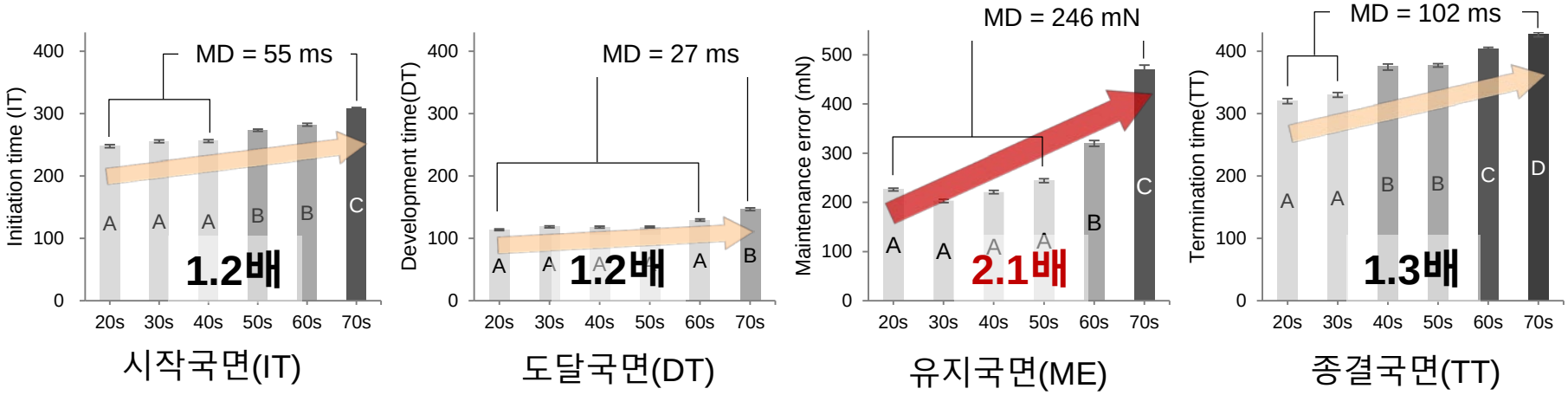
- 모든 국면에서 연령 효과가 유의함
- 유지국면에서만 성별에 따른 힘 특성 차이가 유의함
- 시작, 유지국면에서 연령과 성별의 교호작용이 유의함

		시작시간(IT)	도달시간(DT)	유지오차(ME)	종결시간(TT)
Main effects	Age (A)	< .001	< .001	< .001	< .001
	Gender (G)	.009	.012	< .001	.003
	Hand (H)	.803	.008	.644	.032
Interaction effects	A × G	< .001	.314	< .001	.379
	A × H	.064	.756	.227	.515
	G × H	.310	.667	.705	.242
	A × G × H	.768	.851	.336	.568

※ Shaded area: $p < .001$

S2. 정상인 힘 통제 특성: 연령 효과

- 연령 ↑ → 시작시간, 도달시간, 유지오차, 종결시간 ↑
- 70대의 운동국면별 힘 통제 능력은 20대보다 1.2 ~ 2.1배 저하됨
- 운동국면별 연령에 따른 운동능력 저하 정도: 유지 > 종결 > 시작 ≈ 도달

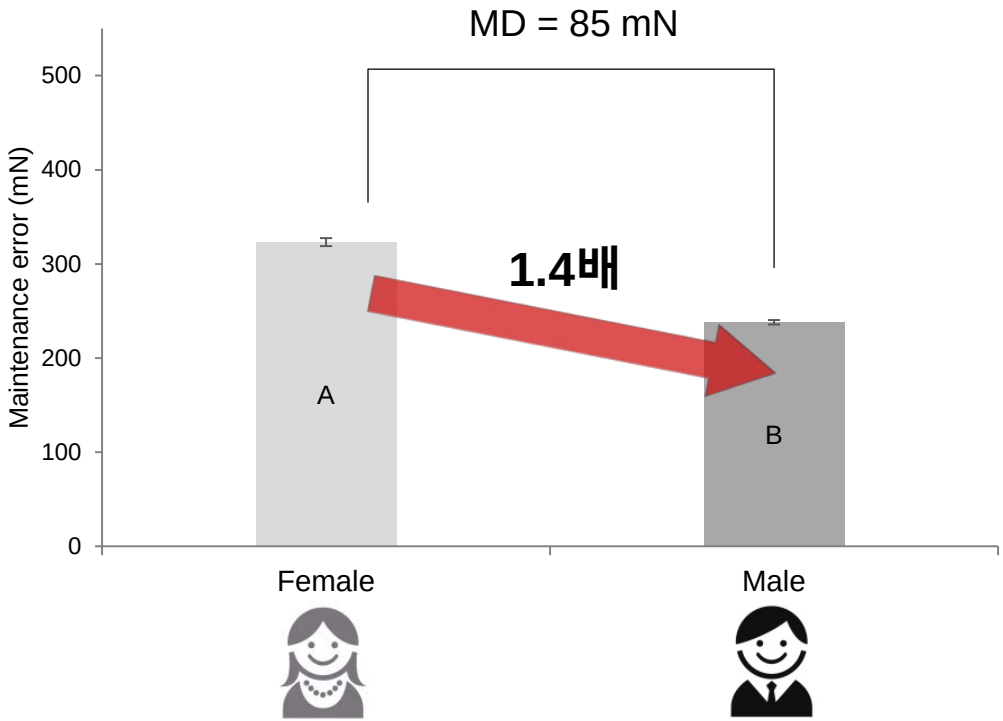


시작국면(IT) 도달국면(DT) 유지국면(ME) 종결국면(TT)

