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HUNTINGTON'S DISEASE IN COLOMBIA: A NEUROPSYCHOLOGICAL ANALYSIS

DIEGO ROSSELLI

Hospital Militar Central, Colombia

MONICA ROSSELLI

Hospital San Juan de Dios, Colombia
Fundacion Universitaria Konrad Lorenz

BEATRIZ PENAGOS

Universidad Javeriana, Colombia

and

ALFREDO ARDILA

Instituto Neurologico de Colombia

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This is the first publication of the presence of Huntington's disease (HD) in Colombia. We studied four families comprising nine adult HD patients and 45 high risk adult offspring; all received complete physical, neurological and neuropsychological examinations. Among affected individuals, intensity of mental involvement varied in direct proportion with duration of the symptoms. The HD patients and some of the asymptomatic offspring displayed similar low scores on standardized tests of memory, language and constructive abilities. Prolonged follow-up of the latter group will allow assessment of the potential value of such tests for early diagnosis. The sequence followed by mental deterioration is discussed.

Keywords: Huntington's disease, dementia, neuropsychological assessment, mental deterioration

Since the first published description of Huntington's disease (HD) in 1872, there have been reports of the syndrome in many populations worldside, e.g., in China and Japan (Narabayashi, 1973), among African blacks (Glass & Saffer, 1979) and among Australian aboriginals (Brothers, 1964). In South American there is a published account of HD in a large group of patients from the western shore of Venezuela's Lake Maracaibo (Avila-Giron, 1973). The present study documents the occurrence of HD in Colombia and presents the results of neuropsychological tests which may ultimately prove useful for evaluating individuals with a genetic predisposition for the disorder.

Neuropsychological studies of HD patients have revealed patterns of severe impairment in memory, motor and conceptual abilities, visuomotor integration and capacity to use spatial directional cues (Albert, Butters & Brandt, 1981; Brandt,

Address for correspondence: Monica Rosselli, Apartado Aereo 17021, Bogota, Colombia, South America.

1984; Fisher et al., 1983; Josiassen, Curry & Mancall, 1983; Rosselli & Rosselli, 1984). Despite the recent genetic studies (Gusella et al., 1983), the demonstration of electrophysiological changes in patients carrying the dysfunctional gene (Jossiassen et al., 1982, 1984) and the attempts to detect mental and electrophysiological changes in the offspring of affected individuals (Fedio et al., 1979; Josiassen, Curry & Mancall, 1983; Josiassen et al., 1986; Lyle & Gottesman, 1977; Oepen et al., 1985; Wexler, 1979), there is still no valid predictive technique for diagnosing the disease in asymptomatic individuals with high genetic risk (Josiassen, 1986).

We have evaluated three generations of four Colombian families with HD (apparently not related to the Venezuelan group) (Figure 1). The size of these families (each has a set of 10 or more living siblings) provides an opportunity to assess the neuropsychological characteristics of a large sample of a population prone to develop the disease and, through several years of follow-up, determine whether there is a predictible sequence of impairment that can be detected in its early, subtle stages.

