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Odor detection, learning, and memory in Huntington's disease

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Abstract

We compared 7 mildly affected Huntington's disease (HD) patients to 7 age- and education-matched healthy controls (NC) on an odor detection test, the California Odor Learning Test, and the California Verbal Learning Test. Results demonstrated that odor detection sensitivity, but not group membership, accounted for significant variance in total olfactory learning. Both groups learned fewer items in the olfactory modality compared to the verbal modality, but retained a similar amount following a delay. No group differences were demonstrated for verbal recognition discriminability, but the HD group demonstrated significantly impaired odor recognition discriminability. Finally, odor detection provided excellent classification sensitivity and specificity between the patients and controls, suggesting that olfactory testing may provide a sensitive measure of the early disease process in HD. (*JINS*, 1999, *5*, 609–615.)

Keywords: Huntington's disease, Olfaction, Learning and memory, Recognition memory, Odor identification, Odor threshold, Dementia

INTRODUCTION

Olfactory ability has been studied in Huntington's disease (HD) using a number of different paradigms (Doty, 1991; Moberg et al., 1987; Nordin et al, 1995). Previous researchers have found impairments in detection (Moberg & Doty, 1997; Nordin et al., 1995), identification (Bylsma et al, 1997; Doty, 1991; Moberg & Doty, 1997; Nordin et al., 1995), strength and quality discrimination (Nordin et al., 1995), and recognition memory (Moberg et al., 1987). In fact, Nordin et al. (1995) demonstrated that deficits in detection, discrimination, and identification were greater for olfaction than for other modalities (i.e., taste and vision). While the exact cause of this impairment is unknown, it is consistent with the known neuropathology associated with HD.

Post-mortem analysis of HD brains has revealed neuronal loss in the entorhinal cortex, which is believed to support olfactory functioning (Braak & Braak, 1992). Braak and Braak (1992) indicate that the entorhinal cortex relays information to both the hippocampal formation and to the ventral striatum. The latter, in turn, sends information to the prefrontal cortex (Alexander et al., 1986). Braak and Braak (1992) have speculated that neuropathology in the entorhinal cortex may disrupt the connections between the neocortex and the hippocampal formation and may result in the personality changes and memory impairments associated with HD. In HD, the cell loss that occurs in the entorhinal area and the striatum (Vonsattel et al., 1985) could disrupt the flow of olfactory information to and from olfactory regions in the prefrontal cortex. Thus, olfactory deficits in HD may be expressed in tasks relying on intact connections between the entorhinal cortex and the prefrontal cortex.

Given that free recall of acquired information may be the most severely impaired memory function in HD (Delis et al., 1991) and that olfactory ability is also significantly impaired, it is possible that an odor-based learning and memory paradigm may be more sensitive to deficits in HD than conventional neuropsychological tests. We examined this possibility by using an odor-based learning and memory task (the California Odor Learning Test; COLT) developed by Murphy et al. (1997). We compared the performances of HD patients and control participants on the COLT and on a commonly used verbal learning and memory task, the California Verbal Learning Test (CVLT; Delis et al., 1987). More specifically, we were interested in investigating three key questions: (1) Do HD and NC participants differ in learning

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and memory on the COLT *versus* the CVLT; (2) What contribution does odor detection sensitivity make to odor learning and memory; and (3) Are olfactory measures more sensitive to the early changes in HD than a traditional neuropsychological test, namely the CVLT?

METHODS

Research Participants

HD patients were selected from the HD Clinical Research Program at the University of California, San Diego. The diagnosis of HD was made by a senior neurologist based on an abnormal neurological examination, positive family history, gene positive status for the HD gene, and dementia according to DSM–IV criteria (American Psychiatric Association, 1994). Exclusionary criteria included (1) Dementia Rating Scale (DRS; Mattis, 1988) total score less than 115; (2) average olfactory thresholds below 2.5, indicating severe hyposmia or anosmia; (3) current or past DSM–IV diagnosis of substance dependence or abuse; (4) neurologic diagnosis other than HD; (5) serious psychiatric diagnosis requiring hospitalization; (6) speech articulation too impaired to be reliably understood; and (7) English as a second language. Based upon these criteria, 10 HD patients were available for study. Odor detection threshold was assessed in 6 additional HD patients, but they were found to be severely hyposmic or anosmic and were excluded from further study.