※ MD = mean difference

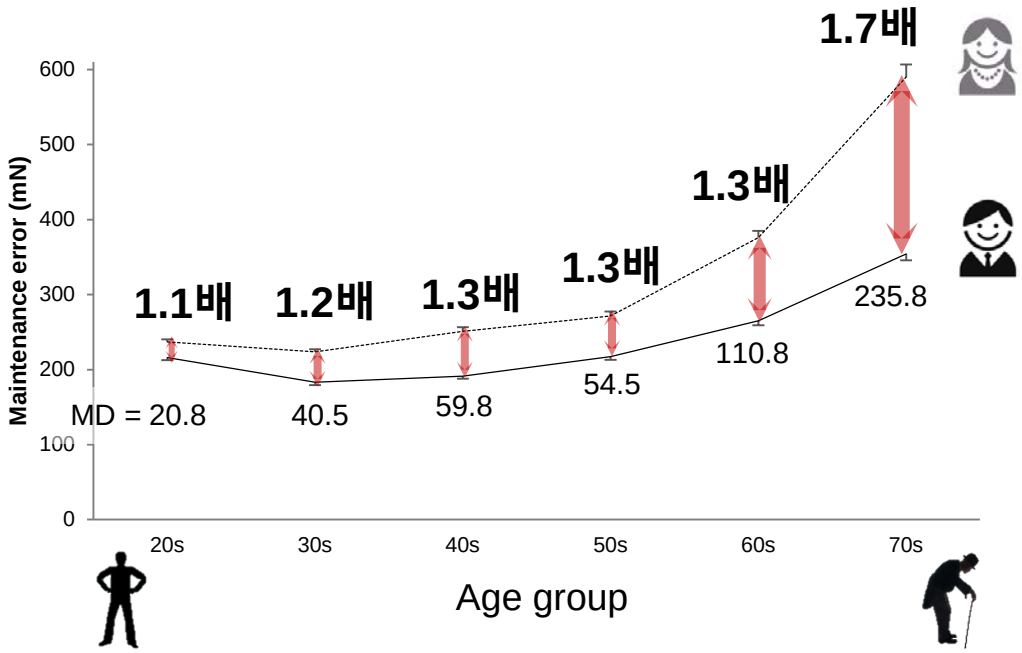
S2. 정상인 힘 통제 특성: 성별 효과

- 유지오차: 남성 < 여성
- 여성의 유지오차는 남성의 1.4배만큼 저하됨



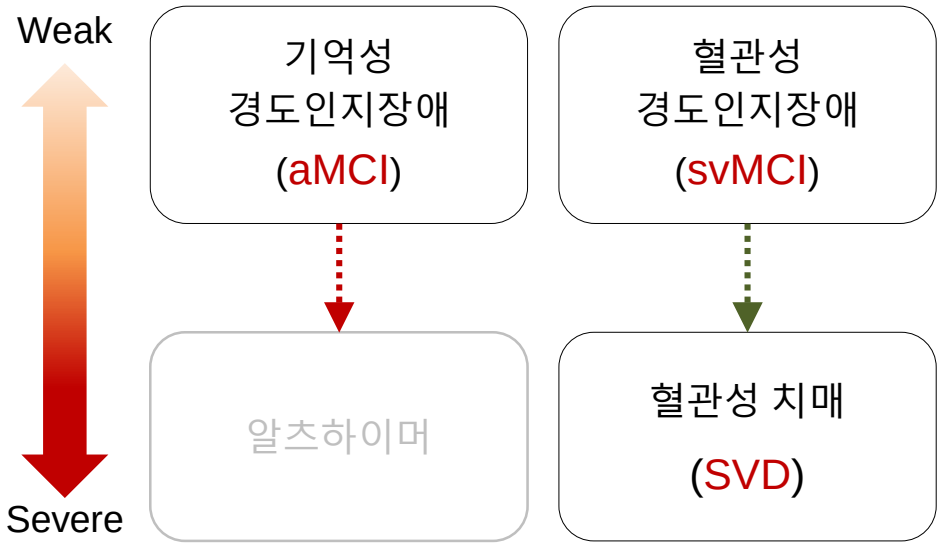
S2. 정상인 힘 통제 특성: 연령 × 성별 효과

- 유지오차: 연령↑ → 남녀 간 유지오차 차이↑



S3. 힘 통제 특성 비교: 정상인 vs. 환자

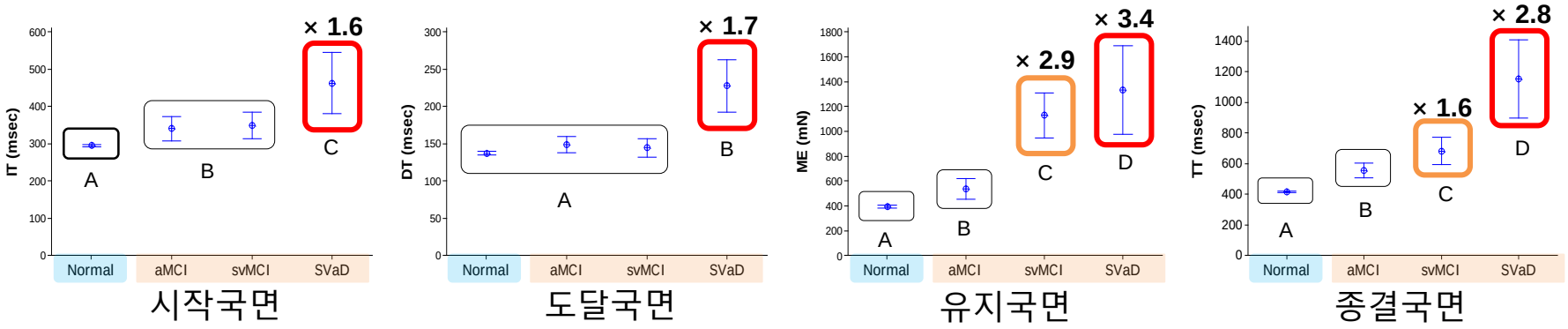
- Yoon et al. (2012)에서 수행된 운동국면별 뇌 손상 환자의 운동능력 평가 결과와 비교
  - ✓ 뇌 손상 환자: 60 ~ 70대 aMCI 17명, svMCI 23명, SVD 10명
  - ✓ 정상인: 본 연구의 60 ~ 70대 정상인 120명



※ Amnestic mild cognitive impairment (aMCI): 기억상실성 경도인지장애, subcorticar vascular MCI: 피질하 혈관성 경도인지장애, subcortical vascular (SVD): 피질하 혈관성 치매

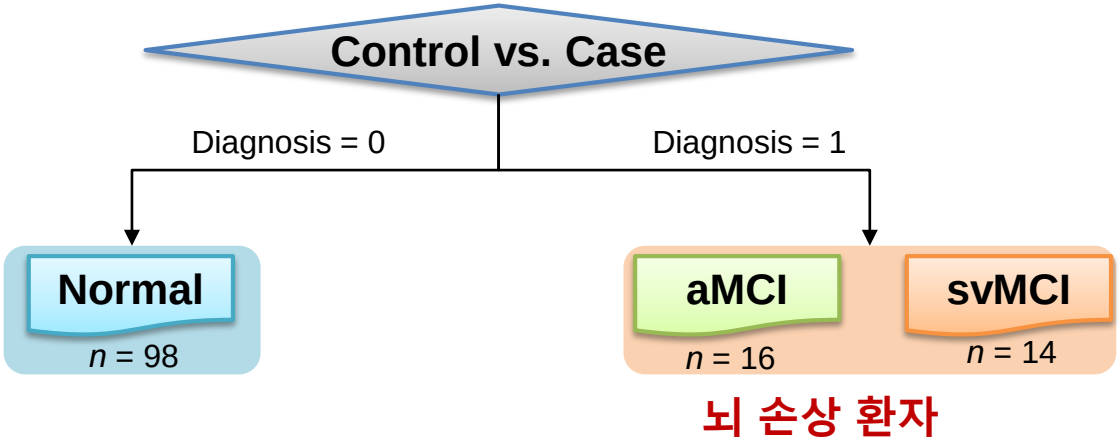
S3. 힘 통제 특성 비교: 정상인 vs. 환자

- 모든 국면에서 뇌 손상 환자의 힘 통제 능력이 저하됨
- 환자 유형별 운동능력 저하 정도: aMCI < svMCI < SVD



S3. 판별 모형 개발: 방법

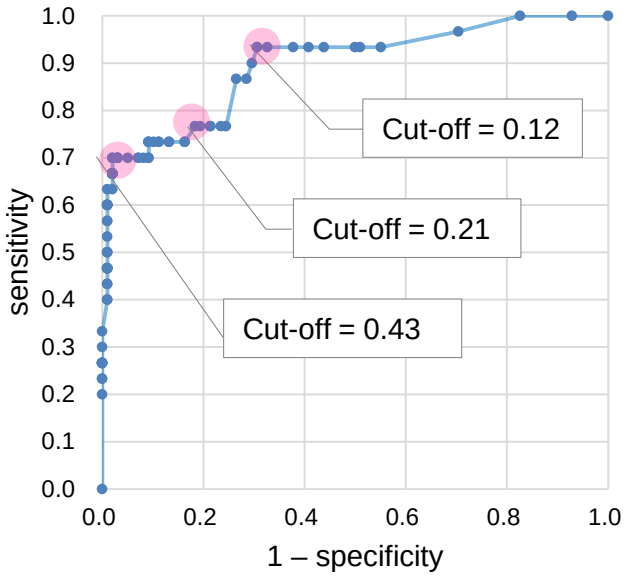
- 판별 모형 개발 목적: 뇌 손상 환자의 조기 선별
- 방법
  - ✓ 분류 기법: binary logistic regression
  - ✓ 변수 선정: TT, ME, IT, age (stepwise method, $\alpha_{in,\ out} = 0.05$)
  - ✓ Data set: normal controls, aMCI + svMCI patients



S3. 판별 모형: 성능

❑ 판별 threshold에 따른 모형 성능 비교

No.	Cut-off	Confusion matrix				Performance (%)		
						Sensitivity	Specificity	Accuracy
1	0.12	*n* = 128		Actual Normal	Actual Patient	93.3	69.4	75.0
		Predicted	Normal	**68**	2			
			Patient	30	**28**			
2	0.21	*n* = 128		Actual Normal	Actual Patient	76.7	81.6	80.5
		Predicted	Normal	**80**	7			
			Patient	18	**23**			
3	0.43	*n* = 128		Actual Normal	Actual Patient	70.0	98.0	91.4
		Predicted	Normal	**96**	9			
			Patient	2	**21**			



