Using the LASSI-L to Detect Robust Interference Effects in Premanifest Huntington Disease

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Background: Diagnosis of manifest Huntington disease (HD) is based primarily on motor symptoms, but premanifest HD (preHD) is often associated with subtle cognitive decline. The Loewenstein–Acevedo Scales for Semantic Interference and Learning (LASSI–L) is a validated verbal learning test that can be used to detect early cognitive decline.

Objective: To determine the utility of the LASSI–L for detecting early cognitive decline in individuals with preHD and to compare the results of the LASSI–L with those of commonly used neuropsychological tests in HD.

Method: We administered the LASSI–L to 13 individuals with preHD and 13 healthy controls matched for age, sex, and education as part of a longitudinal study of disease progression. For comparison purposes, we administered the Mini-Mental State Examination; Stroop Color and Word Test; Symbol Digit Modalities Test; Trail-Making Test, Parts A and B; and category fluency (animals) task.

Results: Five of the seven sections on the LASSI–L captured group differences: Proactive Semantic Interference (PSI; $P < 0.001$), Failure to Recover From PSI ($P = 0.038$), Retroactive Semantic Interference (RSI; $P = 0.013$), Delayed Recall ($P < 0.001$), and B1 Cued Recall Intrusions ($P = 0.036$). Using a false discovery rate of <0.05, PSI, RSI, and Delayed Recall remained significant.

Conclusion: The LASSI–L is a sensitive instrument for detecting early interference effects in individuals with preHD that outperforms commonly used neuropsychological tests. The LASSI–L could be a useful addition to clinical and research protocols involving individuals with preHD.

Key Words: semantic interference, cognitive, Huntington disease, executive function, premanifest HD

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CVLT = California Verbal Learning Test. **FDR** = false discovery rate. **frPSI** = failure to recover from proactive semantic interference. **HC** = healthy controls. **HD** = Huntington disease. **LASSI–L** = Loewenstein–Acevedo Scales of Semantic Interference and Learning. **MMSE** = Mini-Mental State Examination. **preHD** = premanifest Huntington disease. **PSI** = proactive semantic interference. **RSI** = retroactive semantic interference. **SDMT** = Symbol Digit Modalities Test.

Huntington disease (HD) is an autosomal-dominant neurodegenerative disorder that is caused by the pathological expansion of CAG (cytosine, adenine, guanine) repeats in the Huntingtin gene. HD is characterized symptomatically by a progressive decline in motor, cognitive, and psychiatric domains. The diagnosis of *manifest HD* is established with the emergence of unequivocal motor signs, but individuals often show mild cognitive and psychiatric symptoms during the premanifest phase. In fact, more than one-third of individuals with *premanifest HD* (preHD) are considered to have mild cognitive impairment (Duff et al, 2010; Ross et al, 2014).

Cognitive Deficits in preHD

Cognitive deficits in individuals with preHD have been observed in several domains, including psychomotor speed, visuomotor and spatial integration, executive function, sustained attention, and memory retrieval (Tabrizi et al, 2013). Neuroimaging studies of individuals with HD have reliably correlated declining performance on neuropsychological tests to neuroanatomical changes, including a correlation between general cognitive decline and progressive striatal atrophy (Paulsen et al, 2013; Starkstein et al, 1988); executive dysfunction and striatal/insular atrophy (Peinemann et al, 2005); deficits on verbal learning tasks and caudate atrophy (Harrington et al, 2014); and deficits on executive measures such as the Stroop Color and Word Test (Stroop, 1935), the Symbol Digit Modalities Test (SDMT; Smith, 1982), and verbal fluency tasks with regionally specific cortical thinning across motor and premotor, lingual, and occipital regions (Diana Rosas et al, 2008).

Relying solely on clear motor symptoms to establish a conversion to manifest HD is therefore likely to overlook subtle progressive decline in other domains such as cognition and behavior. Refining the assessment of cognitive

decline in individuals with preHD is important for understanding disease progression and building accurate prediction models, which may optimize the timing of any eventual disease-modifying intervention (Tabrizi et al, 2013).

