Magnetic Resonance Imaging in Down's Syndrome

David M. Pelz, Stephen J. Karlik, Allan J. Fox and Fernando Viñuela

ABSTRACT: 100% of brains of Down's adults over age 40 will show Alzheimer-type neuropathologic changes in the frontal and temporal lobes. In an attempt to image these lesions, magnetic resonance imaging (MRI) was performed in seven patients with Down's syndrome, ranging in age from 17 to 45 years, using a resistive unit operating at 0.15 Tesla. All scans were within normal limits except for one 45 year-old patient with severe left temporal lobe atrophy. No areas of abnormal signal were seen in the frontal or temporal lobes and the white matter lesions commonly seen in elderly demented subjects were not visualized in this group. We conclude that these white matter lesions are likely coincidental and not causally related to Alzheimer's changes. The pathologic process leading to the formation and development of Alzheimer's changes in the brains of Down's adults may not be visible on magnetic resonance images.

RÉSUMÉ: L'imagerie par résonance magnétique dans le syndrome de Down. Cent pour-cent des cerveaux d'adultes au-dessus de 40 ans atteints du syndrome de Down présentent des changements neuropathologiques de type Alzheimer dans les lobes frontaux et temporaux. Nous avons procédé à un examen par résonance magnétique nucléaire (RMN) au moyen d'une unité d'impédance réglée à 0.15 Tesla, dans une tentative d'illustrer ces lésions chez sept patients atteints du syndrome de Down et dont l'âge variait de 17 à 45 ans. Tous les scans étaient dans les limites de la normale, à l'exception de celui d'un patient âgé de 45 ans porteur d'une atrophie sévère du lobe temporal gauche. Aucune aire de signaux anormaux n'a été visualisée dans les lobes frontaux et temporaux, et les lésions de la substance blanche souvent observées chez les sujets âgés déments n'ont pas été visualisées chez notre groupe de patients. Nous concluons que ces lésions de la substance blanche sont vraisemblablement une coïncidence et ne sont pas reliées de façon causale aux changements de type Alzheimer. Le processus pathologique conduisant à la formation et au développement des changements de type Alzheimer dans le cerveau des adultes atteints du syndrome de Down peut ne pas être visualisable au moyen de l'imagerie par résonance magnétique.

Can. J. Neurol. Sci. 1986; 13:566-569

It is known that patients with Down's syndrome often experience a preciptious decline in mental functioning in the fifth decade and close to 50% over the age of forty-five years will have a full dementia syndrome.[1,2] There is abundant evidence which indicates that close to 100% of brains of Down's patients over forty years of age will show the presence of Alzheimer's type neuropathological changes, most commonly in the hippocampi and frontal white matter.[3,4] It would seem that the neuropathological and neurochemical processes which occur in Down's syndrome are very similar to those occurring in Alzheimer's disease, but they occur at a much earlier age.[5,6] Patients with Down's syndrome therefore represent an ideal population to study with magnetic resonance imaging (MRI) in an attempt to visualize Alzheimer's changes and to document any chronological pattern in their development.