⇒ 환자의 조기선별이 주 목적인 경우: 환자를 90% 이상(sensitivity > 0.9) 선별 가능

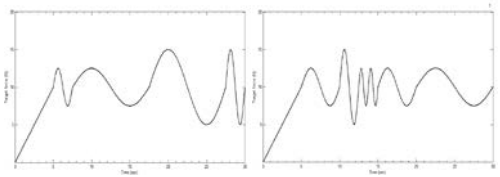
⇒ 임상가가 판별 기준을 조정할 수 있는 시스템으로 개발하면 진단상황에 따라 선호되는 판별 성능을 결정할 수 있음

힘 추적 능력 평가

힘 추적 능력 평가: 연구 절차

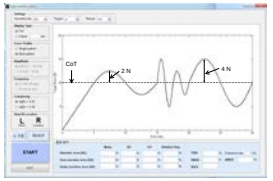
S1. Force tracking 파형 개발

- Composite sinusoidal profile 개발
- ApEn 적용한 파형의 complexity 결정



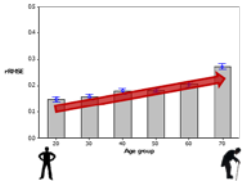
S2. 정상인 힘 추적 능력 실험

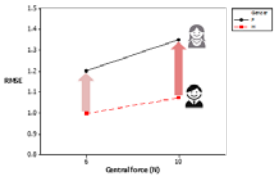
- 실험대상: 정상인 90명(20 ~ 70대)
- 16가지 실험조건에 대하여 평가



S3. 정상인 힘 추적 특성 분석

- 힘 추적 능력에 대한 age, gender, central force, complexity level effect 분석

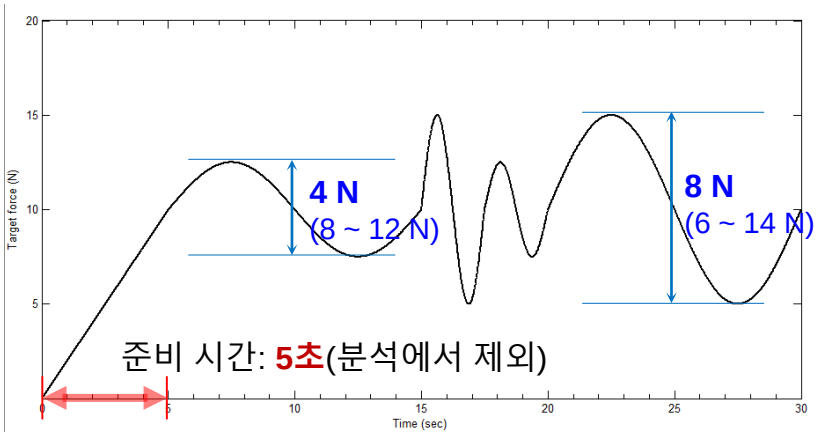




S1. Force Tracking 파형 개발

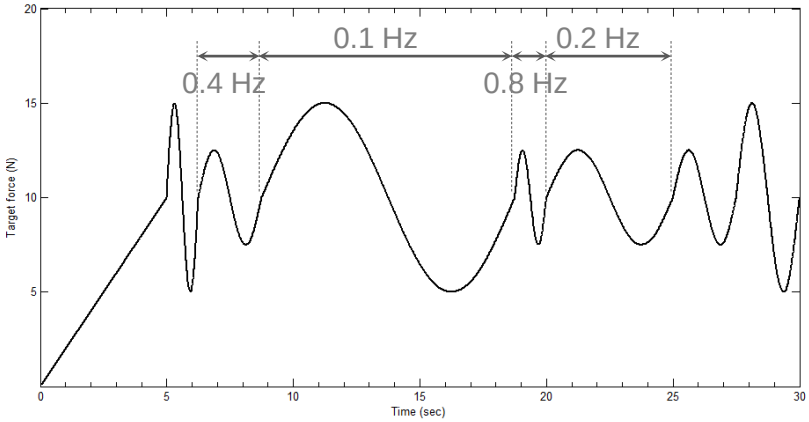
- 파형의 complexity 결정: ApEn 척도 적용
  - ✓ **ApEn** (approximate entropy): regularity(complexity) statistics of time series (Pincus, 1991)
  - ✓ Amplitude: 2 N, 4 N
  - ✓ Frequency: 0.1 Hz, 0.2 Hz, 0.4 Hz, 0.8 Hz

Low complexity



ApEn = 0.03 ± 0.005

High complexity

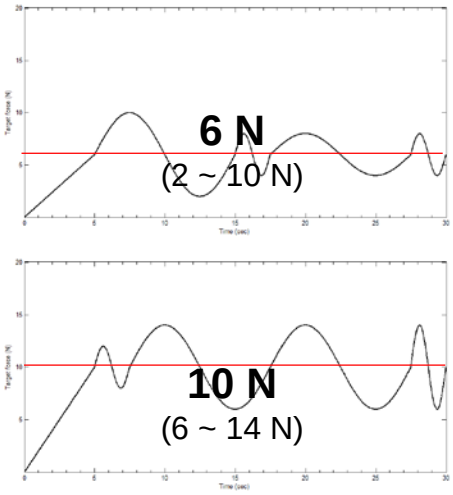


ApEn = 0.06 ± 0.005

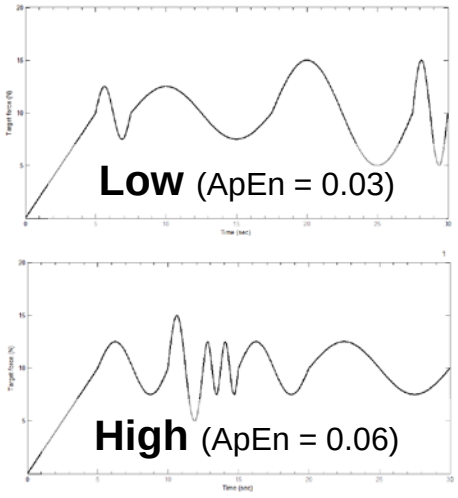
S2. 힘 추적 평가 실험: 설계

- 실험 방법: 30초간 sinusoidal tracking task (실험 조건별 2회 반복)
- 실험 조건: 16가지 (2 central forces × 2 complexity levels × 2 hands × 2 locations)

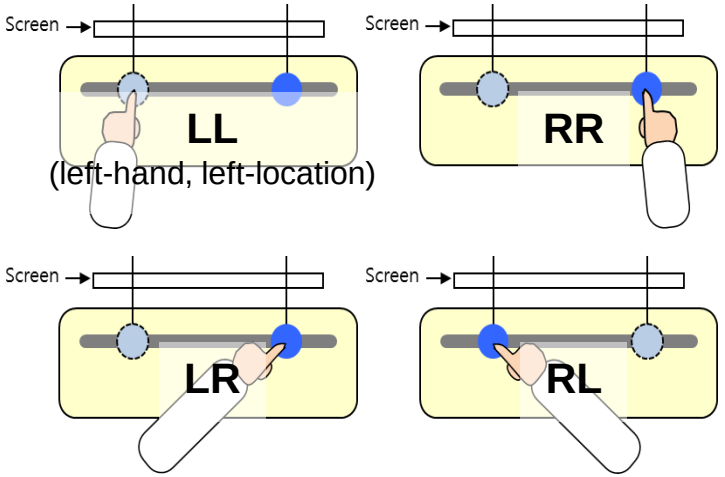
⇒ **총 실험 횟수**: 16 × 2 = 32 trials (소요 시간: 40분)