Ten HD patients volunteered for the olfaction memory battery. Two of these patients were unable or unwilling to complete the protocol. Thus, the HD sample consisted of 8 HD patients (7 women and 1 man). One HD patient lacked motivation and concentration during testing and performed in a haphazard manner. Statistical analyses revealed that his data were more than 3 standard deviations from the mean. Therefore, this patient's data were not included in further analyses. Thus, the odor memory data of 7 HD patients (7 women) were analyzed.

The average age of the HD group was 53.6 ($SD = 6.4$) and the average number of years of education was 13.7 ($SD = 1.8$). The HD gene in 3 patients was maternally transmitted and in 4 patients was paternally transmitted. At the time of testing, the patients had been diagnosed with HD an average of 6.1 ± 3.8 years. The cognitive status of the HD patients was assessed by the DRS ($M = 130.4$, $SD = 9.6$). Six patients were taking psychotropic medications (i.e., 5 patients were taking an antidepressant, 3 were taking an antipsychotic, 2 were taking an anticonvulsant, and one was taking an antianxiety medication).

Seven age- and education-matched normal controls (NC) participated. Average age of the controls was 54.1 ($SD = 13.1$) and the average number of years of education was 14.4 ($SD = 2.3$). The NC participants were free of neurologic disease and dementia. All scored within normal limits on the Mini-Mental Status Examinations (Folstein et al., 1975). No NC participant scored in the anosmic or hyposmic range.

Measures

Absolute odor detection

A two-alternative (odorant and blank), forced-choice, ascending method of limits was used to assess absolute odor thresholds monorhinically (Nordin et al., 1995). Each participant was instructed to choose which of the two stimuli had a stronger smell. Certified grade butanol, in deionized water, was used as the odorant, prepared in a series of 14 aqueous dilution steps, each one-third the dilution of the previous concentration, beginning with 3055 ppm (Dilution Step Zero). Vapor phase from 60-ml solutions was presented in 250-ml squeezable, polyethylene bottles with pop-up spots. Testing proceeded from weakest to strongest concentrations. Because odor detection has previously been demonstrated to be impaired in HD (Nordin et al., 1995), the HD participants were started at Dilution Step 9. If a participant correctly chose the bottle with the odorant, then the same step was repeated to a criterion of five consecutive correct responses. If the participant chose the incorrect bottle, a one-step increase in concentration resulted. The trials occurred 90 s apart to avoid adaptation. The presentation of the odorant and blank was randomized. The order in which the nostrils were tested was also randomized among participants.

California Verbal Learning Test (CVLT)

The CVLT employs a 16 item word list (List A) presented orally for five immediate recall trials. The list consists of four items from each of four semantically distinct categories (e.g., *fruits*, *spices and herbs*, *tools*, *clothing*). Adjacent words on the list are from different categories in order to assess the extent to which the examinee uses the efficient learning strategy of semantic clustering. Following the presentation of List A, an interference list (List B) is presented. Immediately following the presentation of List B, short delay free and cued recall of List A are conducted. After a 20-min delay period, long delay free and cued recall of List A are tested. Finally, recognition memory for List A is assessed, yielding measures of discriminability and response bias.

California Odor Learning Test (COLT)

The COLT, developed by Murphy et al. (1997), follows the same format as the CVLT. Table 1 displays the odors that comprise List A and B of the COLT. The odors presented in the COLT are at a suprathreshold level. Sixteen odors (List A) were distributed into the four semantic categories of spices and herbs, fruits, personal products, and sauces and condiments. The interference list (List B) has been further refined since originally developed by Murphy et al. It employs 16 different odors distributed into four semantic categories (e.g., *spices and herbs*, *fruit*, *snacks*, and *beverages*). Forty-four odors were used in the recognition memory test, which included all 16 List A odors and 28 distracter odors

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Table 1. Odors comprising List A, List B, and recognition distractors of the California Odor Learning Test (COLT)