Cognitive profiles in preHD have been studied using a myriad of paradigms (Mestre et al, 2019; Paulsen, 2011; Paulsen et al, 2013) and have revealed specific deficits in multiple domains, including notable deficits in executive functioning (Duff et al, 2010; Holden et al, 2020; Mestre et al, 2019; Oosterloo et al, 2021; Tabrizi et al, 2013). In the early stages of manifest HD, executive dysfunction leads to difficulties on memory-based tasks. For example, individuals with manifest HD exhibit impaired retrieval but relatively intact encoding on free-recall paradigms (Beatty and Butters, 1986; Butters et al, 1985, 1987; Weingartner et al, 1979), modified Brown-Peterson distractor paradigms (Beatty and Butters, 1986), and associated memory paradigms (Fine et al, 2008).

Deficits in source memory in individuals with manifest HD have been detected by the Rey Auditory Verbal Learning Test (Butters et al, 1985) and the California Verbal Learning Test I (CVLT–I; Delis et al, 1991), and intrusion errors have been detected by the CVLT–3 (Graves et al, 2019) and CVLT–II (Holden et al, 2020). Difficulties with the rate of improvement across trials, increased perseveration, and semantic clustering in individuals with manifest HD have also been detected by the CVLT–I and II (Graves et al, 2017; Kramer et al, 1988; Massman et al, 1990, 1992, 1993).

Despite the substantial evidence indicating executive dysfunction-based memory problems in individuals with manifest HD, fewer studies have looked specifically at the effects in the preHD period. Using the Wechsler Memory Scale (Wechsler, 1987), Giordani et al (1995) were unable to find differences on any individual memory subtest between individuals with preHD and controls. A more recent study using the CVLT–II demonstrated relatively mild deficits in free/cued recall and recognition discriminability in individuals with preHD but was unable to detect an effect of executive dysfunction—such as interference, intrusions, and semantic clustering—on other aspects of memory (Holden et al, 2020).

Current Study

Given this extensive neuropsychological characterization of both individuals with HD and those with preHD, investigators have argued that (a) any additional cognitive test that is used to assess this population should provide unique information that is not found in current tests, and (b) the test should represent an improvement in terms of cost, reliability, and/or effect size (Paulsen, 2010). Taking these criteria into account, we hypothesized that previously obscured effects of executive dysfunction on memory in the preHD period could be elicited by administering a verbal learning test that would sharpen the effects of interference and probe for inhibitory failures during memory retrieval (Crocco et al, 2014). We selected the Loewenstein–Acevedo Scales for Semantic Interference and Learning (LASSI–L; Loewenstein and Curiel Cid, 2021) for the following reasons:

- It is specifically designed to elicit and capture the effect of interference.
- It has been validated.
- It has been shown to exhibit good interrater reliability (Curiel et al, 2013; Matías-Guiu et al, 2020).
- It is efficient/cost-effective to administer.
- To our knowledge, it has not been used previously to characterize the preHD population.

Similar to other verbal learning tests such as the CVLT, the LASSI–L uses free and cued recall of word lists with both short and long delays. However, the LASSI–L also promotes maximal encoding through multimodal presentation (ie, auditory and visual) and explicit semantic category cuing; it also captures the effect of processing speed deficits by imposing time limits for each section (Loewenstein and Curiel Cid, 2021; Loewenstein et al, 2004; Matías-Guiu et al, 2020). In addition, by using two lists that are presented an equal number of times, the LASSI–L enhances the interference effect of both lists on each other while simultaneously probing for failure to recover from interference effects (Curiel et al, 2013). The methodology used by the LASSI–L is outlined in Figure 1 and is described in detail in the Method section.

The overall goals of this study were to determine whether the LASSI–L could detect interference effects in individuals with preHD and to compare these findings to the results of standard neuropsychological tests that are commonly used to detect and monitor cognitive deficits in individuals with HD.

METHOD

Participants

We recruited two groups of individuals for our study: individuals with preHD and healthy controls (HC). Both groups were recruited from the Huntington's Disease Society of America Center of Excellence at the Beth Israel Deaconess Medical Center in Boston, Massachusetts.

Inclusion criteria for the preHD group were 18–65 years of age and confirmed genetic diagnosis of HD (ie, ≥40 CAG repeats in the Huntingtin gene). Inclusion criteria for the HC were 18–65 years of age and no personal history of HD. The HC were selected to match the preHD group across age, sex, and educational parameters in order to minimize confounding effects.