Central force



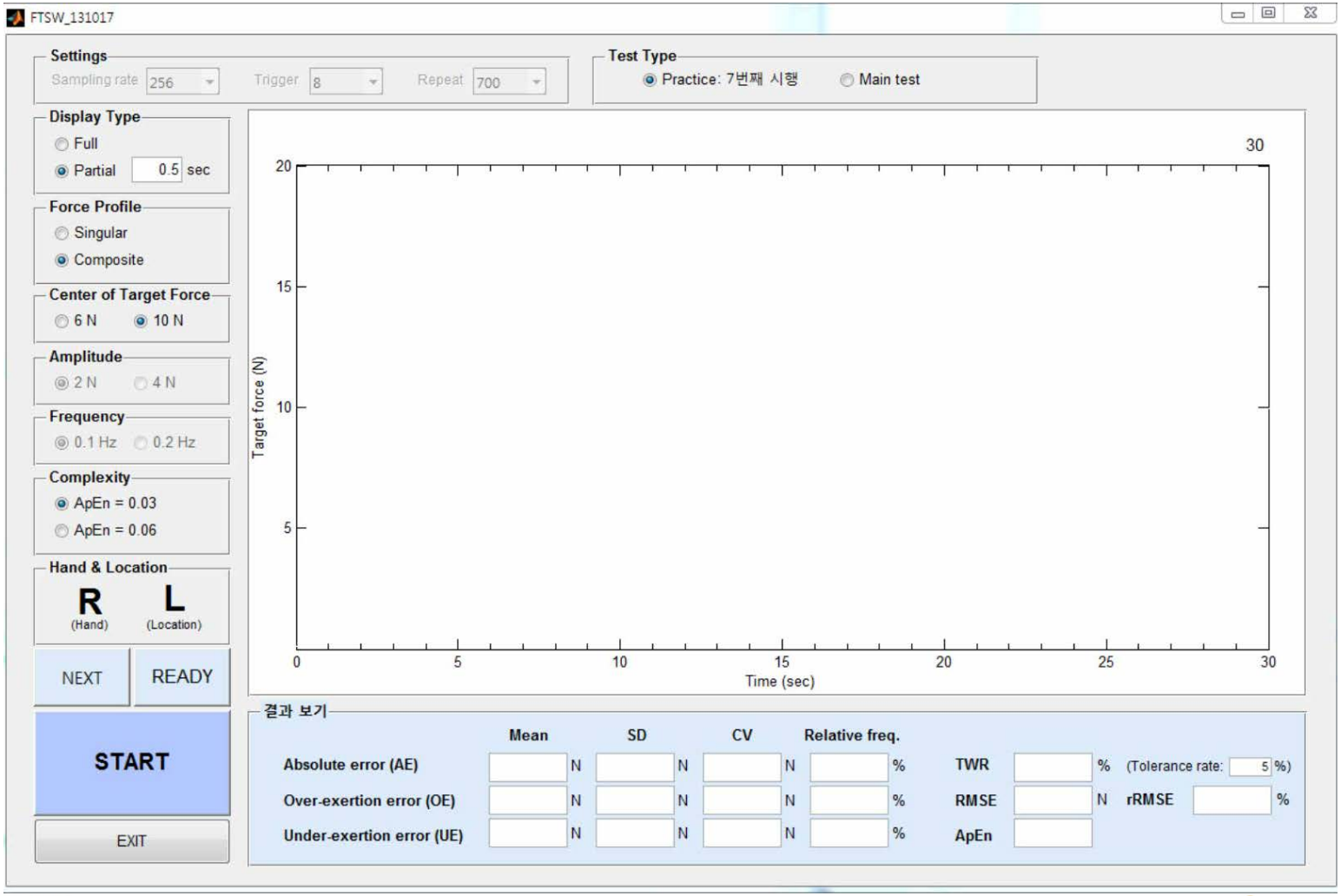
Complexity level



Hand-location

S2. 힘 추적 평가 실험: Task

- 실험 조건 예: central force = 10 N, complexity level = low



S2. 힘 추적 평가 실험: Participants

- 정상인 90명
  - ✓ 연령: 20대 ~ 70대(20 ~ 40대: 각 10명씩, 50 ~ 70대: 각 20명씩)
  - ✓ 남성:여성 = 연령대별 1:1

연령대	20s	30s	40s	50s	60s	70s	Total
n	10 (M: 5, F: 5)	10 (M: 5, F: 5)	10 (M: 5, F: 5)	20 (M: 10, F: 10)	20 (M: 10, F: 10)	20 (M: 10, F: 10)	90 (M: 45, F: 45)
Age (years) (mean ± SD)	25.1 ± 2.8	33.8 ± 2.7	44.6 ± 2.7	53.6 ± 2.3	64.2 ± 2.4	72.5 ± 2.0	53.8 ± 16.0

S2. 힘 추적 평가 실험: 분석 방법

- Independent variables

1) Age: 20s, 30s, 40s, 50s, 60s, 70s
2) Gender: male, female
3) Central force: 6 N(range = 2 ~ 10 N), 10 N(range = 6 ~ 14 N)
4) Complexity level: low(ApEn = 0.03), high(ApEn = 0.06)

4-factor mixed-subjects ANOVA
- b-s-f: age, gender
- w-s-f: central force, complexity level

- Dependent variables

1) TWR (time within the target range; tolerance rate = 5%)

$$TWR\ (\%) = \frac{\sum_{i=1}^{m} x_i}{m} \times 100$$

where, m = # measurements

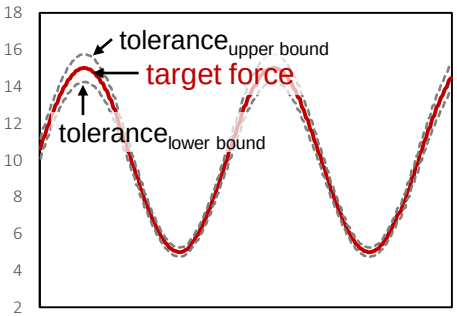
$$x_i = \begin{cases} 1, if\ |\text{발휘 힘}_i - \text{목표 힘}_i| \leq \text{목표 힘}_i \times tolerance\ rate \\ 0, o/w \end{cases}$$

2) RMSE (root mean square error)

$$RMSE\ (N) = \sqrt{\frac{\sum_{i=1}^{m}(\text{발휘 힘}_i - \text{목표 힘}_i)^2}{m}}$$

3) rRMSE (relative RMSE)

$$rRMSE\ (\%) = \sqrt{\frac{1}{m}\sum_{i=1}^{m}\left(\frac{\text{발휘 힘}_i - \text{목표 힘}_i}{\text{목표 힘}_i}\right)^2} \times 100$$



S3. 정상인 힘 추적 특성: 분석 결과

- 정상인 힘 추적 특성에 대한 age, gender, central force, complexity 효과 분석
  - ✓ 힘 추적 능력에 대한 모든 효과가 유의함
  - ✓ Central force와 관련된 일부 교호작용이 유의함

		TWR	RMSE	rRMSE
Main effects	Age (A)	$F(5, 78) = 13.84, p < .001$	$F(5, 78) = 7.97, p < .001$	$F(5, 78) = 10.67, p < .001$
	Gender (G)	$F(1, 78) = 15.10, p < .001$	$F(1, 78) = 9.25, p = .003$	$F(1, 78) = 10.01, p = .002$
	Central force (CF)	$F(1, 83) = 634.15, p < .001$	$F(1, 83) = 48.63, p < .001$	$F(1, 83) = 686.53, p < .001$
	Complexity (C)	$F(1, 83) = 241.80, p < .001$	$F(1, 83) = 510.81, p < .001$	$F(1, 83) = 434.92, p < .001$
Interaction effects	A × G	$F(5, 78) = 0.41, p = .842$	$F(5, 78) = 0.59, p = .707$	$F(5, 78) = 0.59, p = .705$
	A × **CF**	$F(5, 83) = 1.85, p = .112$	$F(5, 83) = 0.59, p = .710$	$F(5, 83) = 12.11, p < .001$
	A × C	$F(5, 83) = 1.91, p = .101$	$F(5, 83) = 2.20, p = .062$	$F(5, 83) = 0.90, p = .486$
	G × **CF**	$F(1, 83) = 11.18, p = .001$	$F(1, 83) = 7.12, p = .009$	$F(1, 83) = 7.74, p = .007$
	G × C	$F(1, 83) = 0.16, p = .694$	$F(1, 83) = 0.79, p = .376$	$F(1, 83) = 1.59, p = .211$
	CF × C	$F(1, 89) = 2.42, p = .123$	$F(1, 89) = 1.03, p = .313$	$F(1, 89) = 168.09, p < .001$