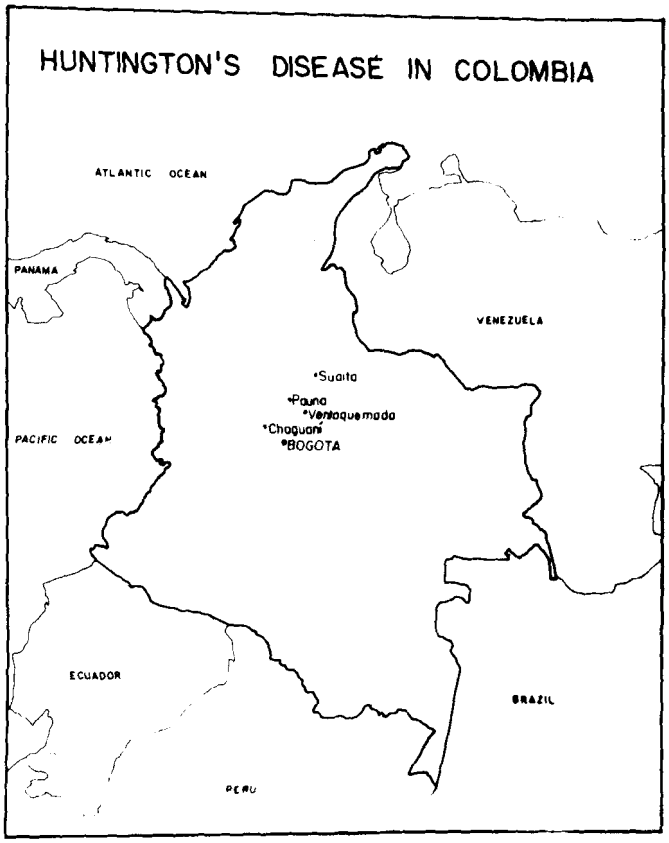

FIGURE 1 Origin of the four studied families. Bogota is shown as a reference.

METHOD

Subjects

A search through ten years of medical records in the files of the principal neurological centers in Bogota disclosed five cases of HD, one of which was lost for follow-up. Criteria for positive diagnosis included clinical signs of chorea and family history confirming dominant inheritance. We visited patients and their relatives in their home towns, and after carefully explaining the purpose of the study, we performed medical and neurological exams to detect the occurrence of HD. In the four involved families there were 11 living afflicted patients. We examined nine of these individuals, those 15 years or older (four in family A, three in family B, one in family C and one in family D). Of the 82 subjects born to an affected parent (i.e., with a 50% probability of developing HD themselves in the future), we took 45, those who were available, with ages between 15 and 50 years (15 in family A, 15 in family B, 8 in family C, and 7 in family D). There are, additionally, 155 related subjects (not including those lost for follow-up) whose chance of suffering the disease is 25%. All the patients of the sample were right handed and had an average of five years of education (see Figure 2).

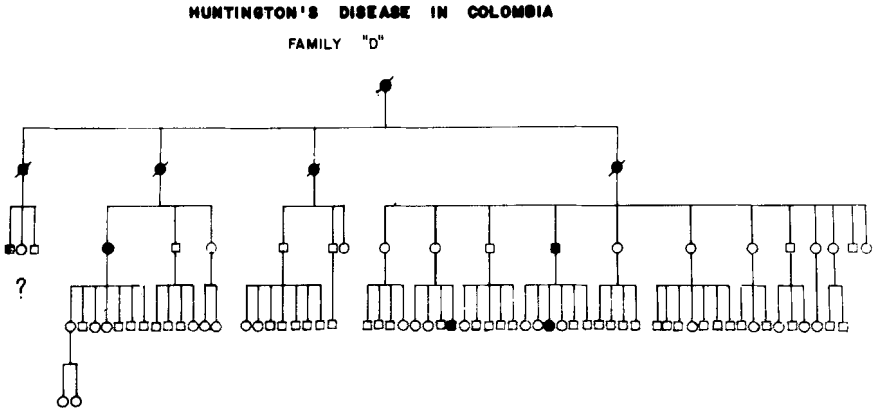

FIGURE 2 Example of a Colombian family with Huntington's disease. Marks represent members with HD (square = males, circles = females, hashed marks = deceased members).

We distinguished two major groups in the sample: the HD group (two men and seven women, 33–66 years old, average age 41.7 years) and the offspring group (45 subjects, 22 men and 23 women, 15–50 years old, average age 31.6 years). Despite the small size of the HD group, we further distinguished two subgroups, based on individual differences in ability to carry out the activities on normal daily life: (1) five patients capable of living independently or with only sporadic supervision [three of these were at stage 2 on Shoulson and Fahn's Functional Scale (1979); the other two at stage 3], and (2) four patients who required frequent or constant institutionalized care (two at stage 4 and two at stage 5). A review of the patients' records revealed that those in the first group had suffered the disease for three

years or less (hence, they are referred to as the "Early HD Group"); those in the second group had been ill for eight years or more (hence, "Advances HD Group"). Due to the difficulty of establishing an exact date of disease onset, we used the date of first consultation to define operationally the duration of the condtion.

