

# How Does the Huntington's Disease Everyday Functioning (Hi-DEF) Scale Correlate with Widely Used Cognitive Tests?

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## Background

- Cognitive impairment in Huntington's disease (HD) is characterized by difficulties in multi-tasking, organizing thoughts, and planning and decision making, and is a key driver of loss of functioning.<sup>1,2</sup>
- The HD Everyday Functioning (Hi-DEF) scale is a novel, 40-item, patient-reported outcome (PRO) measure designed to assess the impact of cognitive abilities on daily functioning early in the course of illness. The Hi-DEF scale was previously demonstrated as a valid and reliable measure of cognitive functioning in HD.<sup>3-6</sup>
- To further validate and aid interpretability of the Hi-DEF scale, we assessed the relationship between Hi-DEF items and established cognitive performance measures used to evaluate cognition in HD.

## Objective

- To examine the correlations between Hi-DEF items and established cognitive performance measures.

## Methods

- The analysis is part of a larger non-interventional study conducted to assess the psychometric properties and validity of the Hi-DEF scale, results of which are presented elsewhere.<sup>5,6</sup>
- Alongside Hi-DEF, the validation study collected data on five cognitive performance measures from the Cambridge Neuropsychological Test Automated Battery (CANTAB) including Paired Associates Learning (PAL), Spatial Working Memory (SWM), Spatial Span (SSP), One Touch Stockings of Cambridge (OTS), and Emotion Recognition Task (ERT).
- Items in the final Hi-DEF scale were qualitatively assessed to identify the cognitive processes involved (e.g. executive function, planning and problem solving) and were grouped to conceptually align with the CANTAB tests that measured similar cognitive processes. CANTAB measure variables of greatest relevance were selected for each Hi-DEF item (TABLE 1).
- CANTAB variables used were PAL first attempt memory score (PAL-FAMS), PAL total errors adjusted (PAL-TEA), SWM total errors 8 boxes (SWM-TE8), SSP forward span length (SSP-FSL), OTS median choices to correct (OTS-MCC), OTS median latency to correct (OTS-MLC), and ERT unbiased hit rate sadness (ERT-UHRS).
- Two-tailed Spearman correlations were used to evaluate relationships among Hi-DEF items and corresponding CANTAB tests. Correlation strengths of <0.3 were considered low, 0.3–0.7 were moderate, and >0.7 were strong.

TABLE 1: CONCEPTUAL ALIGNMENT OF COGNITIVE PROCESSES IN HI-DEF AND CANTAB MEASURES

	EXAMPLE HI-DEF ITEMS	SUGGESTED COGNITIVE CONCEPT	COGNITIVE TEST	TESTING FOCUS
Huntington's Disease Everyday Functioning (Hi-DEF); 40 items	#35: Getting thoughts across in group conversations #36: Getting thoughts across in writing	Information processing speed, sequencing, and working memory	One Touch Stockings of Cambridge (OTS)	Executive function and information processing, including both spatial planning and working memory subdomains
	#28: Driving in an unfamiliar place/route #32: Parking without bumping into things	Visuospatial working memory	Spatial Working Memory (SWM)	Retention and manipulation of visuospatial information to assess executive function and working memory
	#30: Remembering where you are going while driving #34: Driving while following GPS instructions	Following a route and remembering locations	Spatial Span (SSP)	Visuospatial working memory capacity
	#5: Learning how to do a new activity/task #21: Learning new work tasks/procedures	Visuospatial working memory	Paired Associates Learning (PAL)	Visual memory and new learning
	#38: Participating in family activities #40: Participating in recreational activities	Social information processing	Emotion Recognition Task (ERT)	Ability to identify basic emotions in facial expressions along a continuum of expression magnitude