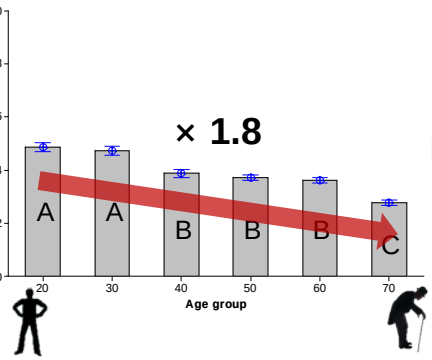
※ Shaded area: $p < .05$

S3. 정상인 힘 추적 특성 분석: 연령 효과

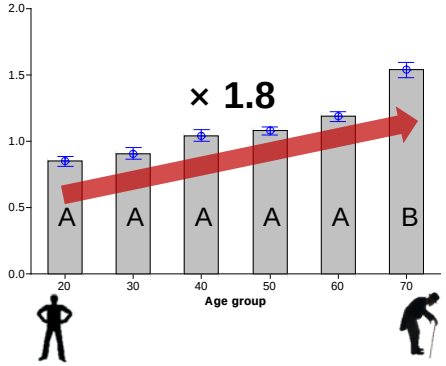
- TWR: 70s < 60s ≈ 50s ≈ 40s < 30s ≈ 20s (F[5, 78] = 13.84, p < .001)
- RMSE: 20s ≈ 30s ≈ 40s ≈ 50s ≈ 60s < 70s (F[5, 78] = 7.97, p < .001)
- rRMSE: 20s ≈ 30s ≈ 40s ≈ 50s ≈ 60s < 70s (F[5, 78] = 10.67, p < .001)

⇒ 70대의 힘 추적 능력 ↓: force accuracy ↓, force variability ↑

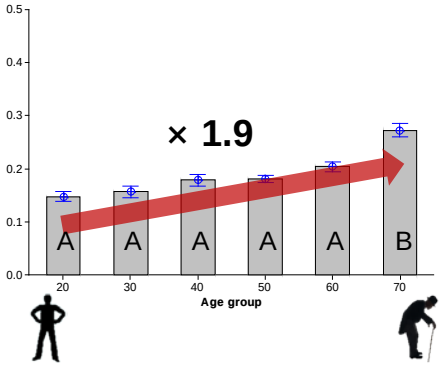
TWR



RMSE



rRMSE

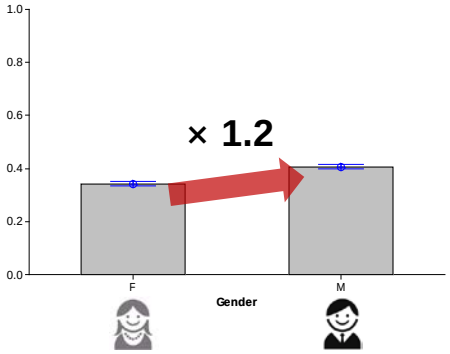


S3. 정상인 힘 추적 특성 분석: 성별 효과

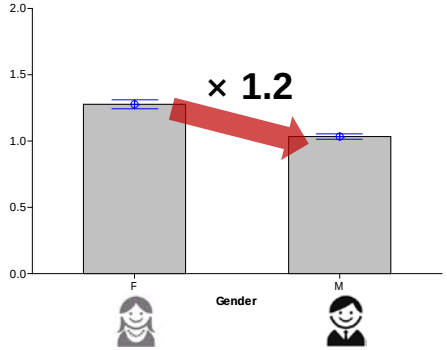
- TWR: female < male (F[1, 78] = 15.10, p < .001)
- RMSE: male < female (F[1, 78] = 9.25, p = .003)
- rRMSE: male < female (F[1, 78] = 10.01, p = .002)

⇒ 여성은 남성보다 힘 추적 능력이 1.2배 저하됨: force accuracy ↓, force variability ↑

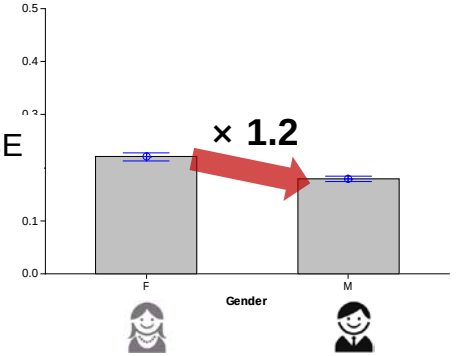
TWR



RMSE

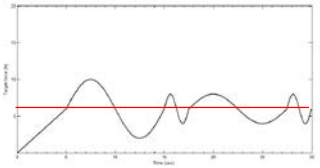


rRMSE

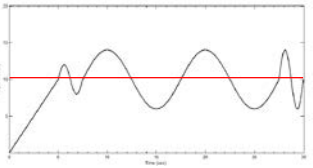


S3. 정상인 힘 추적 특성 분석: Central Force 효과

- TWR: 6 N < 10 N (F[1, 83] = 634.15, p < .001)
- RMSE: 6 N < 10 N (F[1, 83] = 48.63, p < .001)
- rRMSE: 10 N < 6 N (F[1, 83] = 686.53, p < .001)



6 N

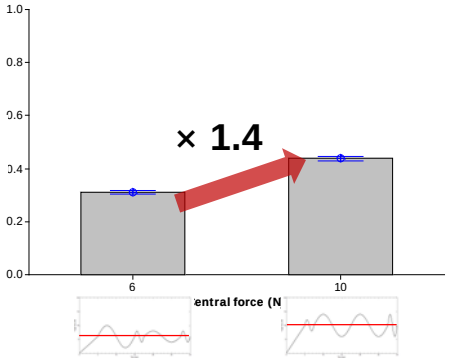


10 N

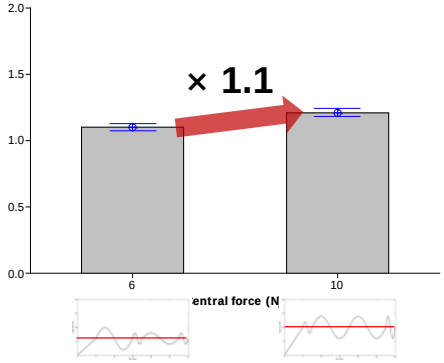
⇒ 적은 힘(fine motor control)을 추적할 때 힘 추적 능력이 1.1 ~ 2.1배 저하됨

⇒ 힘 수준에 대한 힘 추적 능력은 rRMSE를 사용할 때 변별성 ↑

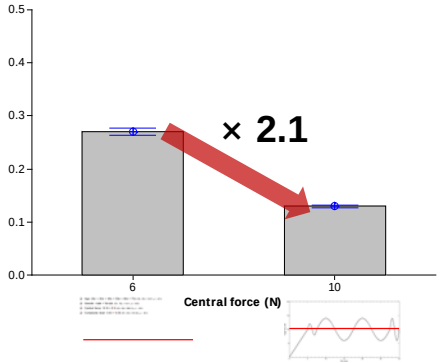
TWR



RMSE

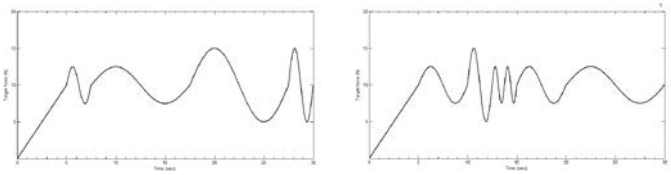


rRMSE



S3. 정상인 힘 추적 특성 분석: Complexity 효과

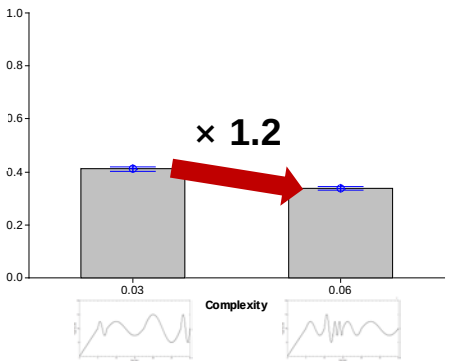
- TWR: 0.06 < 0.03 (F[1, 83] = 241.80, p < .001)
- RMSE: 0.03 < 0.06 (F[1, 83] = 510.81, p < .001)
- rRMSE: 0.03 < 0.06 (F[1, 83] = 434.92, p < .001)