Methods and Materials

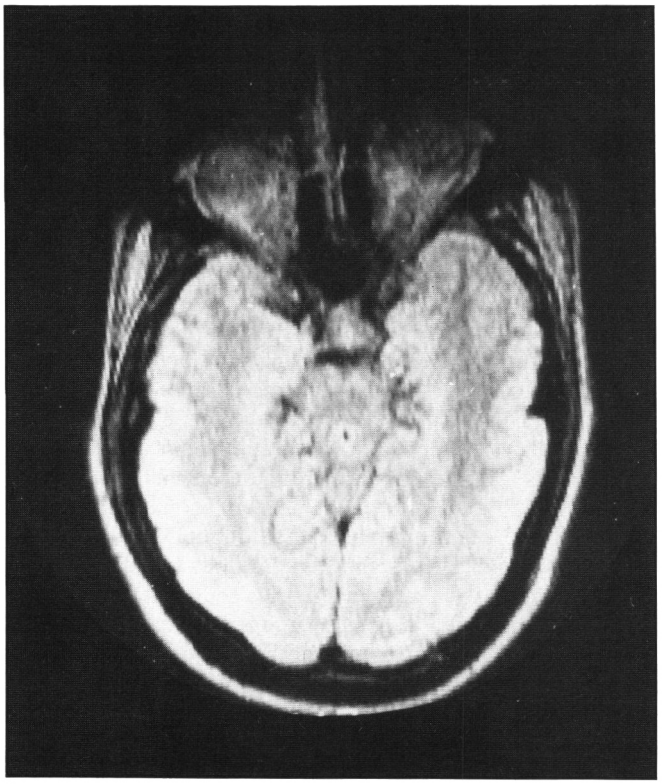
Seven patients with Down's syndrome, ranging in age from 17-45 years, were entered into this study. All patients were living in group homes and functioning well in supervised workshops. They were all able to independently sign informed consents. The studies were performed on a Technicare resistive unit operating at 0.15 Tesla. An attempt was made to perform axial and coronal studies on all patients using as rapid an imaging sequence as possible due to the concern that the patients would become uncooperative in the scanner. The spin echo technique for image acquisition was used. The axial scans were T_2 weighted using a repetition time (TR) of 2,000 milliseconds, echo times (TE) of 60 and 120 milliseconds and a slice thickness of 0.75 cm. Whenever possible, we also performed coronal scans which were more T_1 weighted, using a TR of 700 milliseconds, TE 30 and 60 milliseconds and slice thickness of 1.00 cm. The scans were then analyzed for the presence of any abnormalities. Particular attention was paid to the temporal lobes and hippocampi, frontal lobes and deep white matter. We were interested in areas of abnormal signal, localized atrophy or ventricular enlargement.

Results

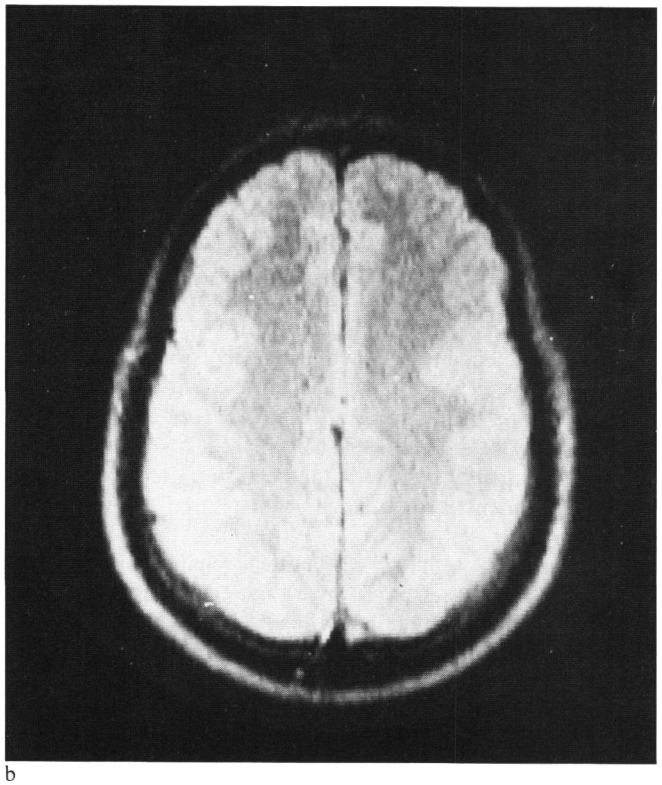
The patients' ages and MR findings are summarized in Table 1. None of the patients were clinically demented. The three patients in the youngest age group (20-29 years) demonstrated

From the Departments of Diagnostic Radiology and Clinical Neurological Sciences (Drs. Pelz, Karlik, Fox and Viñuela) and the Department of Pathology (Dr. Karlik), University Hospital, University of Western Ontario, London, Ontario

Reprint requests to: David M. Pelz, M.D., Department of Diagnostic Radiology, University Hospital, P.O. Box 5339, Postal Stn. "A", London, Ontario, Canada N6A 5A5

