These mucosal units are most commonly circular or elliptical and occasionally rectangular or hexagonal (fig. 1). The vessels are single or multiple and tend to run a tortuous course. The width of the vessels are seldom more than quarter the width of the non-vascular area of the mucosal unit. (With oblique lighting a small, refractile circular or longitudinal "pit" is found in the centre of each unit, and we believe that this is the opening of a crypt of Lieberkühn.) At higher magnifications, the central pit is sometimes surrounded by a slight elevation producing a "volcano" effect and the remainder of the surface of the unit has a roughened appearance with larger elliptical bulges, possibly representing goblet cells.

Ulcerative Colitis

The variations from the normal dissecting-microscope appearance were confined largely to vasculature and consisted of: (*a*) faintness and blurring of the vessels; (*b*) excessive tortuosity, increased size of individual vessels, and widening of the vascular area (fig. 2); (*c*) loss of honeycomb architecture and discontinuity of vessels; and (*d*) complete disorganisation with appearance of larger (perhaps deeper) vessels (fig. 3) and fold formation (resembling large, leaf-shaped villi). No pits were seen, perhaps because they had been plugged by mucus; but "pit" visualisation was not always easy and the changes were too variable to be of value.

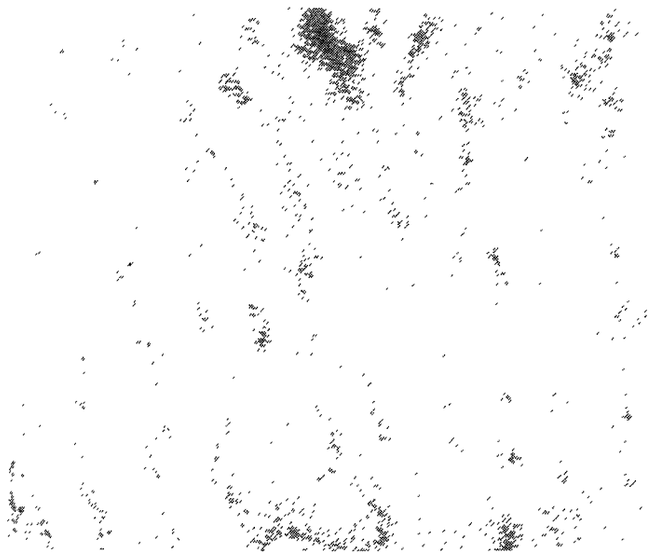

Fig. 2—Widened, tortuous vascular channels and less of honeycomb appearance in patient with mild ulcerative colitis. Reduced slightly from ×40.

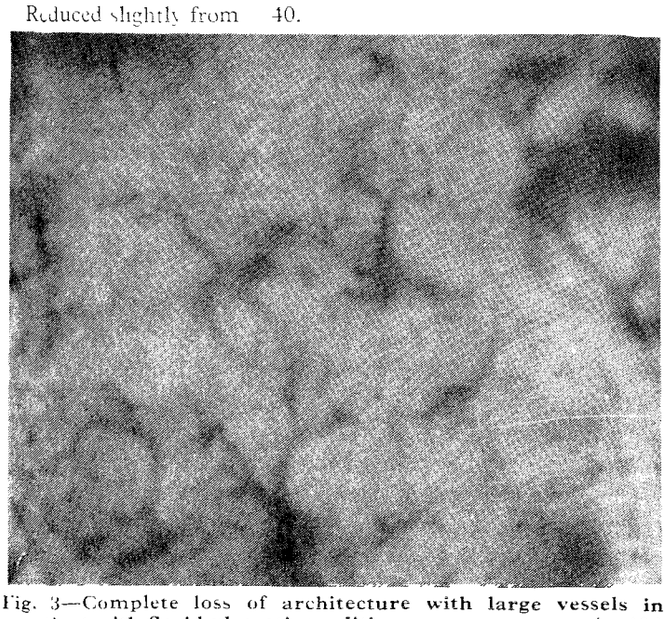

Fig. 3—Complete loss of architecture with large vessels in patient with florid ulcerative colitis. (×40.)

CORRELATION BETWEEN APPEARANCES ON SIGMOIDOSCOPY AND DISSECTING MICROSCOPY

Sigmoidoscopy	No.	Normal vascular pattern	Abnormal vascular pattern characterised by one or more of:				Pits not seen
			Faint and blurred	Widened channels	Loss of architecture	Total disorganisation	
Normal colon	14	11	2	1	0	0	3
Rectal erythema due to diarrhoea	2	0	2	0	0	0	0
Ulcerative colitis:							
Normal	6	4	1	1	0	0	2
Erythema	8	0	5 (*2*)	6 (*3*)	0	0	6
Granular	12	0	4 (*3*)	6 (*1*)	7	1	12
Bleeding	2	0	0	0	1	1	2
Ulceration	2	0	0	0	0	2	2

Italic type shows numbers with only one abnormality.