Exclusion criteria for the preHD group included manifest disease as assessed clinically by a neurologist at any point before or up to 6 months after the initial study visit. Exclusion criteria for both the preHD and HC groups also included the following:

- history of cardiovascular disease;
- other neurologic history, including stroke, seizure, and traumatic brain injury (defined as head trauma with loss of consciousness of >5 minutes or requiring treatment);

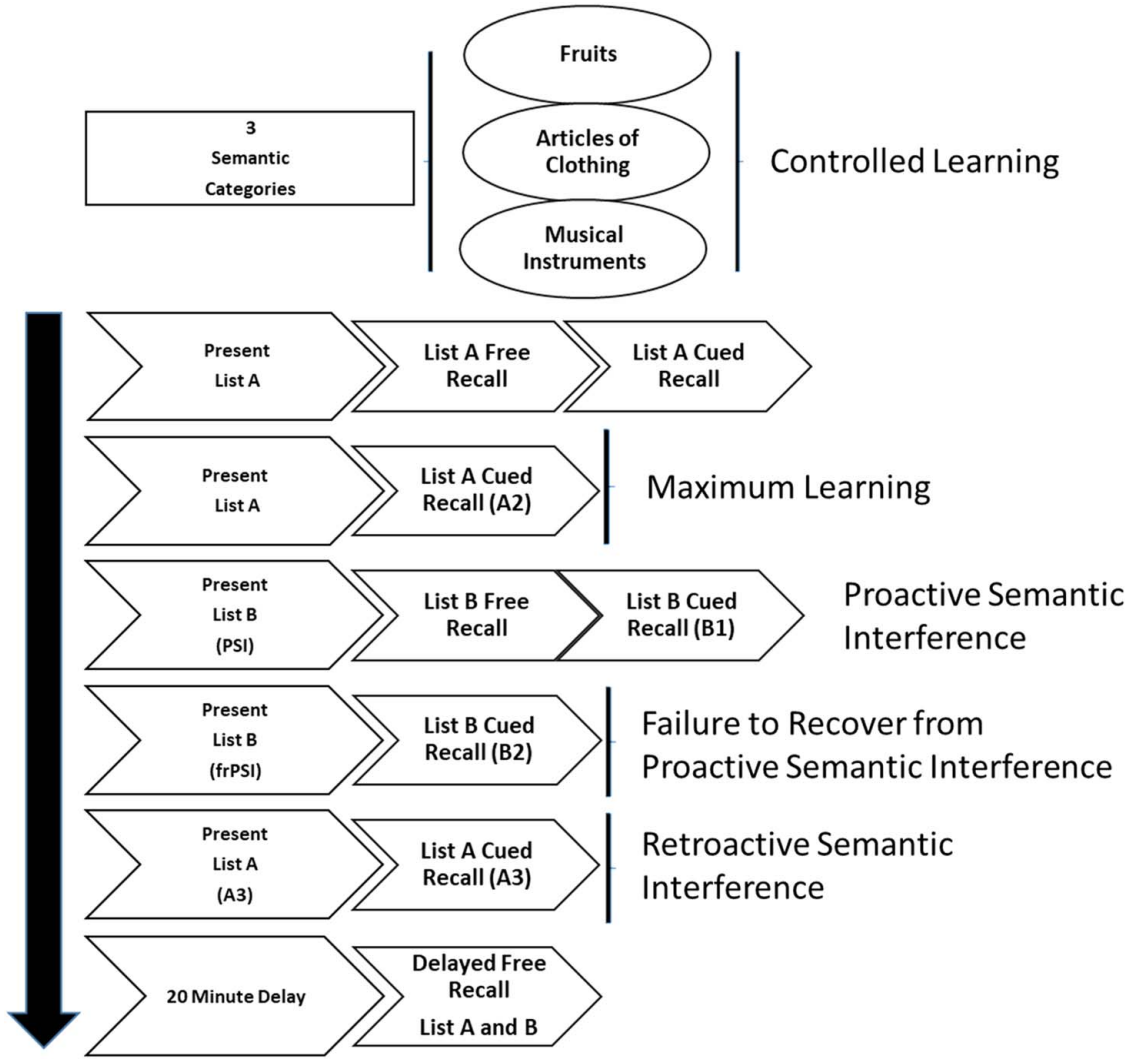

FIGURE 1. Methodology of the LASSI–L. **frPSI** = failure to recover from proactive semantic interference. **LASSI–L** = Loewenstein–Acevedo Scales of Semantic Interference and Learning. **PSI** = proactive semantic interference.