List A	Fruits	Spices	Condiments	Personal products
	Coconuts	Cinnamon	Ranch dressing	Menthylatum
	Lemons	Cloves	Hot sauce	Baby powder
	Grapes	Garlic	Soy sauce	Nail polish remover
	Bananas	Oregano	BBQ sauce	Aftershave
List B	Fruits	Spices	Beverages	Snacks
	Coconuts	Chili powder	Coffee	Peanuts
	Apricots	Dill	Tea	Licorice
	Pineapples	Horse radish	Sherry	Peppermint
	Cherries	Ginger	Beer	Chocolate
Distractors	List B	Prototypical	Perceptual	Unrelated
	Apricots	Soap	Perfume	Rose
	Coconuts	Oranges	Ketchup	Mothballs
	Chili powder	Mustard	Nutmeg	Varnish
	Dill	Pepper	Almond	Glue
	Peanuts		Worcestershire	Machine oil
	Licorice		Wintergreen	Paint thinner
	Beer		Limes	Bleach
	Tea		Onions	Cigarette butts

(8 List B odors and 20 novel odors; see Table 1). The final component of the COLT is a 32-odor, forced-identification task that includes all 16 List A and 16 List B odors randomly ordered and presented to participants in a standardized manner.

Procedures

Absolute odor detection was assessed in all participants prior to assessment of odor and verbal learning and memory performance. The COLT and the CVLT were administered to all participants on separate days. Because the CVLT was given to the HD participants as part of a larger assessment battery, it was not always possible to randomize administration of the COLT and CVLT. However, whenever possible, the administration of the COLT and CVLT was randomized. The CVLT was administered in the standardized manner. The procedure for the COLT followed that of the CVLT with the exception of a 5-s stimulus presentation and a 10-s interstimulus interval (ISI) as suggested by Murphy et al. (1997). The forced identification component of the COLT was completed after the recognition memory portion of the COLT. Participants were not tested if they were experiencing an upper respiratory tract infection, blocked nasal passage due to the common cold, or other respiratory difficulty.

In an effort to assess the ability to recall odors relatively independently of the ability to identify odors, responses on the COLT were considered correct if the response was either present on the target list or was uniquely identified during the forced identification portion of the COLT. For example, if a participant identified "cherries," and only "cherries," as "strawberries" during the forced identification portion of the test, then "strawberries" would be considered a correct response on the recall portion of the test. Responses that were neither on the target list nor were uniquely labeled on the identification portion of the test were considered intrusions.

Performance on the CVLT was scored using the computerized scoring system developed by Fridlund and Delis (1987). Because the odors used in the COLT were matched one-to-one with the words on the CVLT, it was possible to use the CVLT scoring software to score the COLT. Naturally, raw scores were used in all comparisons as the standard scores printed by the CVLT scoring system specific to the CVLT.

RESULTS

Table 2 depicts performance on measures of odor and verbal recall and recognition memory for the two groups.

Absolute Odor Detection

Because paired *t* tests revealed no significant difference in absolute odor threshold between nostrils for the HD or NC groups [$t(6) = -1.45$, $p = .20$; and $t(6) = .83$, $p = .44$, respectively], threshold was averaged between nostrils for all participants and used in all further analyses. An independent samples *t* test revealed that the HD group had significantly higher olfactory thresholds than the NC group, indicating impaired ability to detect odors [$t(12) = -5.39$,

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Table 2. Performance on measures of odor and verbal recall and recognition memory for Huntington's disease (HD) and normal control (NC) participants

	California Odor Learning Test				California Verbal Learning Test			
	HD		NC		HD		NC	
Measure	*M*	(*SD*)	*M*	(*SD*)	*M*	(*SD*)	*M*	(*SD*)
List A, Trials 1–5	12.86	(10.11)	34.71	(13.56)	33.00	(14.74)	48.29	(10.21)
Long delay savings	85.71	(37.80)	106.63	(44.27)	86.46	(15.61)	88.95	(13.69)
Discriminability	52.14	(12.01)	73.29	(6.63)	89.57	(7.83)	91.86	(7.58)
Intrusion rate*	42.85	(27.69)	29.42	17.53	10.83	(12.05)	4.22	(3.13)

*Intrusion rate is the percentage of total responses that were intrusion errors.

$p < .001$]. Mean average thresholds for the HD and NC groups were 5.64 ± 1.77 and 10.57 ± 1.64.