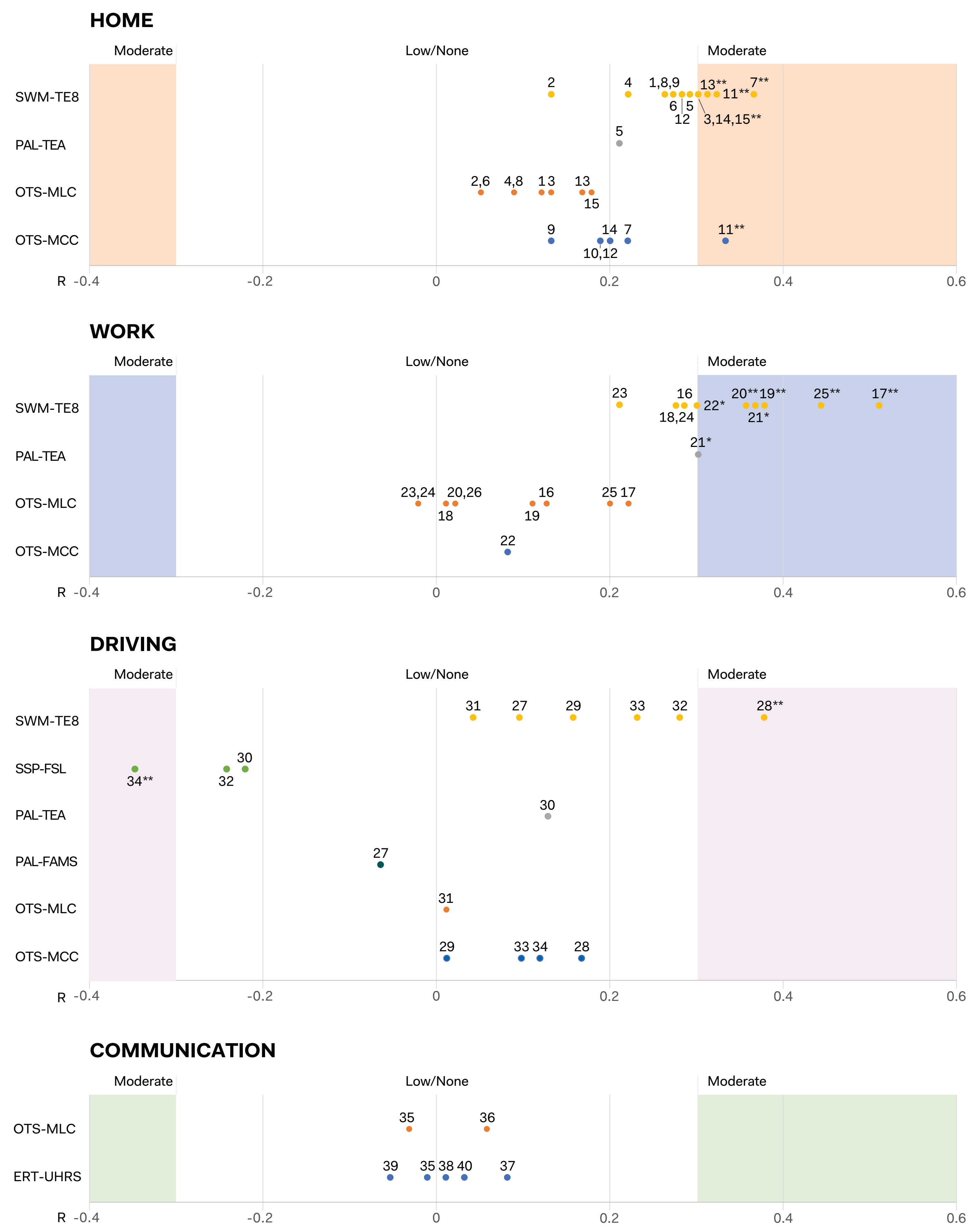
CANTAB, Cambridge Neuropsychological Test Automated Battery; GPS, global positioning system. Petrillo et al. 2022;<sup>5</sup> www.cambridgecognition.com.<sup>7</sup>