- medication regimens that were being actively changed or use of stimulant medication (eg, amphetamine salts/methylphenidate) or sedative (eg, opioid/benzodiazepine) <5 days before the study visit; and
- any current illicit substance use, remote alcoholism or frequent alcohol use (>14 drinks per week), bipolar disease, schizoaffective disorder, active suicidal ideation, history of psychosis, or concern for mild cognitive impairment/dementia.

Because this study was part of a larger longitudinal MRI study, exclusions for both groups also included any contraindication to this type of imaging, including metal in the brain or medical devices (eg, cardiac pacemaker).

At baseline, all of the participants provided their medical history and were examined by a trained neurologist (S.A.F. and S.L.) who determined their Unified Huntington's Disease Rating Scale (Huntington Study Group, 1996) Total Motor score. To reduce the likelihood of enrolling individuals with manifest HD, we excluded individuals whose Total Motor score on the Unified Huntington's Disease Rating Scale ≥10.

The study protocol was reviewed and approved by Beth Israel Deaconess Medical Center's Committee on Clinical Investigations in Boston, Massachusetts. All individuals provided informed written consent before enrolling in the study.

Neuropsychological Tests

We administered a battery of neuropsychological tests to both study groups. The battery included several neuropsychological tests that are already in use in Enroll–HD, which is a large, ongoing international observational study (Landwehrmeyer et al, 2016). Specific tests included the Mini-Mental State Examination (MMSE; Folstein et al, 1975); Stroop Color and Word Test; SDMT; Trail-Making Test, Parts A and B (Reitan, 1956); and category fluency (animals) task (Benton, 1968). After these tests

were completed, we administered the LASSI–L to both study groups, depicted methodologically in Figure 1.

The LASSI–L employs a list-learning paradigm to measure an individual's maximum learning capacity, free recall, cued recall, and delayed recall of 15 target words (List A) followed by 15 separate but semantically related words (List B) (Loewenstein and Curiel Cid, 2021). Each list contains 5 words from 3 semantic categories (ie, fruits, articles of clothing, musical instruments) and is visually cued and verbally read aloud by the participant at a rate of 4 seconds per word.

List A is presented first, after which the participant has 60 seconds to perform a free recall. This section is followed by a 20-second cued recall for each semantic category (ie, participants are given the semantic category cue and have a 20-second limit for each category). List A is immediately presented again, and the participant has 20 seconds to perform a second cued recall of each semantic category. By repeatedly cuing the participant with semantic categories, this approach aims to constrain individual learning strategies and to maximize the number of initially encoded items, which in turn increases the likelihood of detecting interference and prompting intrusions on subsequent steps.

This exact procedure is then repeated using an entirely different set of 15 words (List B) that belong to the same 3 semantic categories. Next, the participant is given 60 seconds to perform a free recall, followed by 20 seconds to perform a cued recall, of the initial list, List A. Finally, after a 20-minute delay, the participant is given 90 seconds to recall any item from either list without being cued. The number of correct items and the number of intrusions are recorded for each section.

Given that both lists include words in the same semantic categories, the LASSI–L probes for proactive semantic interference (PSI) and failure to recover from PSI (frPSI) by measuring the interference of List A on the participant's ability to learn List B. Similarly, the LASSI–L probes for retroactive semantic interference (RSI) by measuring the interference of List B on a subsequent cued recall of List A (A3). The LASSI–L uses standardized rater instructions and time limits on each section in order to mitigate individualized learning strategies (Loewenstein and Curiel Cid, 2021).