Testing Procedure

In single 50–60 minute sessions we administered to each subject a neuropsychological battery consisting of five memory tests, three language tests, and one constructive ability test, as follows:

Memory Tests

1) Digit Retention Span: We used the Digit Retention Span Subtests (Progressive and Regressive sequences) from WAIS (Wechsler, 1955). Scoring: according to criteria outlined in the Manual. Maximum score = 18 (sum of the two sequences).

2) Learning Curve: Each subject was read five time consecutively the same list of 10 disyllabic words. Immediately after each reading (and 20 minutes after the final reading for an evaluation of long-term memory), the subject recalled as many words as possible from the five trials. Maximum score = 50 on immediate and 10 on delayed memory.

3) Logical Memory (Immediate and Delayed): Each subject listened to a story consisting of 11 ideas (adapted from the Wechsler Memory Scale). He/she was then asked to recall the story immediately after its reading and, again, 25 minutes later (delayed memory). Scoring: according to criteria from the Manual of Wechsler Memory Scale (1945). Maximum score = 11 for immediate and 11 for delayed memory.

4) Visual Memory (Immediate and Delayed): We used the Figure B of Plate C (Form 1) from the visual reproduction of Wechsler Memory Scale. After observing the design for 10 seconds, the subject was asked to reproduce it from memory immediately and at the end of the evaluation. Scoring: 1 point for drawing correctly the external rectangle, 1 point for drawing the internal rectangle, 1 point for drawing the internal rectangle towards the right. Maximum score: 3.

5) Memory of Unfamiliar Faces: 24 black and white photos (5×3 cm) of unfamiliar faces were presented, one at a time, to the subject. After the 5th photo, six of the same faces were randomly presented a second time. After each, the subject was asked whether or not he/she had previously seen the face. Scoring: the number of correct identifications. Maximum score = 6.

Language Tests

6) Verbal Fluency: Subjects were asked to say in one minute as many words in a category as possible (the categories used were names, fruits, and animals). Score = the total number of words in the three categories.

7) Object Naming Test: We used the Object Naming Subtest of the Boston Diagnostic Aphasia Examination (BDAE). Scoring: according to criteria established by Goodglass and Kaplan (1972). Maximum score = 20.

8) Written Narrative: We used the Written Idea Production subtest of the BDAE. Each subject as asked to write as much as he/she could about "The Theft of Cookies" (Plate 1). Scoring: according to the criteria of Goodglass and Kaplan (1972). Maximum score = 4.

Constructional Tests

9) Construction Skill: This consisted of items 3 and 7 of the Block Design Subtest of the WAIS. Scoring: 0 = mistakes in both designs, 1 = mistakes in one of the designs, 2 = no mistakes.

RESULTS

Table 1 shows the mean score obtained by HD group and offspring group in each test used. In all tests the offspring group scored better than the HD group, with statistically significant differences in all categories, especially Memory Curve, Verbal Fluence and Written Narrative. The dispersion of scores is apparent in both groups (Table 1).

TABLE 1
Raw scores in the different tests. Mean, standard deviation, t values, and p ($df = 52$) are shown

		Offspring group		HD group			
		$\bar{X}$	σ	$\bar{X}$	σ	t	p
Digit span:	Progression	4.76	1.15	3.44	1.42	3.00	.005
	Regression	3.44	1.20	1.44	1.51	4.38	.0005
Learning curve:	Immediate	37.99	6.02	21.67	9.94	6.49	.0005
	Delayed	7.27	2.60	3.00	2.18	4.60	.0005
Logical Memory:	Immediate	5.80	2.71	2.22	2.05	3.74	.0005
	Delayed	5.44	2.73	.89	1.83	4.77	.0005
Visual memory:	Immediate	1.98	.94	.89	.78	3.25	.005
	Delayed	2.13	.76	1.00	1.00	3.88	.0005
Memory of unfamiliar faces		4.69	1.47	2.67	1.94	3.19	.005
Verbal fluency		54.33	11.08	26.00	13.42	6.72	.0005
Object naming test		19.11	1.70	15.44	4.95	4.03	.0005
Written narrative		3.75	.71	2.11	1.36	5.30	.0005
Construction skill		1.03	.77	.11	.33	3.70	.0005

In order to make a comparison between the results of different tests, the scores of the offspring group were converted into a T scale (mean = 50, standard deviation = 10). The scores of the HD group were also converted to that same scale. T scores were used for all further analysis. An average T score was calculated for each subject.