## Results

### CORRELATION ANALYSIS BY CANTAB TEST

- Overall, Hi-DEF items had the closest relationship to SWM; 30 of the 40 items were grouped with this test, of which 43% had moderate correlations to the SWM total errors (8 box) outcome (FIGURE 1).
- Moderate correlations were found for some Hi-DEF items with four CANTAB measures (FIGURE 1).
  - SWM-TE8 was moderately correlated with 13 Hi-DEF items (p<0.01). The items were Home subscale: **switching between two activities** (#3; r=0.30), **following a recipe** (#7; r=0.36), **completing logic puzzles** (#11; r=0.32), **doing basic mental math** (#13; r=0.31), **managing finances** (#14; r=0.30), and **responding to unexpected situations** (#15; r=0.30); Work subscale: **completing multi-step activities** (#17; r=0.51), **switching between tasks** (#19; r=0.38), **restarting tasks after interruption** (#20; r=0.36), **learning new tasks** (#21; r=0.37), **working without mistakes** #22; r=0.30), **working with mental math** (#25; r=0.45), and; Driving subscale: **driving in unfamiliar places** (#28; r=0.38).
  - PAL-TEA was moderately correlated with the Hi-DEF item **learning new tasks** from the Work subscale (#21; r=0.30; p=0.01).
  - SSP-FSL was moderately correlated to the Hi-DEF item **driving while following GPS directions** from the Driving subscale; (#34; r=-0.35; p<0.001).
  - OTS-MCC was moderately correlated to the Hi-DEF item **completing logic puzzles** from the Home subscale (#11; r=0.33; p<0.001).
- Low correlations were found between Hi-DEF items and PAL-FAMS, OTS-MLC, or ERT-UHRS.

FIGURE 1: HI-DEF ITEM CORRELATIONS WITH ESTABLISHED COGNITIVE TESTS



\*p<0.05; \*\*p<0.001.

Dots represent individual items of the Hi-DEF scale. Shaded regions indicate threshold for moderate correlation. ERT-UHRS, Emotion Recognition Task unbiased hit rate sadness; OTS-MCC, One Touch Stockings median choices to correct; OTS-MLC, One Touch Stockings median latency to correct; PAL-FAMS, Paired Associates Learning first attempt memory score; PAL-TEA, Paired Associates Learning total errors (adjusted); SSP-FSL, Spatial Span forward span length; SWM-TE8, Spatial Working Memory task total errors 8 boxes.

## Conclusions

- The Hi-DEF scale items had the highest correlations with the SWM test, thus demonstrating the ability of the Hi-DEF scale to measure the impact of executive functioning and working memory on daily activities.
- Home and Work subscale items had more moderate strength correlations to the CANTAB tests than items in Driving or Communication subscales, which may indicate that the Hi-DEF scale is more likely to capture the impact of cognitive impairment on daily activities at home or in work environments.
- Low correlations, such as those seen for the Driving and Communication subscale items, may suggest that Hi-DEF items in those subscales measure different concepts than those of the paired CANTAB tests. This is a limitation of the analysis and results may vary with other cognitive tests. Future studies to explore the relationship of Hi-DEF items with other cognitive assessments are needed.
- Overall, this evidence on the relationship of the Hi-DEF scale items and the CANTAB cognitive performance measures suggests there may be a similar relationship with the Hi-DEF scale items and the HD-Cognitive Assessment Battery (HD-CAB), which tests similar constructs as the CANTAB measures.

## References

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A short form version of the Hi-DEF scale has been designed and validated, and is presented separately in Poster #700.

Disclosures: JP, RS, JJ, and SB are employees of Sage Therapeutics, Inc. and may hold stock or stock options. RR, EE, CI, and SC are employees of Modus Outcomes Ltd. (a Division of THREAD) which received payment from Sage Therapeutics, Inc. to conduct this research. SC may hold stock or stock options.

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