Statistical Analysis

We used unpaired two-tailed *t* tests to analyze group differences in both demographics and test performance except for the MMSE and B1/B2 Intrusion sections, which were compared using Mann-Whitney *U* due to floor/ceiling effects and non-normal distribution. Given that the LASSI–L had not previously been administered to any HD cohort, it was challenging to predict a priori which sections of the LASSI–L might show significant group differences. We therefore decided to try to minimize the risk of Type 1 errors by submitting all seven sections of the LASSI–L and all eight of the commonly used neuropsychological tests to multiple comparison testing. The resulting *P* values from all of the neuropsychological tests (total of 15 group comparisons) were corrected for multiple comparisons using a false discovery rate (FDR) <0.05.

We used a χ^2 analysis to analyze differences in the categorical variables (sex). Effect sizes were measured using Cohen's *d*.

Next, we conducted additional analyses on the PSI and RSI sections of the LASSI–L in order to evaluate whether the interference measures might have been confounded by a global difficulty with encoding. In other words, if a participant demonstrated relative difficulty with maximal learning (A2), a lower performance on a subsequent section (B1) might reflect a general inability to encode rather than a demonstration of true interference. We therefore also calculated the relative change in performance from the maximal encoding section for both PSI (B1 − A2) and RSI (A3 − A2) for each participant and compared the relative performance across the two groups using another *t* test.

We used Pearson's *r* to assess for collinearity/shared variance between tests that might probe similar cognitive domains in order to compute correlations between any significant section of the LASSI–L and the eight commonly used neuropsychological tests.

RESULTS

We enrolled 14 individuals with preHD and 13 HC in our study. One individual with preHD was later excluded because of a clinical diagnosis of manifest HD (within 6 months of the initial study visit).

Participants ranged in age from 19 to 57 years; the mean age of the preHD group was 37.3 (SD = 11.04, range 24–57 years), and of the HC was 32.2 (SD = 10.98, range of 19–53 years). The mean years of education in the preHD group was 14.8 (SD = 3.0), and in the HC was 16.0 (SD = 1.83). Seventy-six point nine percent of the preHD group was female; 38.5% of the HC group was female. These baseline demographics were not statistically different.

Among the preHD group, the mean CAG repeat length for the expanded allele was 42.4 (SD = 1.3) (Table 1). Compared with the HC, the preHD group exhibited significant deficits across five of the seven sections of the LASSI–L: PSI, frPSI, RSI, Delayed Recall, and B1 Intrusions. PSI, RSI, and Delayed Recall remained significant after adjusting for multiple comparisons with an FDR <0.05 (Table 2 and Figure 2). Relative performance on PSI and RSI—when computed as the relative change from maximal encoding (A2)—also remained significant. (See Table 1 in the supplementary digital content [SDC], http://links.lww.com/CBN/A120, which illustrates the difference in A2 to B1 scores and A2 to A3 scores.) PSI showed a moderate positive correlation to the MMSE ($r = 0.559$, $P = 0.047$) and to the Stroop Interference subtest ($r = 0.618$, $P = 0.024$). RSI and Delayed Recall did not show significant correlations with any other neuropsychological test. (See Table 2 in the SDC, http://links.lww.com/CBN/A120.)

TABLE 1. Clinical Characteristics of the Group With Premanifest Huntington Disease

Age	CAG Length	UHDRS Total Motor Score
26	42	2
56	42	2
36	42	0
33	43	0
51	40	0
36	44	8
29	44	0
24	40	1
29	44	0
35	41	0
27	43	1
55	43	4
41	43	0

CAG = cytosine, adenine, guanine. **UHDRS** = Unified Huntington's Disease Rating Scale.

Performance on most of the commonly used neuropsychological tests (ie, Stroop Interference subtest; SDMT; Trail-Making Test, Part B; and category fluency task) was not significantly different between the preHD and HC groups. Of the four tests that were significantly different between the two groups, only the Stroop Word Reading subtest remained significant using an FDR <0.05 (Table 3). Interestingly, the Stroop Word Reading subtest was not significantly correlated with PSI, RSI, or Delayed Recall. (See Table 2 in the SDC, http://links.lww.com/CBN/A120.)

DISCUSSION

We demonstrated that the LASSI–L is a sensitive instrument that captures proactive interference, retroactive interference, and impairments in delayed recall in a preHD group. Even with a small sample size, the LASSI–L was able to detect early cognitive deficits with large effect sizes. Deficits captured by this instrument were not readily apparent on several neuropsychological tests that are commonly used in HD-related research, including the Stroop Interference subtest; SDMT; Trail-Making Test, Part B; and category fluency task.