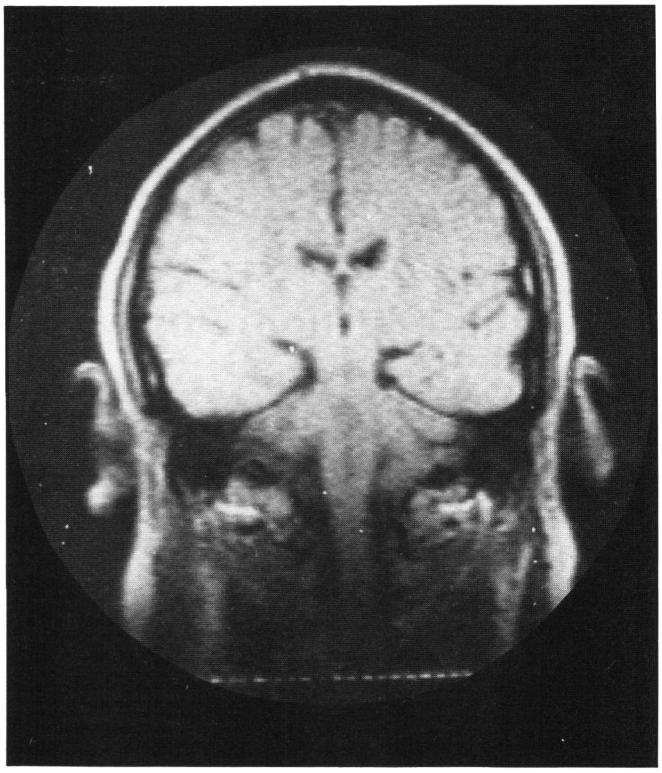


a



b

Figure 1 — Case 1: (a) SE Scan, TR 2,000, TE 60. An axial scan through the temporal lobes demonstrates no abnormality. (b) SE Scan, TR 2,000, TE 60. No abnormalities are seen in the deep white matter of either hemisphere. (c) SE Scan, TR 700, TE 30. A coronal scan demonstrates no abnormalities in the temporal lobes.



c

Table 1: Patients ages and MR findings.

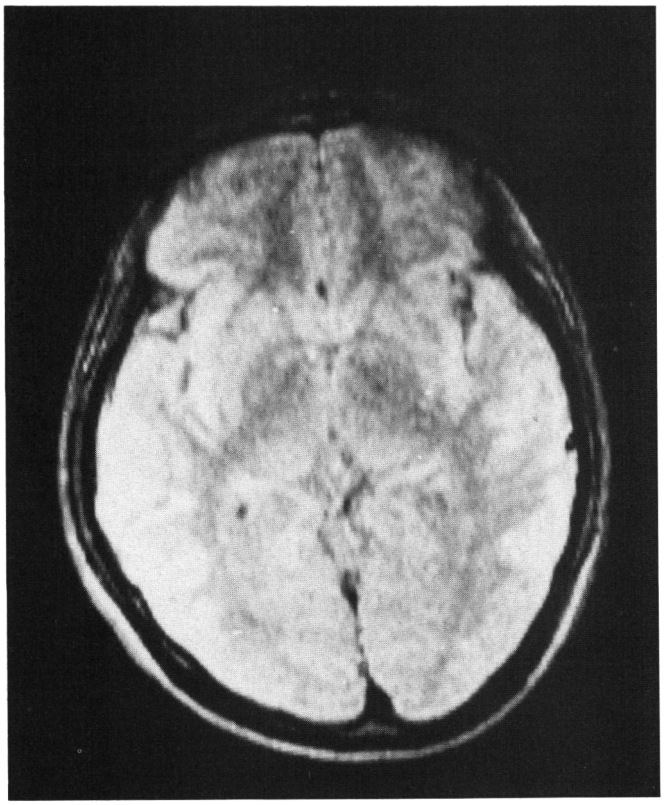
Case	Age	MR Findings
(1) BB	29	no abnormality
(2) DM	32	no abnormality
(3) LS	35	poor quality no abnormality
(4) FL	35	motion artifact no abnormality
(5) JAM	45	— mild generalized atrophy — marked focal atrophy in left temporal lobe with enlarged sylvian fissure
(6) AW	25	— motion artifact — mild generalized atrophy
(7) WC	26	— mild frontal and temporal atrophy

no significant lesions on their scans (Figure 1) although two patients showed mild atrophic changes in the temporal regions and generous ventricles which suggested mild central atrophy (Figure 2). There were three patients in the 30-39 year age group. Two patients became restless and agitated while in the magnet and consequently only axial studies were performed. Although two scans were degraded by artifact, no abnormalities were seen in this group. The scan on the oldest patient (45 years) demonstrated marked left temporal lobe atrophy with a very prominent left sylvian fissure (Figure 3). No other lesions could be identified.