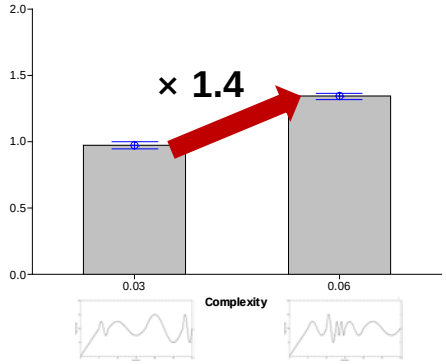
Complexity ↑ Complexity ↓

⇒ Complexity가 높은 파형을 추적할 때 힘 추적 능력이 1.2 ~ 1.4배 저하됨

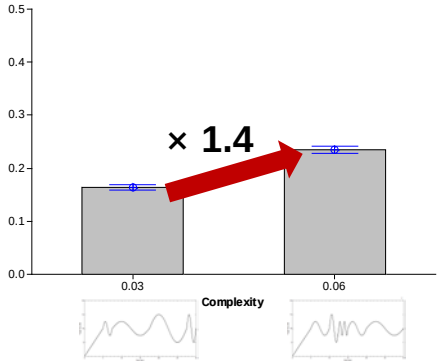
TWR



RMSE

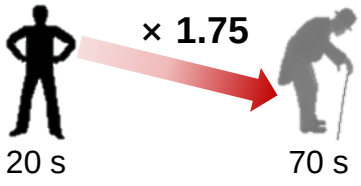
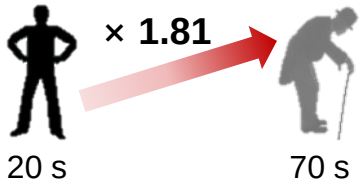
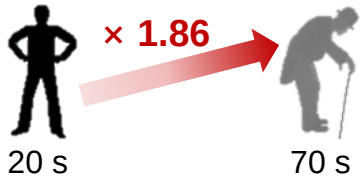
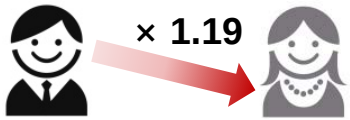
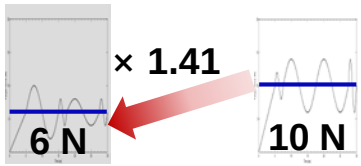
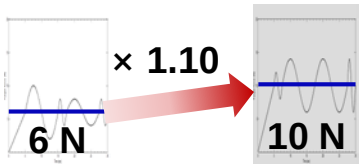
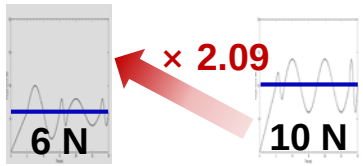
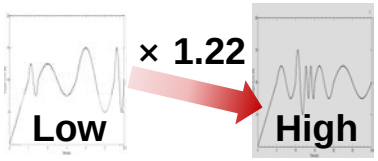
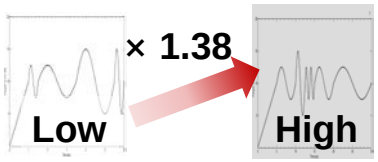
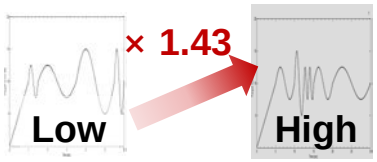


rRMSE



S3. 정상인 힘 추적 특성 분석: Summary

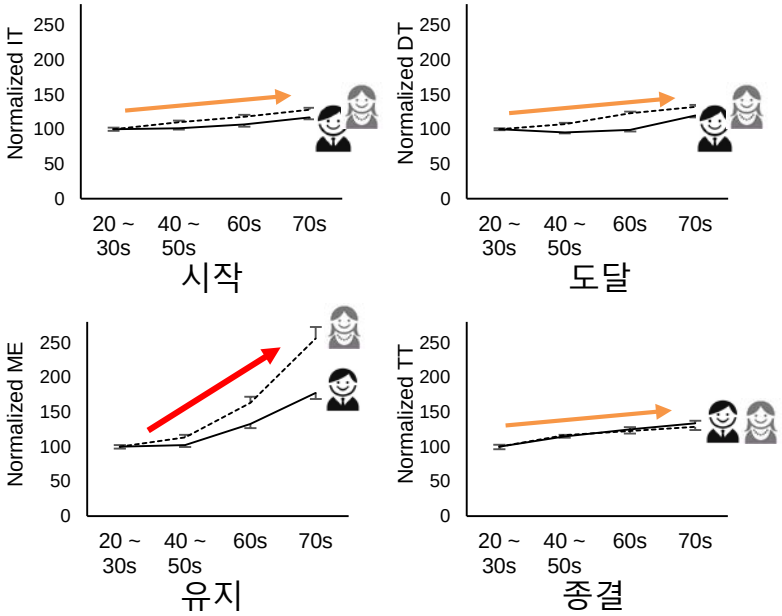
❑ Age↑, female, central force↓, complexity↑ ➔ force tracking performance ×1.1 ~ ×2.1⬇

	TWR	RMSE	rRMSE
Age			
Gender			
Central force			
Complexity			

Discussion (1/3)

- 운동국면(시작, 도달, 유지, 종결)별 정상인의 힘 통제 특성에 대한 운동능력 규준 수립
  - ✓ 유지오차(ME): 연령과 성별에 따른 변별성이 가장 높음

