Lifelong cognitive engagement slows symptom progression and neurodegeneration in Huntington's disease: a six year follow-up study

Barcelona, Spain

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Research Question: How does lifelong cognitive engagement affect...

1. **Longitudinal progression** of other symptom domains (i.e., motor, psychiatric)?
2. Underlying **structural brain modulation**?

BACKGROUND

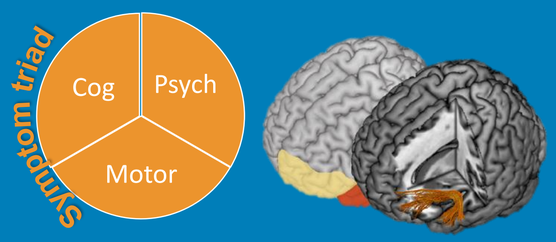
What is cognitive engagement?

Confers benefits in aging and neurodegeneration[1]

- Cognitive reserve (resilience)
- Brain reserve (resistance)

Why Huntington's disease?

Model for neurodegeneration[4]



In HD, cognitively active lifestyle

- Delayed disease onset[5]
- Less severe symptoms severity[6]
- Reduced degeneration in basal ganglia[7]

DESCRIPTION OF ORGANIZATION

To study individual differences and symptom profiles in Huntington's disease

METHODS

- **Participants:** 45 HD gene-expansion carriers (21 pre-, 24 manifest at baseline)
  - **Clinical evaluation**[9,10] (4.28±1.6 assessments, 13.52±4.1 mon inter-assessment interval)
  - **Cognitive Reserve Questionnaire (CRQ)**[11]
  - **T1-weighted MRI** (follow-up at 18 ± 6 mon)

1 Can CRQ score predict symptom progression?

- Generalized linear mixed-effects models in R[8]

CRQ model

Null model

CRQ × Time (days) + Disease state (CAP) + Subject-specific random effects + Random slopes for time ~ Symptom progression

- Three sets of nested models (one for each symptom domain)
- Likelihood ratio test: goodness-of-fit of null vs. CRQ model
- Akaike's information criteria weight (*W*): effect size

UHDRS-cogscore
UHDRS-motor
PBA-s

2 How may cognitive engagement modulate change in gray matter volume over time?

- Longitudinal VBM in cat12 package in SPM[12]
- Controls: CAG-Age Product[13], days b/w scans, TIV
- $P < .005$ (uncorrected) and threshold of $P < .05$ applied at cluster-level; k = 100

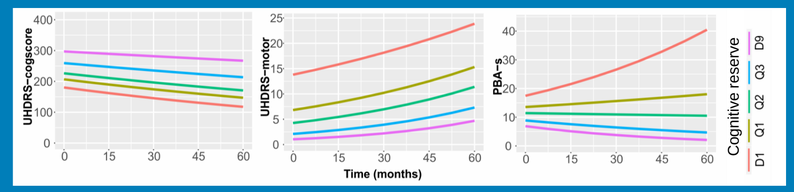
Lifelong cognitive engagement may...

- **Ameliorate clinical progression in motor and psychiatric domains** as well as cognitive
- **Confer brain reserve** in executive regions that integrate action and behavioral regulation

✓ Encourage therapeutic interventions that promote reserve, even prior to diagnosis

RESULTS

1 Higher CRQ scores predict lower overall severity and rate of progression across time and symptom domains

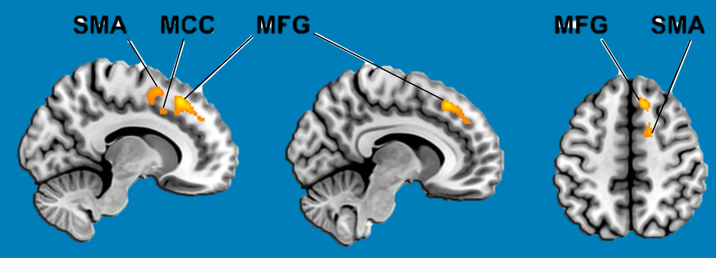


CRQ model was a better fit than null in all three sets

	W	$\chi^2(2)$	*P*
UHDRS-cogscore	.996	15.2	< .001
UHDRS-motor	.991	13.5	.001
PBA-s	.999	17.8	< .001

CRQ score and CRQ x Time variables significant in all three models ($P < .05$)

2 Higher CRQ scores confer structural neuroprotection (reduced gray matter volume loss)



x = 11 x = 8 z = 50 R

MCC = middle cingulate cortex (BA32); MFG = medial frontal gyrus; SMA = supplementary motor area
Slice position labeled in MNI coordinates.

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