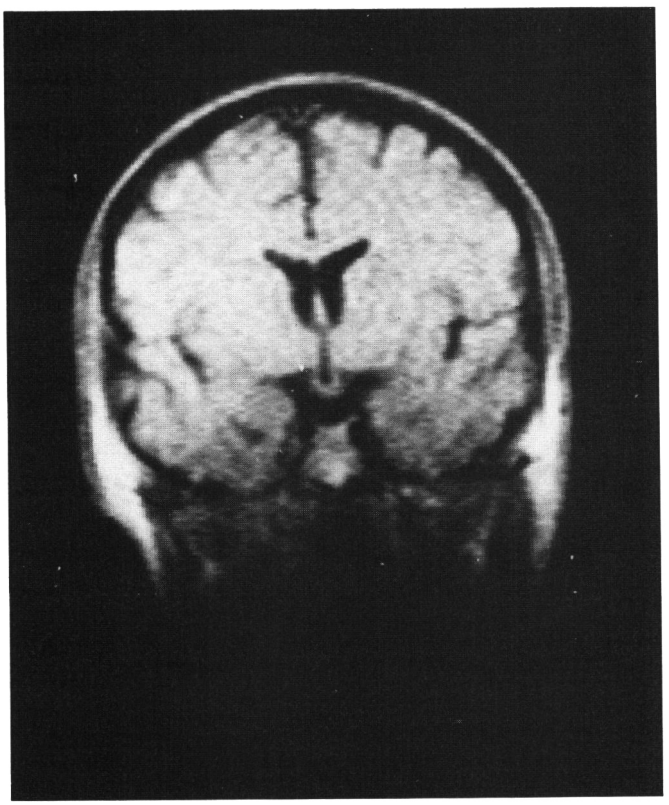
Discussion

Dementia is defined as a dysfunction in more than one of the four major cognitive ability areas — language, memory, reason-

https://doi.org/10.1017/S0317167100037318 Published online by Cambridge University Press



a



b

Figure 2 — Case 7: (a) SE Scan, TR 2,000, TE 60. This axial image demonstrates mild atrophic changes in both temporal lobes. (b) SE Scan, TR 700, TE 60. The coronal image shows mild frontal atrophic changes.

ing and construction. More than 50% of the senile dementias are of the Alzheimer's type with the remainder usually resulting from cerebrovascular atherosclerosis. The neuropathologic changes of Alzheimer's disease typically include cell loss, neurofibrillary tangle formation in the neocortex, amygdala and hippocampus and extensive senile plaque formation. These changes may be seen in the normal elderly population but occur at an earlier age in Alzheimer's, clustering in the 55-65 year age group.

There are striking similarities seen between the brains of Alzheimer's patients and those of Down's subjects who survive into the third decade. Many investigators[1-6] have found nearly identical patterns of cell loss and neurofibrillary tangle formation in the brains of adult Down's patients but these occur at least ten years earlier than in Alzheimer's patients. Nearly 90% of brains of Down's patients over the age of 30 and 100% over age 40 will show the typical neuropathological changes of Alzheimer's. This group therefore represents an ideal population in which to study the development and formation of plaques and tangles. Despite the anticipated difficulties with patient co-operation, our purpose in this study was to define imaging correlates of these changes in an early sequential manner using the newest, most sensitive technique available, MRI.

CT scanning of elderly demented and nondemented subjects has been of little value in either predicting the level of cognitive function or demonstrating features specific for Alzheimer's disease.[7,8] Nonspecific cortical atrophy, ventricular enlargement and deep white matter lucencies have been seen with CT in demented and non-demented subjects.