Correlation with Sigmoidosopy

The dissecting-microscope findings in 14 patients with normal appearance on sigmoidoscopy and considered to be free of bowel disease, 30 patients with known ulcerative proctocolitis (classified according to the sigmoidoscopic appearance), and 2 patients with rectal "erythema" due to continued small-bowel diarrhœa are shown in the table.

COMMENT

Immediate examination of rectal-mucosa biopsy specimens under the dissecting microscope has proved to be a useful additional guide in the diagnosis and grading of ulcerative disease of the colon. Alterations in the small mucosal vessels would seem to be a fairly consistent finding in ulcerative colitis. The study is being extended to include other types of ulcerative disease of the colon and rectum.

We thank Mr. J. Atkinson for the excellent photography. Requests for reprints should be addressed to S. B.

SUPERIOR INTELLIGENCE IN RECESSIVELY INHERITED TORSION DYSTONIA*

ROSWELL ELDRIDGE ANNE HARLAN

Section on Genetics in Epidemiology, Epidemiology Branch, Collaborative and Field Research, National Institute of Neurological Diseases and Stroke, Bethesda, Maryland, U.S.A.

IRVING S. COOPER MANUEL RIKLAN

Department of Neurological Surgery, St. Barnabas Hospital, New York, N.Y., U.S.A.

Summary The association between intelligence and the recessive form of torsion dystonia has been evaluated in a retrospective study. Psychometric data were available from a period before the appearance of symptoms for fourteen patients with this disease. Similar data were available for a control group matched for age, sex, ethnic back-

* Based on a paper presented at the Second Conference on the Clinical Delineation of Birth Defects, held at the Johns Hopkins Hospital, Baltimore, Maryland, on May 26–30, 1969.

ground (Jewish), and, so far as possible, socioeconomic background. The mean I.Q. of the patients was 121 (range 104–170) and that of their controls was 111 (range 76–147). This difference is significant ($P<0.03$). These data suggest that the gene for torsion dystonia enhances I.Q.

INTRODUCTION

THERE are probably at least two hereditary forms of torsion dystonia [1]: neither has been characterised pathologically or biochemically but there are general clinical differences between the two. The autosomal recessive form generally presents between ages 4 and 16 as inability to control fine movements in one of the limbs, usually on the dominant side. Symptoms may progress rapidly over several years and lead to death. The gene is especially common in those of Ashkenazi Jewish background from eastern and central Europe. Improvement after L-dopa suggests that there may be a basic abnormality in biogenic-amine metabolism in this trait.[2] In the less common autosomal dominant form the age of onset and clinical course are more variable. Neck and trunk are often involved first and torticollis may be the initial diagnosis. Often, in the early stages of sporadic cases, the organic basis of the abnormal movements is not appreciated, and patients undergo a period of unrewarding psychiatric treatment.[3]

One of us (I. S. C.) has been impressed with the intelligence and social maturity of many children with this disorder.[4] This impression is supported by the numerous published reports of Jewish patients, whose family history is compatible with recessive inheritance, which invariably describe such patients as " alert ", " bright ", or " of at least average intelligence ". To evaluate the association between intelligence and recessive torsion dystonia we have compared group intelligence tests for patients, sibs, and matched controls.

METHODS

Commencing in late 1966, a clinical and genetic study of torsion dystonia was undertaken in the United States with cases ascertained through neurosurgery and neurology departments with teaching services. We asked the parents of all Jewish patients whose illness was suggestive of recessive inheritance (i.e., dystonia presenting spontaneously between 4 and 16 years of age and not present in either parent) for permission to use school psychometric data of patients and their sibs. A control for each patient and each sib was obtained by selecting the next student in alphabetical order who was the same age, sex, religion (Jewish), and, whenever possible, who attended the same primary school. Scores were used only if the patient (or sibling) and control had had the same intelligence test in the same year. For the patient group, we analysed results obtained from tests given before the onset of symptoms. When more than one test result was available, the mean of the scores was used.

RESULTS

One hundred and one patients with a diagnosis of dystonia were evaluated, and of this group thirty-nine were Jewish patients whose clinical features and family history are suggestive of the autosomal recessive form of torsion dystonia. Useful psychometric data are now available for fourteen of these patients and for ten of their sibs plus controls for each. Of the remainder, results for five patients could not be used since symptoms were present when the first tests were administered; no data were available for four; data for seven were not recorded in usable form; no response to the request was received from the schools of five patients; and the parents of four patients did not wish to participate.