Olfactory and Verbal Learning and Memory

To examine group differences on the CVLT and COLT, four planned comparisons were tested using separate 2 (HD, NC) × 2 (CVLT, COLT) repeated measures analysis of variance (ANOVA). Table 3 demonstrates the groups' means and standard deviations on all variables that were analyzed from the CVLT and the COLT. Variables were examined for normality of distribution and homogeneity of variance. When necessary, variables were transformed using square root transformations to correct nonnormality (i.e., total learning on the Monday List and intrusion rate). A Bonferroni adjustment for four planned comparisons was established to protect the Type 1 error rate at a .05 level.

Figure 1 illustrates the total number of items each group correctly recalled on each of the five trials of the CVLT and the COLT. A repeated measures analysis of variance (ANOVA) for total learning revealed that averaged across the two measures, the HD patients learned significantly less than the NC participants [$F(1,12) = 11.62$, $p = .005$, $\eta^2 = .49$]. The analysis indicated that there was no significant interaction between Group × Test [$F(1,12) = .79$, $p = .39$, $\eta^2 = .06$], but a significant main effect existed for test [$F(1,12) = 20.72$, $p = .001$, $\eta^2 = .63$]. Both groups learned significantly more on the CVLT than on the COLT.

In order to determine whether the groups differed in their rate of forgetting on the two tasks, the groups' savings ratios on the CVLT and the COLT were compared. The utility of savings scores for assessing rate of forgetting has been outlined by Tröster et al. (1993). Briefly, savings scores allow for an assessment of the amount of information that is forgotten given the amount of information originally encoded. A repeated measures ANOVA for savings (long delay free recall/list A, Trial 5 recall) revealed no significant between subjects effects [$F(1,12) = 1.39$, $p = .26$, $\eta^2 = .12$], main effects [$F(1,12) = .41$, $p = .53$, $\eta^2 = .03$], or interaction effects [$F(1,12) = 1.39$, $p = .26$, $\eta^2 = .12$], indicating that the groups did not differ in their levels of forgetting on either the CVLT or the COLT.

A repeated measures ANOVA for discriminability revealed a between subjects effect, which indicates that when discrimination was averaged across the two tests, the HD

Table 3. Results of logistic regression analyses predicting group membership from California Odor Learning Test (COLT) discriminability, California Verbal Learning Test (CVLT) discriminability, and average threshold

Variables in equation	Sensitivity	Specificity	χ^2	p
COLT discriminability	85.7	85.7	11.9	<.001
CVLT discriminability	42.9	57.1	.35	>.50
Average threshold	100	100	19.51	<.0001

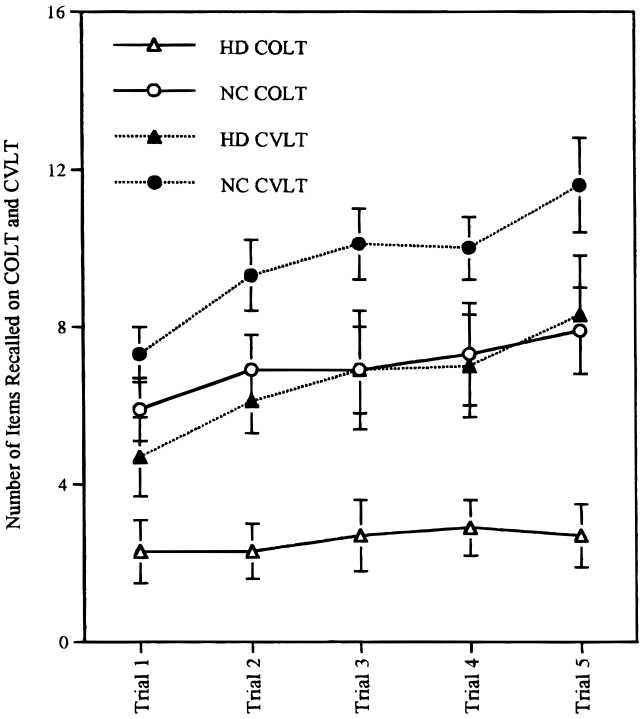

Fig. 1. Huntington's disease and normal control participants' learning curves across Trials 1–5 on the California Odor Learning Test (COLT) and the California Verbal Learning Test (CVLT). *Note*: Performance is expressed as mean and standard errors.