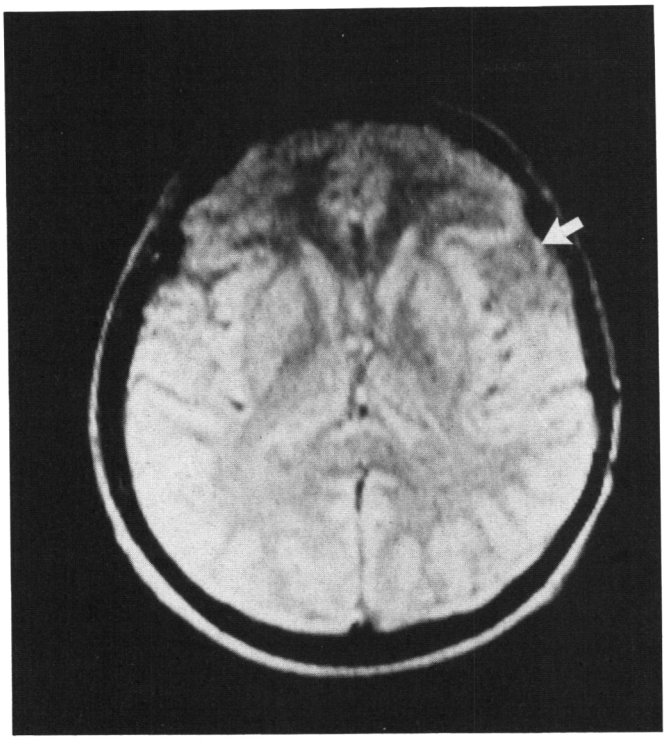
In our group of Down's subjects, we were unable to visualize any specific abnormalities which would correlate with the known underlying neuropathologic changes. Mild to moderate generalized cortical and localized temporal lobe atrophy are expected findings in Down's syndrome.[9] We did not visualize any deep white matter lesions in the temporal and frontal lobes or periventricular regions. There have been studies which suggest an association between the presence and severity of patchy white matter lesions and advancing age, cerebrovascular disease and cognitive loss.[10] These areas of abnormal signal have not however been seen in the few patients with Alzheimer's disease who have been imaged with MR to date.[11,12] The inability to detect any deep white matter lesions in the Down's group adds weight to the premise that the pathological process leading to the formation and development of Alzheimer's changes may not be visible on MR images. It is also likely that these white matter lesions often seen in elderly patients are likely coincidental and not causally related to Alzheimer's changes.

Despite the technical difficulties regarding patient co-operation, a larger series of Down's patients, particularly those in the older age groups and those with a clinical dementia syndrome, should be imaged to verify these preliminary findings.

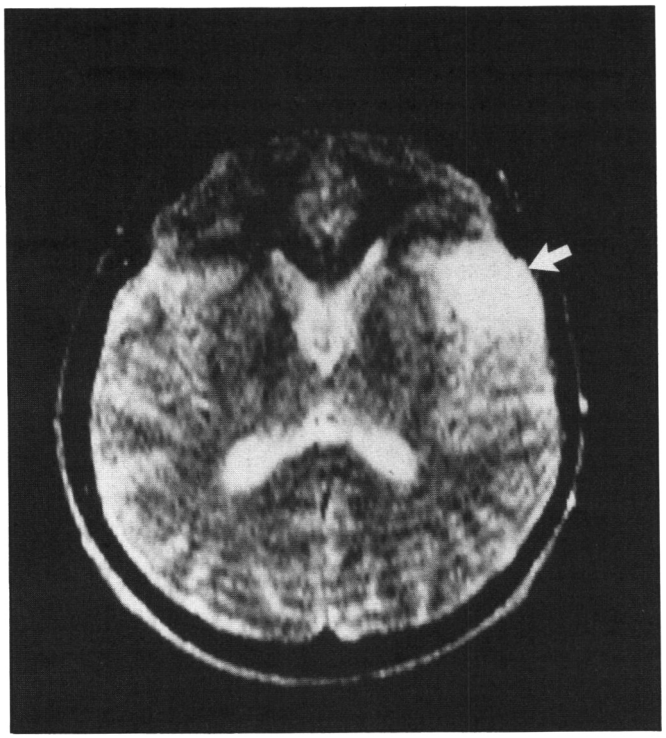
References

1. Wisniewski KE, Dalton AJ, Crapper McLachlan DR, Wen GY, Wisniewski HM. Alzheimer's disease in down's syndrome: clinicopathologic studies. Neurology 1985; 35: 957-961.
2. Wisniewski KE, Howe J, Williams DG, Wisniewski HM. Precocious aging and dementia in patients with down's syndrome. Biol Psychiatry 1978; 13: 619-627.