Family	Patient group				Sibling group		
	Sex	Age at onset (yr.)	Mean I.Q. (range)		Sex	Mean I.Q. (range)	
			Patient	Control		Sib	Control
1	F	10·5	151 (131–170)	123 (118–127)		.. ..	.. ..
2	F	7	150	121	F	125 (120–129)	110 (98–121)
3	M	6·5	121	92		..	..
	F	16	134	114		..	..
4	F	10	111	127	M	113	115
5	M	8	116	101	F	130 (112–146)	101 (94–109)
6	F	10	111 (104–117)	111 (106–114)	M	108 (107–110)	105 (101–111)
7	M	9·5	111 (105–117)	93 (86–99)		..	..
	F	8·5	125 (123–127)	139 (131–147)		.. ..	.. ..
8	F	10	113	101	M	103 (93–114)	124 (112–136)
	F	10	123 (119–127)	111 (104–117)	F	121 (113–131)	112 (104–119)
9	M	9	111 (109–112)	92 (76–107)	M	110 (103–116)	101 (95–103)
					F	134	112
10	F	12	108	113	F	107	112
11	M	9	115	116	F	135 (130–139)	130
Total		9·7	121* (104–170)	111* (76–147)		119 (93–146)	112 (94–136)

* Differences significant at level $P<0.03$.

The I.Q. of each patient, sib, and control is indicated in the table. Using a *t*-test for paired samples, the probability that the differences in I.Q. between patients and their controls is due to chance is less than 3%. The difference in I.Q. of clinically normal sibs and their controls is not significant.

DISCUSSION

These data suggest that recessively inherited torsion dystonia is associated with superior intelligence. The sibling group did not show a significant increase in I.Q.; but, on the basis of simple mendelian segregation, only two out of every three in this group would be expected to have the gene, and this would reduce the performance of the group as a whole.

Traits which may have a genetic basis reported to be associated with superior intelligence include retinoblastoma [5,6] and hyperuricæmia.[7,8] Also, the sibs of patients with phenylketonuria [9,10] and the parents of patients with childhood autism [11] are reported to be unusually bright. However, in these reports, the positive association noted may be a function of unavoidable bias in selection of patients and/or controls. Also, attaching significance to I.Q. data obtained from a group with significant handicap may be hazardous.

By choosing controls of the same ethnic background and, whenever possible, the same school, we have tried to avoid a bias based on cultural and/or socioeconomic background. We think any bias in the selection of controls has been in the direction of minimising their differences with patients. Also, controls were chosen

from regular schools, thereby excluding any who would have been in special education, a factor which might also raise the mean I.Q. of the control group.

These results are based on a small sample and there is a 3% probability they may be explained by chance alone. However, the implications for understanding both the chemistry of intellectual growth and the high frequency of the gene in the Ashkenazim prompts communication at this time.

Dr. Morris B. Gross, Department of Education, Hunter College in the Bronx, Bronx, New York; Dr. John W. Money, Johns Hopkins Hospital, Baltimore, Maryland; and Dr. Jacob A. Brody, Epidemiology Branch, C. & F.R., National Institute of Neurological Diseases and Stroke, National Institutes of Health, Bethesda, Maryland, assisted in the design of the study. Dr. Helen Abbey, Department of Biostatistics, Johns Hopkins Hospital, Baltimore, Maryland, provided useful advice in analysis of the data. This work was supported in part by the John A. Hartford Foundation and the Allan P. and Josephine Green Foundation.

Requests for reprints should be addressed to R. E.

REFERENCES

1. Eldridge, R., Ryan, E., Brody, J. A., Cooper, I. S. *in* Progress in Neurogenetics (edited by A. Barbeau and J. R. Brunett); p. 772. Amsterdam, 1969.
2. Coleman, M. P., Barnet, A. *Trans. Am. Neurol. Ass.* (in the press).
3. Eldridge, R., Riklan, M., Cooper, I. S. *J. Am. med. Ass.* 1969, **210**, 705.
4. Cooper, I. S. Involuntary Movement Disorders, chap. 4. New York, 1969.
5. Thurrell, R. J., Josephson, T. S. *Psychosomatics*, 1966, **7**, 368.
6. Williams, M. *Archs Dis. Childh.* 1968, **43**, 204.
7. Stetton, D., Jr., Hearon, J. Z. *Science*, 1959, **129**, 1737.
8. *J. Am. med. Ass.* 1969, **208**, 1180.
9. Munto, T. A. *Ann. Eugen.* 1947, **14**, 60.
10. Fuller, R. *in* Phenylketonuria and Allied Metabolic Diseases (edited by J. A. Anderson and K. F. Swaimson); p. 133. U.S. Government Printing Office, 1967.
11. Rimland, B. Infantile Autism: the Syndrome and Its Implications for a Neural Theory Behaviour; p. 23. New York, 1964.