In the HD group a high correlation was observed between disease duration and score obtained ($r = -.70$; $df = 8$; $p < .01$). Considering this correlation and the great dispersion of the scores, the HD group was divided into two subgroups: Advanced HD Group (four patients with more than 8 years with the disease, average age 50.5), and Early HD Group (five patients with less than three years with the disease, average age 44.2). Coincidentally, no patient was in the range of three to 8 years of disease duration. Table 2 shows the results obtained by Advanced and Early HD Subgroups in all tests. There was a significant difference in Digit Retention (Regression), Learning Curve (Immediate), Verbal Fluency, and Written Narrative.

TABLE 2
T scores in advanced and early HD subgroups in the different tests, *t* values and *p* ($df = 7$)

		Early HD	Advanced HD	*t*	*p*
Digit span:	Progression	43.44	32.58	1.38	NS
	Regression	39.61	25.42	1.95	.05
Memory curve:	Immediate	33.92	12.82	3.30	.01
	Delayed	37.42	28.76	1.72	.10
Logical memory:	Immediate	37.46	35.98	.27	NS
	Delayed	32.28	34.66	.50	NS
Visual memory:	Immediate	39.61	36.96	.45	NS
	Delayed	40.31	28.42	1.43	.10
Memory of unfamiliar faces		41.23	33.07	.91	NS
Verbal fluency		31.64	14.71	2.38	.025
Object naming test		41.09	21.72	1.49	.10
Written narrative		37.23	15.72	1.95	.05
Construction skill		39.05	36.72	.88	NS

In the subjects of the offspring group we also found a negative correlation ($r = -.47$; $df = 42$; $p < .01$) when relating age with total score. In other words, performance decreased with age. Considering the obvious dispersion of the scores, the offspring group was also divided arbitrarilly into two subgroups: Low Score Offspring (LSO) (19 subjects, 5 males, 14 females, average age 34.4), and High Score Offspring (HSO) (26 subjects, 17 males, 9 females, average age 27.0). Those individuals with an average score below the mean for the offspring group were included in the first subgroup, while those with a score above the mean formed the latter subgroup. When both subgroups were compared, the latter scored significatively better in all tests, except Memory of Faces and Written Narrative (Table 3).

TABLE 3
T scores in HSO and LSO subgroups in the different tests, *t* values and *p* ($df = 43$)

		HSO	LSO	*t*	*p*
Digit span:	Progression	53.79	44.81	3.29	.005
	Regression	54.00	44.53	3.52	.005
Learning curve:	Immediate	55.06	42.90	4.97	.0005
	Delayed	54.60	43.70	4.25	.0005
Logical memory:	Immediate	55.00	43.17	4.80	.0005
	Delayed	55.69	42.22	5.96	.005
Visual memory:	Immediate	54.32	44.09	3.90	.0005
	Delayed	53.83	44.76	3.33	.005
Memory of unfamiliar faces		50.60	49.18	.46	NS
Verbal fluency		54.56	44.23	3.89	.0005
Object naming test		54.56	43.76	4.20	.0005
Written narrative		51.97	47.53	1.48	.10
Construction skill		53.73	44.89	3.18	.005

A comparison was made between LSO group and Early HD group. When these groups were compared, no significant differences were found, except in the tests of Logical Memory (Delayed) and Verbal Fluency (Table 4), which implies certain similarity between both subgroups.