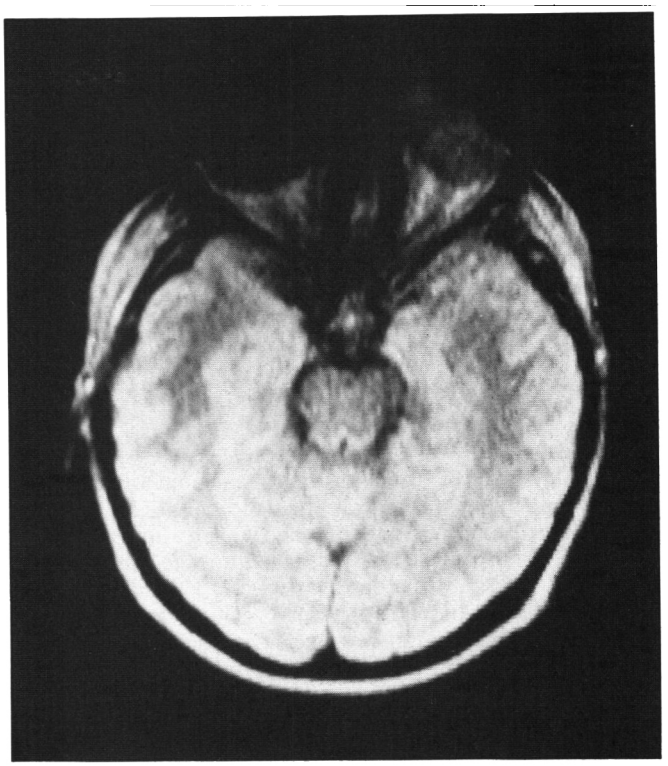
https://doi.org/10.1017/S0317167100037318 Published online by Cambridge University Press



a



b



c

Figure 3 — Case 5: (a) SE Scan, TR 2,000, TE 60. Axial images through the temporal lobes show prominence of the left Sylvian fissure due to marked localized atrophy (arrow). (b) This localized atrophy shows as a high signal with TE 120. (c) SE Scan, TR 2,000, TE 60. No other abnormalities are seen in the temporal lobes.

3. Malamud N. Neuropathology of organic brain syndrome associated with aging. *In:* Gantz CM, ed. Aging and the brain. New York: Plenum Publishing Corp., 1972: 63-87.
4. Crapper DR, Dalton AJ, Skopitz M, Scott JW, Hachinski V. Alzheimer degeneration in down syndrome: electrophysiologic alterations and histopathologic findings. Arch Neurol 1975; 32: 618-623.
5. Ropper AH, Williams RS. Relationship between plaques, tangles, and dementia in down syndrome. Neurology 1980; 30: 639-644.
6. Ball MJ, Nuttall K. Neurofibrillary tangles, granulovacuolar degeneration and neuron loss in down syndrome: quantitative comparison with alzheimer dementia. Ann Neurol 1980; 7: 462-465.
7. George AE, DeLeon MJ, Rosenbloom S, Ferris SH, Gentes C, Emmerich M, Kricheff II. Ventricular volume and cognitive deficit. A computed tomographic study. Radiology 1983; 149: 493-498.
8. Hughes CP, Cado M. Computed tomography and aging of the brain. Radiology 1981; 139: 391-396.
9. Ball MJ, Schapiro MB, Rapoport SI. Neuropathological relationships between down syndrome and senile dementia alzheimer type. *In:* Epstein C, ed. The neurobiology of down syndrome. New York: Raven (in press).
10. Brant-Zawadzki M, Fein G, VanDyke C, Kiernan R, Davenport L, de Groot J. MR imaging of the aging brain: patchy white-matter lesions and dementia. AJNR 1985; 6: 675-682.
11. Friedland RP, Budinger TF, Brant-Zawadzki M, Jagust WJ. The diagnosis of alzheimer-type dementia: a preliminary comparison of positron emission tomography and proton magnetic resonance. JAMA 1984; 252: 2750-2752.
12. Erkinjuntii T, Sipponen JT, Iivanainen M, Ketonen L, Sulkava R, Sepponen RE. Cerebral nmr and ct imaging in dementia. J Comput Assist Tomogr 1984; 8: 614-618.

https://doi.org/10.1017/S0317167100037318 Published online by Cambridge University Press