⇒ 정상인 운동능력 규준은 검사자의 연령과 성별에 해당하는 정량적 지표를 제시하여 운동능력 평가 시 유용하게 활용될 수 있을 것으로 기대됨

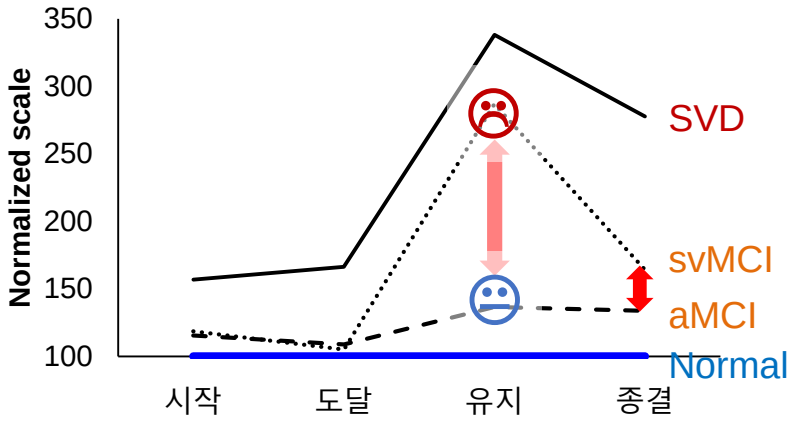


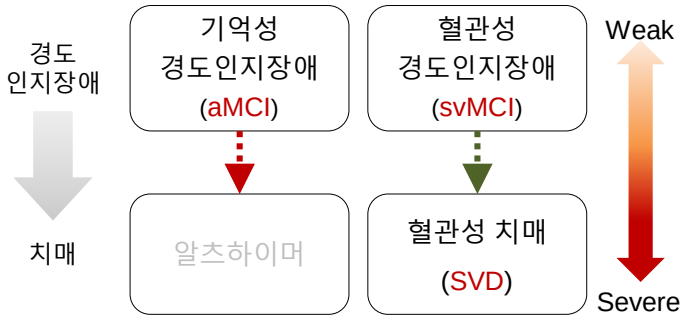
Descriptive statistics	20s ~ 30s		40s ~ 50s		60s		70s	
	M	F	M	F	M	F	M	F
Initiation time (msec)								
*n**	811	782	874	766	451	449	448	449
Mean	264.3	238.5	268.1	262.6	282.6	281.6	309.9	305.9
SD	62.8	64.2	52.5	62.9	66.8	59.0	64.6	58.4
99% LCL	258.6	232.6	263.5	256.7	274.5	274.4	302.0	298.8
99% UCL	270.0	244.4	272.7	268.5	290.7	288.8	317.8	313.0
Development time (msec)								
*n**	836	860	891	891	445	456	448	449
Mean	117.0	115.4	111.8	124.1	116.0	142.1	140.4	152.7
SD	42.93	44.73	38.32	51.33	46.36	49.35	61.32	61.93
99% LCL	113.7	111.6	108.4	121.0	109.2	136.1	132.1	144.2
99% UCL	121.5	119.6	115.0	130.6	120.6	148.1	147.7	159.4
Maintenance error (mN)								
*n**	907	912	913	912	466	458	459	438
Mean	199.5	230.5	204.2	261.2	264.8	375.8	354.2	590.1
SD	76.9	78.8	80.4	122.8	130.1	190.2	187.7	344.2
99% LCL	192.9	223.8	197.3	250.7	249.2	352.8	331.5	547.6
99% UCL	206.1	237.2	211.1	271.7	280.4	398.8	376.9	632.6
Termination time (msec)								
*n**	890	758	912	789	455	460	458	459
Mean	318.7	333.6	365.9	389.1	397.8	409.0	425.6	428.6
SD	82.3	104.5	76.2	102.8	77.0	77.0	82.8	97.4
99% LCL	311.6	323.8	359.4	379.7	388.5	399.7	415.6	416.8
99% UCL	325.8	343.4	372.4	398.5	407.1	418.3	435.6	440.4

Discussion (2/3)

- 운동국면별로 뇌 손상 환자 유형(aMCI, svMCI, SVaD)에 따라 운동능력 저하 정도가 상이함을 파악함
  - ✓ SVD: 모든 국면에서 가장 저하
  - ✓ aMCI, svMCI 환자: 유지와 종결 국면에서 변별성 높음

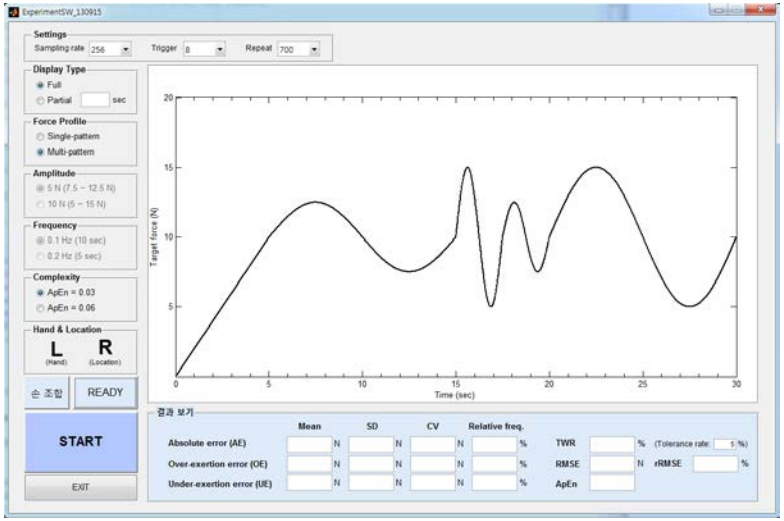
⇒ 운동국면별 운동능력 평가는 뇌 손상 환자의 조기 선별에 유용하게 활용 기대

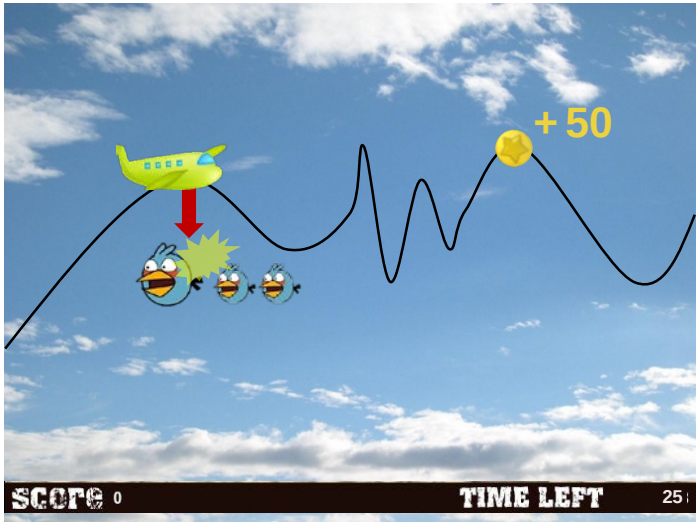




Discussion (3/3)

- 힘 추적은 네 가지의 운동국면을 종합적으로 평가하는 방법으로 평가의 효율성이 기대되나, 평가의 변별성에 대해서는 추후 임상 검증이 필요
- Composite sinusoidal profile이 적용된 힘 추적 평가 방법은 재미 요소를 추가하여 게임으로 개발되면 보다 효과적으로 운동능력을 평가할 수 있을 것으로 기대됨





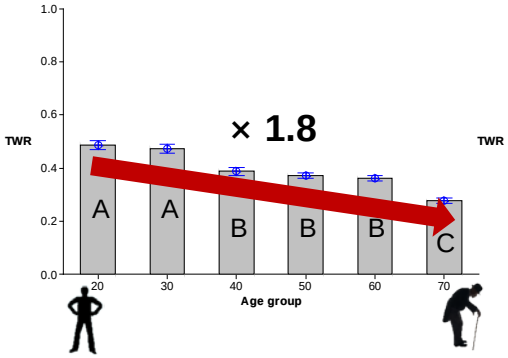
Q & A

Thank you for your attention

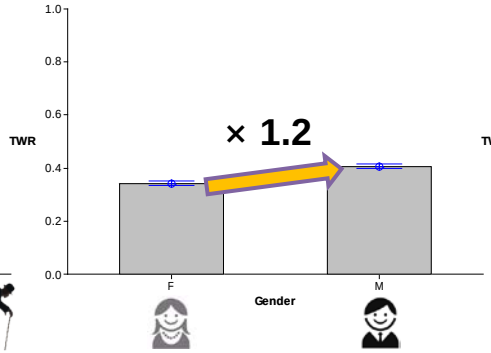
Appendix

S3. 정상인 힘 추적 특성 분석: TWR

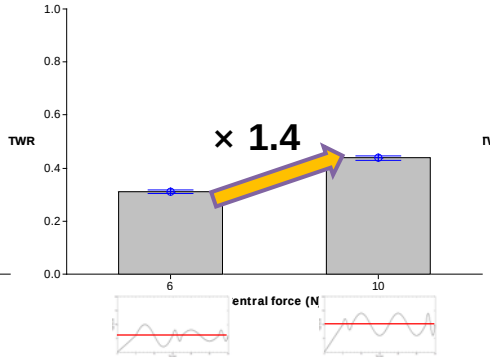
- Age: 70s < 60s ≈ 50s ≈ 40s < 30s ≈ 20s (F[5, 78] = 13.84, p < .001)
- Gender: female < male (F[1, 78] = 15.10, p < .001)
- Central force: 6 N < 10 N (F[1, 83] = 634.15, p < .001)
- Complexity level: 0.06 < 0.03 (F[1, 83] = 241.80, p < .001)