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patients performed more poorly than the NC participants [$F(1,12) = 9.36$, $p = .01$, $\eta^2 = .43$]. The Group × Test interaction effect was also statistically significant [$F(1,12) = 12.25$, $p = .004$, $\eta^2 = .51$]. Figure 2 illustrates this interaction. Follow-up analyses (i.e., ANCOVA (using average threshold as a covariate) for COLT discriminability and ANOVA for CVLT discriminability) indicated that the HD patients performed significantly worse than the NC participants on COLT discriminability, but performed similarly to the NC participants on CVLT discriminability. The average discriminability scores for the COLT were 52% for HD and 73% for NC [$F(1,11) = 4.92$, $p < .05$]. In comparison, the average discriminability scores for the CVLT were 90% for HD and 92% for NC [$F(1,12) = .31$, $p = .59$]. There was also a significant main effect for test [$F(1,12) = 108.01$, $p < .0001$, $\eta^2 = .90$] which indicates that both groups performed better on the CVLT than the COLT.

A repeated measures ANOVA for intrusion rate found no between subjects effect [$F(1,12) = .08$, $p = .78$, $\eta^2 = .01$] and no interaction of Group × Test [$F(1,12) = 1.20$, $p = .30$, $\eta^2 = .09$]. A significant main effect for test was revealed [$F(1,12) = 68.04$, $p < .001$, $\eta^2 = .85$] with both groups committing significantly fewer intrusion errors on the CVLT than the COLT.

Contribution of Absolute Detection to Olfactory Learning and Memory

Correlational analyses indicated that absolute odor detection (i.e., average threshold) was correlated with total learning on the COLT Monday list ($R^2 = .77$, $p = .001$) and COLT discriminability ($R^2 = .65$, $p < .02$). Therefore, model comparisons using multiple regression were conducted to determine what proportion of variance in COLT learning and memory performance group membership accounted for above average threshold. These analyses demonstrated that average threshold accounted for 62% of the variance in COLT total learning [$F(1,12) = 19.57$, $p < .001$]. Group membership did not account for a significant amount of unique variance in COLT total learning. Group membership did, however, contribute significantly to the regression equation for COLT discriminability [$R^2 = .19$, $F(1,11) = 4.92$, $p < .05$]. Average threshold accounted for 39% of the variance in COLT discriminability [$F(1,12) = 7.88$, $p < .05$].

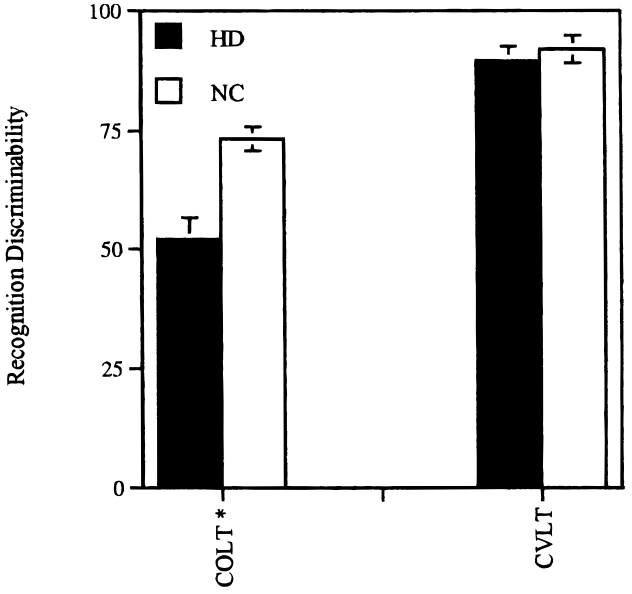

Fig. 2. Mean percent discriminability (and standard error) achieved by Huntington's disease and normal control participants on the California Odor Learning Test (COLT) and the California Verbal Learning Test (CVLT). *Note*: *$p < .05$.