TABLE 4
T scores in LSO and early HD subgroups in the different tests, *t* values and *p* ($df = 22$)

		LSO	Early HD	*t*	*p*
Digit span:	Progression	44.81	43.44	.31	NS
	Regression	44.53	39.61	1.04	NS
Learning curve:	Immediate	42.90	33.92	2.01	.10
	Delayed	43.70	37.42	1.14	NS
Logical memory:	Immediate	48.17	37.46	1.35	.20
	Delayed	42.22	32.28	3.35	.01
Visual memory:	Immediate	44.09	39.61	.91	NS
	Delayed	44.76	40.31	.77	NS
Memory of unfamiliar faces		49.18	41.23	1.33	.20
Verbal fluency		44.23	31.64	2.70	.02
Object naming test		43.76	41.09	.43	NS
Written narrative		47.53	37.23	1.53	.20
Construction skill		44.89	39.05	1.67	.20

Finally, the score of the four subgroups were plotted in order to visualize the neuropsychological profile of each one and compare the differences. Figure 3 illustrates these profiles.

DISCUSSION

This is the first report of the presence of HD in Colombia. Its incidence will almost certainly increase in the near future, given the large number of offspring in the affected families and the absence of genetic counseling services in the past.

Our results confirm earlier studies which demonstrated that in HD mental involvement tends to increase in direct proportion to the duration of the motor signs (Butters et al., 1978; Fisher et al., 1983). In our study, the patients with advanced HD had lower scores than the early HD patients in all tests, especially in Digit Retention Span, Learning Curve, Verbal Fluency, and Written Narrative, which consequently are the most sensitive to deterioration in HD patients. The attentional deficits described in these patients (Caine, 1981), as well as the frontal lobe compromise (Freedman & Albert, 1985) may partially explain the low scores in these tests and particularly the first, since it is the most sensitive to such problems. Deficits in Verbal Fluency and Written Narrative tests reflect the great compromise in "productivity" and "generativity" of the late stages of HD, in the first case in the semantic level and in the latter with regard to interpretation of complex visual stimulus. The contrast between the low scores of HD patients in the Learning Curve and their much better scores in Logical Memory suggests a greater capacity for them to retain information that has a relationship between its elements.

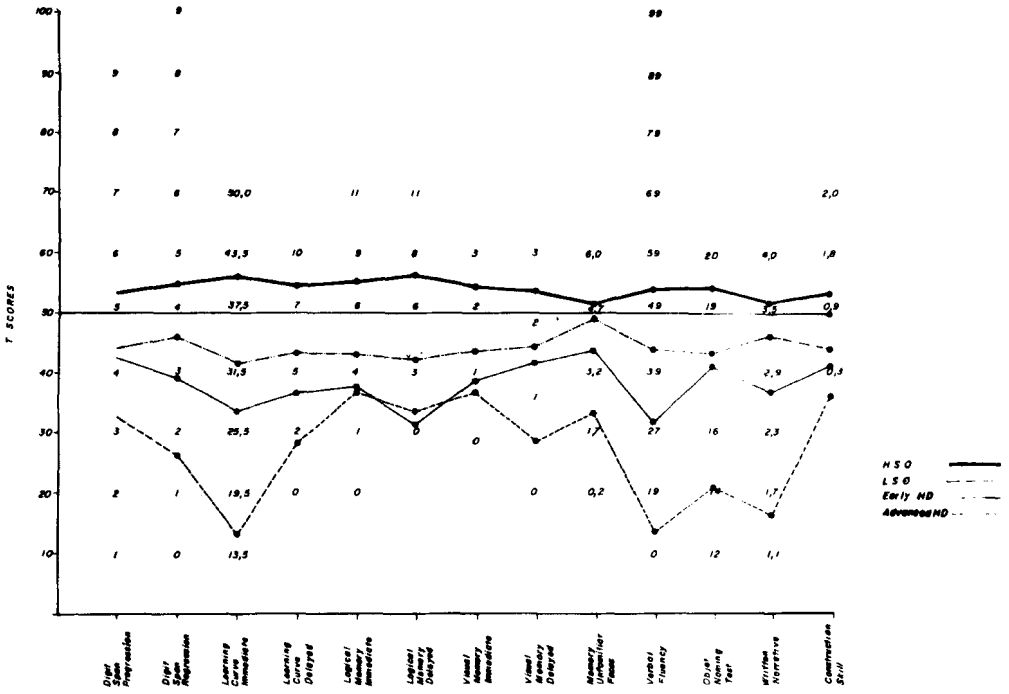

FIGURE 3 Average *T* scores for the four subgroups considered.