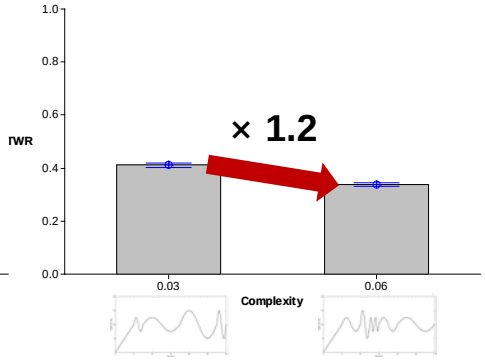
Age effect



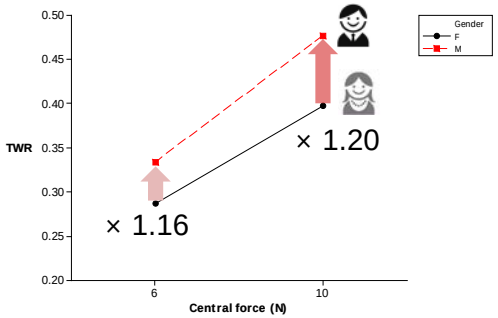
Gender effect



Central force effect



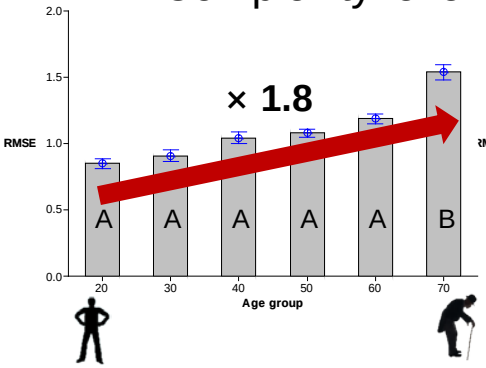
Complexity effect



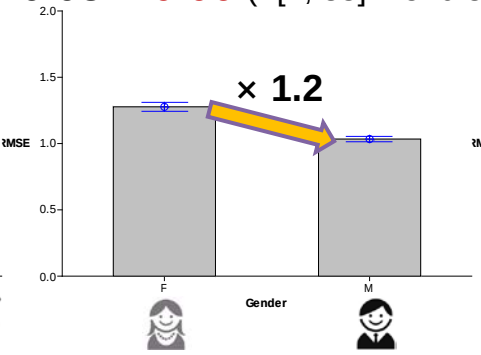
Central force × gender effect (F[1, 83] = 11.18, p = .001)

S3. 정상인 힘 추적 특성 분석: RMSE

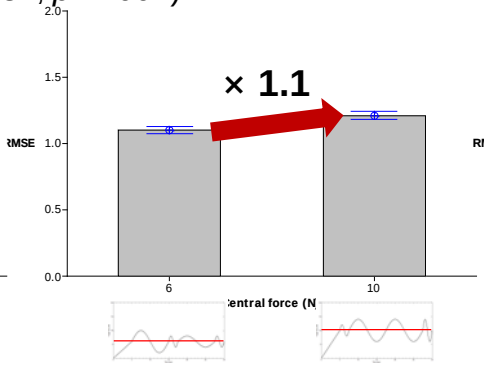
- Age: 20s ≈ 30s ≈ 40s ≈ 50s ≈ 60s < 70s (F[5, 78] = 7.97, p < .001)
- Gender: male < female (F[1, 78] = 9.25, p = .003)
- Central force: 6 N < 10 N (F[1, 83] = 48.63, p < .001)
- Complexity level: 0.03 < 0.06 (F[1, 83] = 510.81, p < .001)



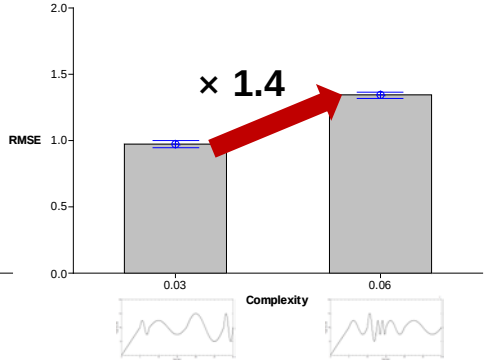
Age effect



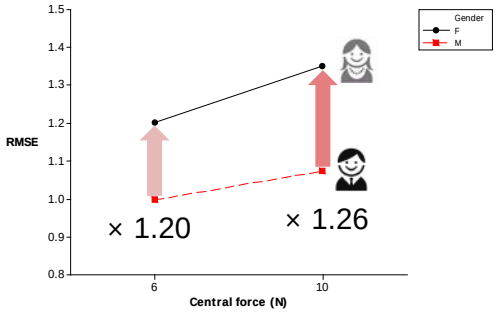
Gender effect



Central force effect



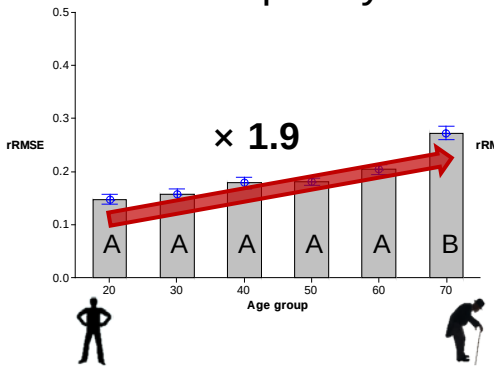
Complexity effect



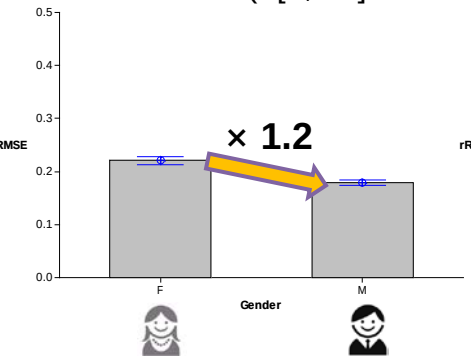
Central force × gender effect (F[1, 83] = 7.12, p = .009)

S3. 정상인 힘 추적 특성 분석: rRMSE

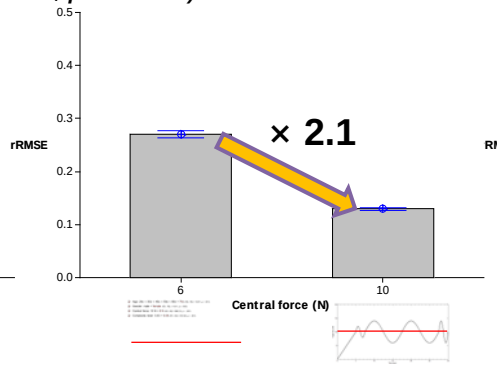
- Age: 20s ≈ 30s ≈ 40s ≈ 50s ≈ 60s < 70s (F[5, 78] = 10.67, p < .001)
- Gender: male < female (F[1, 78] = 10.01, p = .002)
- Central force: 10 N < 6 N (F[1, 83] = 686.53, p < .001)
- Complexity level: 0.03 < 0.06 (F[1, 83] = 434.92, p < .001)



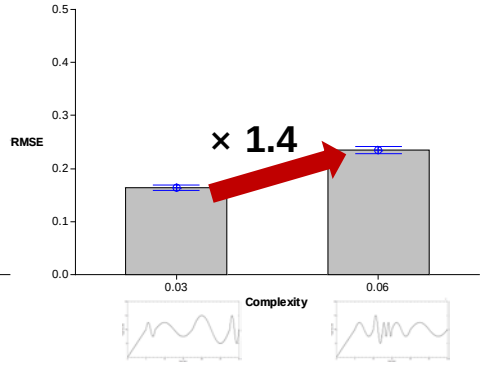
Age effect



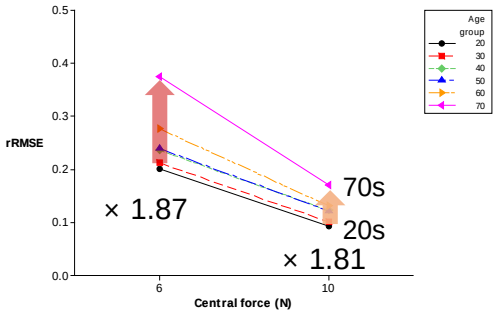
Gender effect



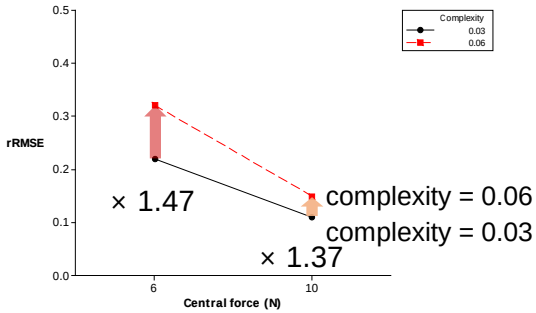
Central force effect



Complexity effect



Age × Central force effect
(F[5, 83] = 12.11, p < .001)



Central force × complexity effect
(F[1, 89] = 168.09, p < .001)