Group Classification Analyses

A logistic regression with backwards elimination was conducted to evaluate the predictive power of absolute odor detection, the COLT, and the CVLT. Table 3 displays the results of the logistic regressions. A logistic regression with backwards elimination using average threshold and COLT discrimination as predictors indicated that average threshold correctly classified 100% of the participants [7/7 HD and 7/7 NC; Model $\chi^2(1) = 19.41$, $p < .0001$]. When indices of discrimination from the CVLT and the COLT were compared without average threshold, results indicated that COLT discrimination alone was capable of correctly classifying 85.7% of the HD (6/7) and 85.7% of the NC (6/7) participants [Model $\chi^2(1) = 11.9$, $p = .0006$]. CVLT discrimination alone was capable of correctly classifying 42.9% of the HD (3/7) and 57.1% of the NC (4/7) participants [Model $\chi^2(1) = .35$, $p = .55$]. A chi-square analysis comparing the predictive power of these models indicated that COLT discriminability was a better predictor of early HD than CVLT discriminability [$\chi^2(1) = 7.92$, $p < .01$].

DISCUSSION

The study sought to determine whether HD and NC participants performed differently on an odor learning and memory test compared to a verbal learning and memory test. A comparison of learning and memory across modalities (i.e., olfactory and verbal) indicated that the NC and HD groups learned fewer items across the learning trials, made a greater rate of intrusions, and were poorer at discriminating old items from new items on the COLT compared to the CVLT. These findings are consistent with our expectations because the COLT is likely to be a more complex learning task than the CVLT (Murphy et al., 1997). More specifically, learning olfactory information (i.e., COLT items) requires the participant to detect the odor, conduct a memory search for an appropriate verbal label, encode the appropriate label, store the label, and then actively retrieve the label. Learning verbal information (i.e., CVLT items), on the other hand, may not require the extra steps of searching for and encoding an additional verbal label. Rather, it is more likely that individuals directly encode, store, and retrieve the target words that are presented to them.

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The increased number of intrusions committed on the COLT compared to the CVLT may be indicative of the fact that the groups experienced difficulties attaching the correct verbal label to the items. Alternatively, the increase in intrusions committed on the COLT may also be the result of greater susceptibility to interference when stimuli are less distinct. Although the odorants were suprathreshold, it is possible that individuals have more difficulty distinguishing specific odors that are smelled than distinguishing specific words that are heard.

Unlike learning, rate of intrusion, and discriminability, no significant differences were found in rate of forgetting (i.e., savings scores) on the COLT compared to the CVLT. Instead the analyses demonstrated that the HD group did not exhibit a significant loss of information in either modality compared to the NC group. This finding is consistent with the notion that HD patients do not suffer from a primary storage problem (Delis et al., 1991). In other words, although the HD patients encoded fewer items on the COLT than the CVLT, the items that they did encode were not forgotten. Care must be taken in interpreting these negative results, however, because the current study may not have had sufficient power to detect small differences between the groups.

Our findings did reveal a dissociation in discriminability across modalities for the HD participants. HD patients were significantly worse than the NC participants on the COLT discriminability index, but performed comparably to the NC participants on the CVLT discriminability index. In the current study, the HD participants performed at chance level on COLT discriminability. This finding is consistent with those of previous studies that have demonstrated impaired odor discriminability (Moberg et al., 1987) and intact verbal discriminability (Delis et al., 1991) in HD patients.

These results suggest that the etiology of memory impairment differs for HD patients on olfactory tests versus verbal tests. On tests of verbal learning and memory, HD patients have been shown to have severely impaired recall, but demonstrate relatively intact performance on recognition testing (Delis et al., 1991; Massman et al., 1990). This pattern of results has prompted researchers to posit that the memory impairment associated with HD is primarily due to a retrieval deficit. In contrast, the current study demonstrates that on tests of olfactory learning and memory, HD patients performed significantly poorer on a measure of recognition discriminability than NC participants. Additionally, analyses indicate that this finding is not solely due to group differences in odor detection ability. One possible explanation for these data is that the HD patients failed to initially encode the olfactory stimuli and thus, were unable to distinguish new items from previously presented items.