The memory disorders in HD have classically been most associated with the process of evocation (Caine et al., 1978) and less with recognition tasks. Recently, Butters et al. (1986) found severe compromise in tests of verbal generation in HD patients (who score worse than patients with Korsakoff's amnesia); we found similar results in our HD group, though few perseverations were found. When testing an HD patient, a prolonged process of search for the information is noticeable.

In spite of the general recognition that HD patients suffer severe cognitive deterioration, only in recent years has there been an interest in assessing the neuropsychological and electrophysiological profiles of the at-risk population. Lyle and Gottesman (1977) described subtle memory loss in early premotor stages of the disease. Josiassen, Curry and Mancall (1983) found special deficits in auditory memory in high-risk subjects, while Oepen et al. (1985) found visuomotor manifestations in asymptomatic offspring. At this point in time, however, there is still no neuropsychological test with the predictive power to identify the very early manifestations of the disease.

Our study revealed strong similarities in the neuropsychological profiles of some high-risk offspring and those of positively diagnosed early HD patients, especially in the organizational, constructional and memory processes (see Figure 3) which have been shown to be affected in the HD sufferers (e.g., Caine & Fisher, 1985). We thus propose that low score on certain tests could be an initial indication of the progressive dementia associated with HD. We predict that at later stages there should be compromise of verbal memory and tasks which require capacity to

generate words or ideas, since apparently, deterioration in these areas continue even though construction skills remain less affected as the disease progresses.

Only a prolonged follow-up will show whether the asymptomatic individuals who scored low in Learning Curve, Verbal Fluency and Written Narrative have a higher risk of developing the disease. Future studies will enable us to assess the usefulness of these tests for the early diagnosis of HD.

REFERENCES

Albert, M. S., Butters, N., & Brandt, J. (1981). Development of remote memory loss in patients with Huntington's disease. *Journal of Clinical Neuropsychology*, **3,** 1–12.

Avila-Giron, R. (1973). Medical and social aspects of Huntington's chorea in the state of Zulia, Venezuala. In A. Barbeau, T. N. Chase & G. W. Paulson (Eds.), ***Huntington's chorea 1982–1972.*** New York: Raven Press.

Brandt, J. (1984). Access to knowledge in the dementia of Huntington's disease. *Paper presented at the XII Annual Meeting of the International Neuropsychological Society.* Houston.

Brothers, C. R. (1964). Huntington's chorea in Victoria and Tasmania. *Journal of Neurological Sciences*, **1,** 405–420.

Butters, N., Wolfe, J., Granholm, E., & Martone, M. (1986). An assessment of verbal recall, recognition and fluency abilities in patients with Huntington's disease. *Cortex*, **22,** 11–32.

Butters, N., Albert, N. S., Sax, L. S., Montgomery, K., & Tarlow, S. (1978). Comparison of the neuropsychological deficits associated with early and advanced Huntington's disease. *Archives of Neurology*, **35,** 585–589.

Caine, E. D. (1981). Pseudodementia. *Archives of Genetics and Psychiatry*, **38,** 1359–1364.

Caine, E. D. & Fisher, J. M. (1985). Dementia in Huntington's disease. In J. A. M. Frederiks (Ed.), ***Handbook of clinical neurology, Volume 46, neurobehavioural disorders.*** Amsterdam: Elsevier Science Publisher.

Caine, E. D., Hunt, R., Weingartner, H., & Ebert, M. (1978). Huntington's dementia: Clinical and neuropsychological features. *Archives of Genetics and Psychiatry*, **35,** 377–384.