REDUCED MUSCLE α-GLUCOSIDASE (ACID-MALTASE) ACTIVITY IN HYPOTHYROID MYOPATHY

L. J. HURWITZ D. MCCORMICK
INGRID V. ALLEN

Department of Neurology, Royal Victoria Hospital, and Department of Pathology, Queen's University, Belfast

Summary A detailed biochemical study of muscle from a patient complaining of disabling cramps revealed a lowered activity of α-glucosidase (acid-maltase), which was the only abnormality detected. A year after the onset of symptoms hypothyroidism was diagnosed. Treatment with L-thyroxine relieved all symptoms, and the muscle acid-maltase activity was found to be normal six months after the initiation of treatment.

INTRODUCTION

IN the following case the presenting symptoms suggested McArdle's disease (type-v glycogenosis: lack of muscle phosphorylase), and for this reason a detailed biochemical investigation was undertaken.

CASE-REPORT

A fire officer, aged 28 years, noticed painful cramps and stiffness in the muscle with exercise in January, 1968. The cramps affected only those muscles involved in any particular exercise and were not affected by cold weather. His exercise tolerance progressively decreased, and some six months after the onset he would have severe cramp on walking 100 yards or after gripping objects for a few minutes. During this period he became aware of considerable muscle development with an increase in weight of 2–3 stone (12–18 kg.). From being a man of slender frame he developed the physique of a professional weight-lifter though he never engaged in any body-building activities. During 1967 and 1968 he had nine brief episodes of central chest pain accompanied by breathlessness. On examination the most notable finding was the massive enlargement of all muscle-groups: there was no obesity and the muscles were normal on palpation. The initial muscle action was always strong, but weakness with the onset of severe cramp followed sustained activity. During the cramp the appropriate muscles became tender and were shortened, and electromyography revealed motor-unit potentials so that the shortening was due to muscle contraction and not contracture. The thyroid was palpable but not enlarged. There were no other abnormal signs either in the nervous system or on general examination. Electrocardiograms (E.C.G.) taken over intervals showed low-voltage or inverted T waves in all leads and QRS complexes of low-normal amplitude. In April, 1969, the patient began to complain of some intolerance to cold, and it was noted clinically that the skin was excessively dry with keratosis of the hands and there was some coarseness of the voice. The ankle-jerk reflex-time was normal. Primary myxœdema was diagnosed clinically, and this was confirmed by tests of thyroid function. On May 3 daily L-thyroxine therapy was started; the initial dose was 0·05 mg. and this was increased over 18 days to a maintenance dose of 0·2 mg. Within 4 weeks of first taking the L-thyroxine the patient could exercise lightly without cramps. The E.C.G. $3^1/_2$ months after the start of treatment was entirely normal. On examination in October, 1969, 21 months after the onset of symptoms, he had no complaints and was back at work. Muscle bulk had decreased, and forearm girth was 3 cm. less than in September, 1968.

Investigations

The following were normal: full blood-count; Wasserman reaction; glucose-tolerance test; glucose-assimilation test; lactate increase on ischæmic exercise; serum electrolytes, urea, B_{12}, folic acid, alkaline phosphatase and carotene; blood-pH before and after exercise; urinary creatine/creatinine ratio; D-xylose excretion; urinary aminoacids;

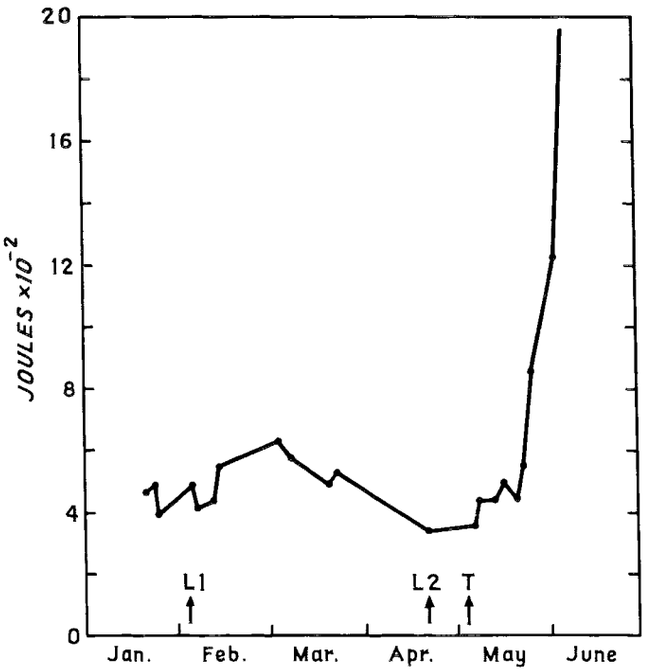

Fig. 1—Work tolerance on handgrip ergometer.

L1, L2 = start and withdrawal of low-carbohydrate diet. T = start of L-thyroxine therapy.