Given that the HD patients did not exhibit savings scores that were significantly different from those of the NC participants, however, it is also possible that they encoded the olfactory information that they detected normally. The HD patients may have an impaired ability to discriminate between the odors that had been stored during the learning phase of the COLT and the new odors that were presented during the recognition portion of the test. It is possible that neuropathological changes occurring in the entorhinal cortex (Braak & Braak, 1992) and/or the striatum (Vonsattel et al., 1985) disrupts olfactory information projected towards the prefrontal cortex. The orbitofrontal cortex has been implicated as an important structure for olfactory discrimination in animal (Eichenbaum, 1998; Tanabe et al., 1975a, 1975b) and human (Potter & Butters, 1980) studies. Neuropathological changes in the entorhinal region, orbitofrontal cortex, or prefrontal–striatal circuit (Alexander et al., 1986) may disrupt the ability to compare stored olfactory data to novel, incoming olfactory stimuli. Therefore, it is possible that HD does not disrupt the ability to encode detected olfactory stimuli, but rather impairs the patient's ability to compare the encoded information with newly presented information.

The conclusions drawn from these results, however, should be viewed with caution because of limitations of the study. First, interpreting direct comparisons across modalities or tests may be problematic because potential test artifacts (e.g., differences in reliability between the COLT and CVLT) can produce findings that do not reflect true group differences. Second, the COLT requires the participant to attach a verbal label to the odorant. Because of the verbal label, the COLT may not be a pure olfactory learning and memory test, but instead may be a memory test with both a semantic and an olfactory component. It is possible that the delayed recall portions of the COLT are particularly reliant on verbal memory. Finally, limitations in the intensity of natural odors may have resulted in certain odors being more salient for some participants than others. While we were careful to include only suprathreshold stimuli, we cannot guarantee that the HD patients were able to perceive the stimuli as strongly as the NC participants.

We were also interested in determining what contribution odor detection made to odor learning and memory. In accordance with previous findings (Bylsma et al., 1997; Moberg & Doty, 1997; Nordin et al., 1995), we found that the HD group experienced reduced odor detection sensitivity compared to the NC group. Multiple regression analysis demonstrated that average odor threshold, but not group membership, significantly accounted for variance in total learning. These findings suggest that an individual's performance on the learning and recall measures of the COLT is significantly related to his or her ability to detect odors. In the current study the participants met criteria for absolute detection ability in the hyposmic range, and therefore, it is assumed that they detected at least a portion of the odors presented in the COLT. Poor detection undoubtedly accounts for a proportion of the variance in the learning measures, but it does not completely define performance on the COLT. With average threshold controlled, group membership significantly accounted for variance in COLT discriminability suggesting that some process inherent to HD is contributing to the patients' poorer discriminability performance.

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It is possible that the HD patients' medication profiles contributed to their decreased abilities to detect odors. Schiffman (1983) has indicated that some of the medications that the HD patients were prescribed may negatively affect their ability to smell. However, it is also possible that decreased ability to detect odors in HD may be an important characteristic of the early stages of the disease and may signal the beginning of the neurologic process that occurs in the disease. Bylsma and colleagues (Bylsma et al., 1997) have reported that performance on an odor identification measure (i.e., University of Pennsylvania Smell Identification Test; Doty et al., 1984) correlated with predicted age of disease onset in a sample of presymptomatic HD gene-carriers. Our findings demonstrate that odor detection may also be useful in discriminating between mildly affected HD patients and neurologically healthy individuals. Absolute odor threshold was demonstrated to provide excellent classification sensitivity and specificity (100%). While our findings also indicated that an odor learning and memory test (i.e., the COLT) more accurately classified mildly affected HD patients (86%) than a verbal learning and memory test (i.e., the CVLT; 43%), it is likely that this result is influenced by significant differences in odor threshold. While it remains to be shown that olfactory tasks possess the discriminative power to distinguish between neurologic diseases (Moberg et al., 1987), it would appear that olfactory tasks may be a useful means of detecting HD.

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REFERENCES

Alexander, G.E., DeLong, M.R., & Strick, P.L. (1986). Parallel organization of functionally segregated circuits linking basal ganglia and cortex. *Annual Review of Neuroscience*, *9*, 357–381.

American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disease* (4th ed.). Washington, D.C.: Author.

Braak, H. & Braak, E. (1992). Allocortical involvement in Huntington's disease. *Neuropathology and Applied Neurobiology*, *18*, 539–547.

Bylsma, F.W., Moberg, P.J., Doty, R.L., & Brandt, J. (1997). Odor identification in Huntington's disease patients and asymptomatic gene carriers. *The Journal of Neuropsychiatry and Clinical Neurosciences*, *9*, 598–600.