Fedio, P., Cox, C. S. Neophytides, A., Canal-Frederick, G., & Chase, T. N. (1979). Neuropsychological profile of Huntington's disease: patients and those at risk. In T. Chase, N. S. Wexler, & A. Barbeau (Eds.), ***Dementia in Huntington's disease: Advances in Neurology,*** Vol. 23, New York: Raven Press.

Fisher, J., Kennedy, J. L., Caine, E. D., & Shoulson, I. (1983). Dementia in Huntington's disease: A cross-sectional analysis of intellectual decline. In R. Mayeux & W. G. Rosen (Eds.), *The dementias: Advances in Neurology*, Vol. 38, New York: Raven Press.

Freedman, M. & Albert, M. L. (1985). Subcortical dementia. In J. A. M. Frederiks (Ed.), ***Handbook of clinical neurology, Volume 46, neurobehavioural disorders.*** Amsterdam: Elsevier Science Publishers.

Glass, J. & Saffer, D. S. (1979). Huntington's chorea in a black family. *African Medicine Journal*, **56,** 685–688.

Goodglass, H. & Kaplan, E. (1972). *Assessment of the aphasia and related disorders.* Philadelphia: Lea and Febiger.

Gusella, J. F., Wexler, N. S. Conneatly, P. N., Naylor, S. L., Anderson, M. A., Tanzi, R. E., Watkins, P. C., Ottina, K., Wallace, M. A., Sakaguchi, A. Y., Young, A. B., Shoulson, I., Bonilla, E. & Martin, J. B. (1983). A polymorphic DNA marker genetically linked to Huntington's disease. *Nature*, **306,** 234–238.

Huntington, S. (1872). On chorea. *Medical and Surgery Reporter*, **26,** 317.

Josiassen, R. C., Curry, L. M., Mancall, E. L., Shagass, C., & Roemer, R. A. (1986). Relationship between evoked potentials and neuropsychological findings in persons "at risk" for Huntington's disease. *Journal of Clinical and Experimental Neuropsychology*, **8,** 21–36.

Josiassen, R. C., Shagass, C., Mancall, E. L., & Roemer, R. A. (1984). Auditory and visual evoked potentials in Huntington's disease. *Electroencephalography and Clinical Neurophysiology*, **57,** 113–118.

Josiassen, R. C., Curry, L. M., & Mancall, E. L. (1983). Development of neurospychological deficits in Huntington's disease. *Archives of Neurology*, **40,** 791–796.

Josiassen, R. C., Shagass, C., Mancall, E. L., & Roemer, R. A. (1982). Somatosensory evoked potentials in Huntington's disease. *Electroencephalography and Clinical Neurophysiology*, **54,** 483–493.

Lyle, O. E. & Gottesman, I. I. (1977). Premorbid psychometric indicators of the gene of Huntington's disease. *Journal of Clinical Psychology*, **45,** 1011–1022.

Narabayashi, H. (1973). Huntington's chorea in Japan: A review of the literature. In A. Barbeau, T. N. Chase, & G. W. Paulson, (Eds.), ***Huntington's chorea 1872–1972,*** New York: Raven Press.

Oepen, G., Mohr, U., Willmes, K., & Thoden, U. (1985). Huntington's disease: visuomotor disturbances in patients and offspring. *Journal of Neurology, Neurosurgery and Psychiatry,* **48,** 426–433.

Rosselli, D. & Rosselli, M. (1984). Neuropsicologia de la enfermedad de Huntington. *Paper presented at the National Meeting of Neurosciences,* Paipa, Colombia.

Shoulson, I. & Fahn, S. (1979). Huntington's disease: clinical care and evaluation. *Neurology,* **29,** 1–3.

Wechsler, D. (1945). A standardized memory scale for clinical use. *Journal of Psychology,* **19,** 87.

Wechsler, D. (1955). ***Wechsler adult intelligence scale: manual.*** New York: Psychological Corporation.

Wexler, N. S. (1979). Perceptual, motor, cognitive, and emotional characteristics of persons at risk for Huntington's disease. In T. Chase, N. S. Wexler, & A. Barbeau (Eds.), ***Huntington's disease: Advances in neurology,*** Vol. 23, New York: Raven Press.