An additional advantage of the LASSI–L is that unlike many cognitive tests that are currently used with individuals with preHD, the LASSI–L does not rely on motor coordination or speed, thereby reducing any confounding effect from declining motor control in this population. Overall, these findings suggest that the LASSI–L meets the criteria outlined in Paulsen (2010) and might represent an improvement over many current tests. The LASSI–L also demonstrates large effect sizes at low cost. After being subjected to larger reliability studies, the LASSI–L could be a valuable addition to neuropsychological batteries that are currently used to assess and monitor the preHD population.

Sections of the LASSI–L, including PSI, RSI, and Delayed Recall, were sensitive to subtle changes in the preHD group, likely because these sections captured deficits in domains that are known to be affected in individuals with preHD, including executive function, processing speed, and memory retrieval (Tabrizi et al, 2013). As expected, the LASSI–L's multimodal, semantically constrained, and cued learning paradigm allowed for effective initial encoding of List A, and both study groups exhibited similarly good performance after the second cued recall (A2 Cued Recall).

In the next measured section (B1 Cued Recall), although both groups exhibited a relative drop in performance, the preHD group was markedly more affected than the HC, indicating stronger interference of List A on the initial learning of List B in the preHD group. Although the group comparison of B1 Cued Recall Intrusions did not survive FDR correction, every intrusion generated by the preHD group (23/23) on that section originated from List A. The LASSI–L also captured group differences in RSI, demonstrating that the preHD group was also sensitive to the interference of List B on List A.

TABLE 2. Comparison of LASSI–L Section Performance for the preHD and HC Groups

LASSI–L Section	preHD (n = 13) M (SD)	HC (n = 13) M (SD)	*P* (FDR-adjusted)	Cohen's *d*
A2 Cued Recall (correct responses)	12.92 (2.06)	14.15 (1.21)	0.104 (0.120)	0.728
B1 Cued Recall (PSI) (correct responses)	5.62 (2.63)	10.38 (2.47)	0.0001 (0.002)***	1.866
B2 Cued Recall (frPSI) (correct responses)	10.54 (2.57)	13.15 (2.27)	0.038 (0.063)	1.076
A3 Cued Recall (RSI) (correct responses)	8.31 (2.87)	11.38 (2.93)	0.013 (0.049)*	1.059
Delayed Recall (correct responses)	17.85 (3.87)	23.77 (3.27)	0.0003 (0.002)***	1.652
B1 Cued Recall Intrusions	1.69 (2.06)	0.31 (0.48)	0.036 (0.077)	0.923
B2 Cued Recall Intrusions	1.31 (1.25)	0.31 (0.48)	0.085 (0.106)	1.056
B1 Cued Recall Intrusion (group total)	23	3		
B2 Cued Recall Intrusion (group total)	15	4		

FDR = false discovery rate. **frPSI** = failure to recover from proactive semantic interference. **HC** = healthy controls. **LASSI–L** = Loewenstein-Acevedo Scales for Semantic Interference and Learning. **preHD** = premanifest Huntington disease. **PSI** = proactive semantic interference. **RSI** = retroactive semantic interference.

*Significant at $P < 0.05$.