Delis, D.C., Kramer, J.H., Kaplan, E., & Ober, B.A. (1987). *The California Verbal Learning Test*. New York: The Psychological Corporation.

Delis, D.C., Massman, P.J., Butters, N., Salmon, D.P., Cermak, L.S., & Kramer, J.H. (1991). Profiles of demented and amnesic patients on the California Verbal Learning Test: Implications for the Assessment of Memory Disorders. *Psychological Assessment*, *3*, 19–26.

Doty, R.L. (1991). Olfactory dysfunction in neurodegenerative disorders. In T.V. Getchell, R.L. Doty, L.M. Bartoshuk, & J.B.J. Snow (Eds.), *Smell and taste in health and disease* (pp. 735–751). New York: Raven Press.

Doty, R.L., Shaman, P., & Dann, M. (1984). Development of the University of Pennsylvania Smell Identification Test: A standardized microencapsulated test of olfactory function. *Physiology and Behavior*, *32*, 489–502

Eichenbaum, H. (1998). Using olfaction to study memory. *Annals of the New York Academy of Sciences*, *855*, 657–669.

Folstein, M.F., Folstein, S.E., & McHugh, P.R. (1975). Mini mental status. *Journal of Psychiatric Research*, *12*, 189–198.

Fridlund, A.J. & Delis, D.C. (1987). *IBM user's guide for the CVLT* [Computer software]. New York: The Psychological Corporation.

Massman, P.J., Delis, D.C., Butters, N., Levin, B.E., & Salmon, D.P. (1990). Are all subcortical dementias alike? Verbal learning and memory in Parkinson's and Huntington's disease patients. *Journal of Clinical and Experimental Neuropsychology*, *12*, 729–744.

Mattis, S. (1988). *Dementia Rating Scale: Professional manual*. Odessa, FL: Psychological Assessment Resources.

Moberg, P.J. & Doty, R.L. (1997). Olfactory function in Huntington's disease patients and at-risk offspring. *International Journal of Neuroscience*, *89*, 133–139.

Moberg, P.J., Pearlson, G.D., Speedie, L.J., Lipsey, J.R., Strauss, M.E., & Folstein, S.E. (1987). Olfactory recognition: Differential impairments in early and late Huntington's and Alzheimer's diseases. *Journal of Clinical and Experimental Neuropsychology*, *9*, 650–664.

Murphy, C., Nordin, S., & Acosta, L. (1997). Odor learning, recall, and recognition memory in young and elderly adults. *Neuropsychology*, *11*, 126–137.

Nordin, S., Paulsen, J.S., & Murphy, C. (1995). Sensory- and memory-mediated olfactory dysfunction in Huntington's disease. *Journal of the International Neuropsychological Society*, *1*, 281–290.

Potter, H. & Butters, N. (1980). An assessment of olfactory deficits in patients with damage to the prefrontal cortex. *Neuropsychologia*, *18*, 621–628.

Schiffman, S.S. (1983). Taste and smell in disease. Part 1. *New England Journal of Medicine*, *308*, 1275–1279.

Tanabe, T., Iino, M., & Takagi, S.F. (1975a). Discrimination of odors in olfactory bulb, pyriform-amygdaloid areas, and orbitofrontal cortex of the monkey. *Journal of Neurophysiology*, *38*, 1284–1296.

Tanabe, T., Yarita, H., Iino, M., Ooshima, Y., & Takagi, S.F. (1975b). An olfactory projection area in orbitofrontal cortex of the monkey. *Journal of Neurophysiology*, *38*, 1269–1283.

Tröster, A.I., Butters, N., Salmon, D.P., Cullum, C.M., Jacobs, D., Brandt, J., & White, R.F. (1993). The diagnostic utility of savings scores: Differentiating Alzheimer's and Huntington's diseases with Logical Memory and Visual Reproduction tests. *Journal of Clinical and Experimental Neuropsychology*, *15*, 773–788.

Vonsattel, J.P., Myers, R.H., Stevens, T.J., Ferrante, R.J., Bird, E.D., & Richardson, E.P. (1985). Neuropathological classification of Huntington's disease. *Journal of Neuropathology and Experimental Neurology*, *44*, 559–577.