***Significant at $P < 0.001$.

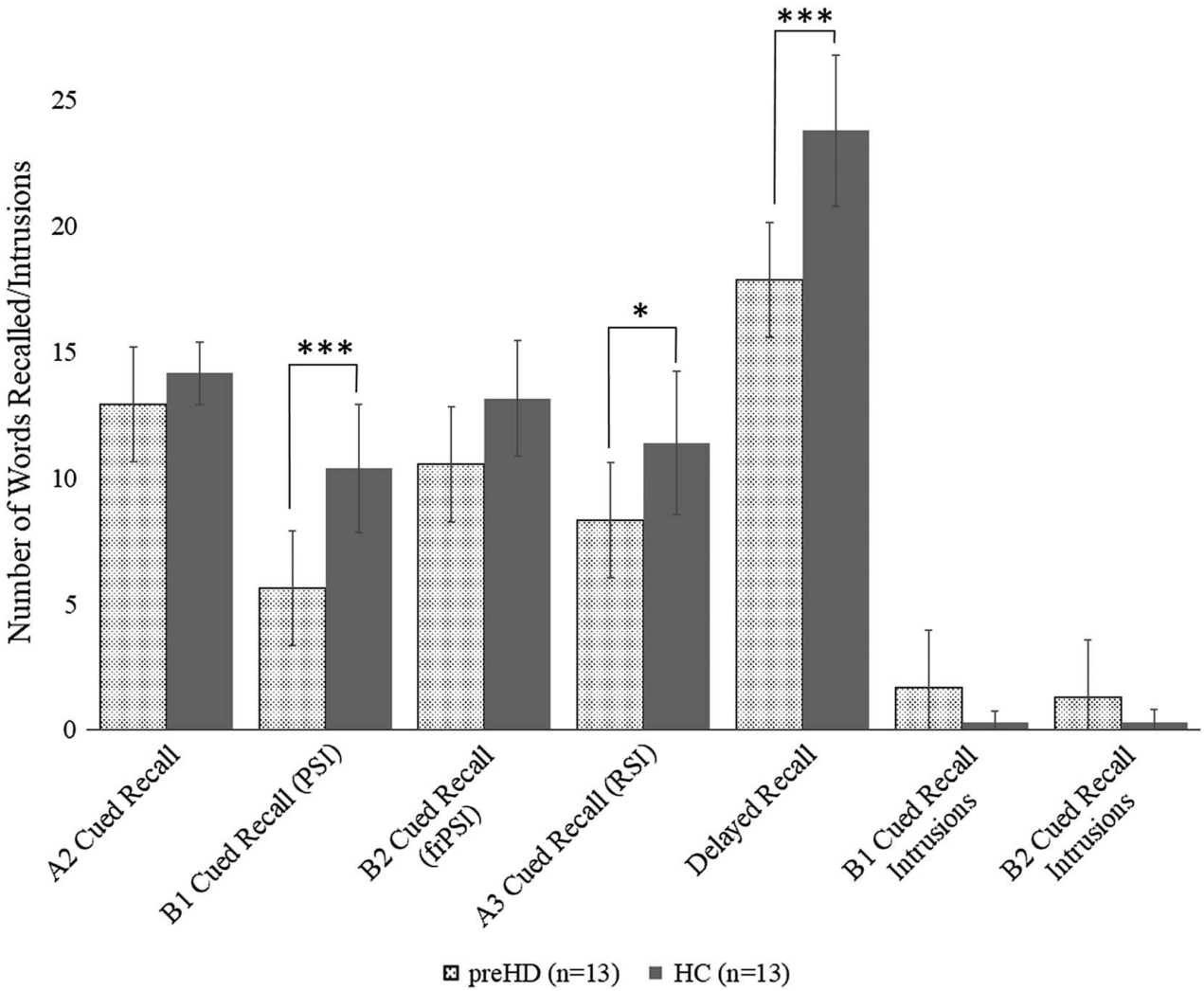

FIGURE 2. Mean performance on each section of the LASSI–L. **frPSI** = failure to recover from proactive semantic interference. **HC** = healthy controls. **LASSI–L** = Loewenstein–Acevedo Scales of Semantic Interference and Learning. **preHD** = premanifest Huntington disease. **PSI** = proactive semantic interference. **RSI** = retroactive semantic interference. *Significant at $P < 0.05$. ***Significant at $P < 0.001$.

Overall, these findings suggest that the cued learning paradigm that is used by the LASSI–L led to robust interference through increased semantic competition, which in turn prompted failures of inhibitory control during learning and retrieval.

As with other list-learning tasks studied by Holden et al (2020) and Rohrer et al (1999), our preHD group exhibited memory retrieval deficits in delayed free recall. However, our results suggest that by allowing for the recall of any item from either learned list (A or B), the LASSI–L paradigm enhanced the combined effects of both proactive and retroactive interference on the final Delayed Recall section. This overall effect may have contributed to the larger effect size that was recorded on the Delayed Free Recall section in our study ($d = 1.652$, $P \leq 0.001$) compared with the effect that was reported for Long Delay Free Recall on the CVLT–II in a similar preHD population ($d = 0.40$, $P = 0.05$) (Holden et al, 2020). Performance on the Interference sections (PSI and RSI) of the LASSI–L was not significantly correlated with performance on the Stroop Word Reading subtest (the only other neuropsychological test that survived multiple comparisons in our battery) ($r = 0.257$, $P = 0.397$). This finding suggests that the LASSI–L was capturing data that were nonredundant with the Stroop Word Reading subtest and that combining both tests would provide complementary information.

Study Limitations

Our study had a small sample size that would benefit from validation across larger groups. Sections of the LASSI–L that did not survive comparison testing in our preHD group (frPSI and B1/B2 Cued Recall Intrusions) may demonstrate adequate sensitivity and reliability in

TABLE 3. Demographics and Baseline Cognitive Performance Comparison Between UHDRS and LASSI–L Assessments for preHD and HC Groups

Variable/Test	preHD (n = 13) M (SD)	HC (n = 13) M (SD)	*P* (FDR-adjusted)	Cohen's *d*
Age (M years)	37.3 (11.04)	32.2 (10.98)	0.249	
Education (M years)	14.8 (3.00)	16.0 (1.83)	0.230	
Sex (% female)	76.9%	38.5%	0.112	
MMSE score	28.54 (0.78)	29.38 (0.77)	0.020 (0.060)	1.084
Stroop Word Reading subtest (correct word count)	84.31 (11.80)	106.62 (12.24)	0.0001 (0.001)***	1.856
Stroop Color Naming subtest (correct word count)	70.69 (11.10)	81.92 (11.12)	0.032 (0.080)	1.011
Stroop Interference subtest (correct responses)	47.23 (12.64)	57.46 (12.61)	0.083 (0.113)	0.810
SDMT (correct responses)	51.77 (9.64)	56.85 (15.21)	0.335 (0.359)	0.399
TMT, Part A (seconds)	30.77 (9.08)	23.23 (5.63)	0.037 (0.069)	0.998
TMT, Part B (seconds)	61.62 (18.02)	61.00 (26.04)	0.959 (0.959)	0.0277
Category fluency (animals) (correct responses)	20.00 (6.63)	24.23 (5.82)	0.061 (0.092)	0.678

FDR = false discovery rate. **HC** = healthy controls. **LASSI–L** = Loewenstein-Acevedo Scales for Semantic Interference and Learning. **MMSE** = Mini-Mental State Examination. **preHD** = premanifest Huntington disease. **SDMT** = Symbol Digit Modalities Test. **TMT** = Trail-Making Test. **UHDRS** = Unified Huntington's Disease Rating Scale.
***Significant at $P < 0.001$.

larger follow-up studies of individuals with preHD. Similarly, follow-up studies might benefit from using different iterations of the LASSI–L (eg, by increasing semantic categories, number of lists, or number of words in each list), which in turn might lead to an inability to recover from interference (eg, frPSI) and/or more frequent intrusions.

It remains possible that our control group was not entirely matched across all possible dimensions—including race/ethnicity—and that factors unaccounted for in our matching paradigm might have influenced our results. Once again, future studies using larger preHD groups would help minimize these concerns. In addition, future studies focused on correlating the LASSI–L with neuroimaging may indicate further underlying mechanisms of memory dysfunction.

Given that similarities in task design could risk confounding participant performance, our study design purposefully avoided administering both the LASSI–L and other verbal learning tests during the same visit. Future direct comparisons of the LASSI–L to verbal learning tests such as the CVLT in the same group could help identify the test, or test sections, having the highest overall sensitivity in individuals with preHD. Each test has relative advantages: The CVLT allows measures of learning strategies (eg, semantic clustering and serial order); the LASSI–L has robust measures of interference. Regardless, our results provide further evidence that verbal learning tests are sensitive to early cognitive changes in individuals with preHD, and they should be incorporated with greater frequency in the assessment and monitoring of this specific population (Holden et al, 2020).

CONCLUSION

The LASSI–L is an efficient learning test that can detect early cognitive decline by capturing subtle interference effects in individuals with preHD. Because the LASSI–L appears to outperform other commonly used neuropsychological tests in individuals with preHD and demonstrates large effect sizes at low cost, it could prove to be a useful addition to current protocols that seek to detect and monitor the earliest cognitive changes in this population.

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