Normal Memory After Damage to Medial Thalamus

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We studied two patients with nonhemorrhagic infarcts of the thalamus and assessed their cognitive functions comprehensively using standardized neuropsychological probes. Neither patient had any discernible memory impairment for verbal or nonverbal material. Analysis of magnetic resonance images with a stereotaxic method revealed that one subject had a right-sided lesion involving about 15% of the dorsomedial nucleus (DM). The other had bilateral lesions that affected about 15% of the left DM and less than 5% of the right DM. The mamillothalamic tract appeared intact in both patients. Considering that medial thalamic lesions commonly cause amnesia in human beings as well as nonhuman primates, there are two possible reasons, alone or in combination, that may explain why these patients failed to have amnesia: the amount of DM damage was less than required to cause amnesia; or the amnesia related to thalamic lesions requires damage to a second structure, such as the mamillothalamic tract or the anterior nucleus.

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Diencephalic structures, and, in particular, the dorsomedial nucleus of the thalamus (DM), appear to play an important role in memory. Victor et al¹ found damage in the DM of all patients with amnesia in the setting of Wernicke-Korsakoff disease. Ischemic infarction of the medial thalamus has also been associated with amnesia. Left- or right-sided lesions impair memory for verbal or nonverbal material, respectively.²⁻⁶ The wellknown patient NA, an example of traumatic thalamic damage, has amnesia for verbal material in association with a left medial thalamic lesion.7 Bilateral damage of DM has been associated with amnesia, both in human beings6.8.9 and in nonhuman primates.10-13

Here we describe two patients who did not develop any memory defect after DM damage. We also describe a stereotaxic method for the analysis of thalamic lesions identified on magnetic resonance imaging (MRI) scans.

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REPORT OF CASES

CASE 1.—A 32-year-old right-handed man, while driving home from work on Jan 10, 1986, noted the sudden onset of vertical double vision and difficulty with judgment of depth. On leaving the car, he had difficulty walking. His wife noticed a mild weakness of the face on the left side and slurred speech. During admission to a local hospital the neurologic signs were confirmed, but results of all laboratory investigations were normal, including a computed tomographic (CT) scan of the head with and without contrast, which was performed one day after onset.

Examination at the University of Iowa Hospital (Iowa City) on Jan 20 showed some flattening of the left nasolabial fold, a mild left pronator drift, slowness of rapid alternating movements of the left fingers, and moderate difficulty with tandem gait. Results of a complete blood cell count, erythrocyte sedimentation rate, VDRL, blood chemistry studies, urinalysis, coagulation profile, electrocardiogram, chest roentgenogram, and echocardiogram were normal. An MRI scan showed a lesion in the medial right thalamus (see anatomic description below). The aortic arch, right carotid, and right vertebral angiograms were normal.

No neurologic deficits were found on a follow-up examination on May 27, 1986.

CASE 2.—A 25-year-old right-handed female nurse awoke at 6 AM on Jan 9, 1986, and had a transient episode of numbness of the left hand. Shortly after dressing she felt nauseated and lightheaded. She left her apartment to call a neighbor, but lost consciousness and fell in the hallway. About 20 minutes later, she awoke spontaneously and returned to her apartment, noting that her vision was blurred and double, that she was unable to look down, and that her gait was unbalanced. Again, she went for help, and was then taken to the University of Iowa Hospital.

On arrival, the patient was sleepy but oriented to person, place, and time. She responded to commands slowly. She incorrectly stated that her husband was in Chicago. She was unable to look up or down, had right-sided facial paralysis, limited movement of the right side of the palate and pharynx, and rightward deviation of the tongue on protrusion. Moderate weakness of her right arm was noted. Two hours after admission, she was alert and had become normal on neurologic examination, except for a slightly unsteady gait. The patient had discontinued taking oral contraceptives 41/2 weeks previously, after having taken them for three years.

Results of a complete blood cell count, erythrocyte sedimentation rate, VDRL, antinuclear antibody test, blood chemistry studies, coagulation profile, electrocardiogram, chest roentgenogram, and echocardiogram were normal. Head CT without contrast (Jan 9) was normal. An MRI brain scan (Jan 10) showed a 1-cm lesion in the left medial thalamus and a smaller lesion in the right medial thalamus (see anatomic description below). The aortic arch, left carotid, and right vertebral angiograms were normal.

At a follow-up examination on Jan 24, 1986, she had no neurologic signs and was subjectively back to baseline.

METHODS Neuropsychologic Studies

Patient 1 was studied at 11 days and 4.5 months following stroke. Patient 2 was studied at four and 18 days after stroke. The procedures used are listed in Table 1.

Neuroanatomical Studies

An MRI scanner (Picker International Superconducting 0.5 tesla) was used to obtain 5-mm thick horizontal and coronal T1-weighted inversion recovery images. The method used for lesion localization was a modification of that described by Archer et al¹⁴ and Graff-Radford et al.¹⁵

If the lesion was seen on one horizontal and one coronal scan only, the following technique was used:

1. On the midline sagittal $MR \, cut$ (Fig 1), the computer was instructed to place lines H and C. These corresponded, respectively, to the horizontal and coronal cuts in which the lesion was seen. Point O was the intersection of these two lines and corresponded to the center of the lesion. The position of the anterior commissure (AC) was marked inferior to the junction of the anterior corpus callosum and fornix. The position of

Table 1Neuropsychologic Studies
Wechsler Adult Intelligence Scale, Revised ²⁹
Temporal Orientation Test ³⁰
Rey auditory verbal learning test (AVLT) ^{31(p422)}
Wechsler memory scale (WMS) ³²
logical memory, paired associates,
and visual reproduction subtests
Twenty-minute delayed recall of WMS
subtests
Release from proactive inhibition
(adapted from Wickens) ³³
Rey-Osterrieth or Taylor figure copy
and 20-minute delayed recall ^{31(p395)}
Kimura recurring figures test ^{34,35}
Benton visual retention test
(administration A, form C) ^{31, p447}
Recall of past presidents
Boston famous faces test ³⁶
Autobiographic reconstruction
Wisconsin Card Sorting Test ³⁷
Serial hand positions ^{38, p423}
Verbal associative fluency
(controlled oral word association) ³⁹
Design fluency ⁴⁰
Multilingual and Boston Diagnostic
Aphasia Examination Subtests ^{39,41}
Benton-Van Allen Facial Discrimination Test ³⁰
Judgment of line orientation ³⁰
Three-dimensional block
construction ³⁰
Hooper Visual Organization Test ^{31, p357}
Right-left discrimination ³⁰
Dichotic listening

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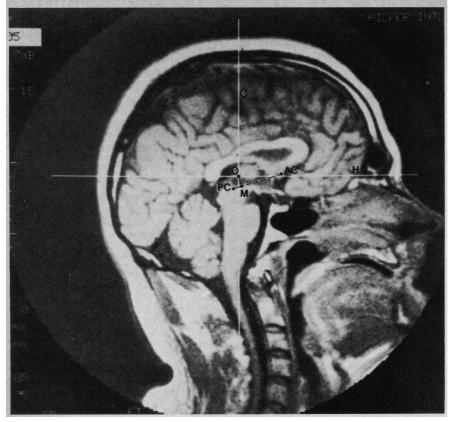


Fig 1.—Midline sagittal magnetic resonance cut from patient 1. Lines H and C denote locations of horizontal and coronal cuts on which lesion was seen. Point O corresponded to center of lesion. AC and PC denote locations of anterior and posterior commissures. Point M identifies intersection of AC-PC line with perpendicular line through point O.

Memory Tests	Patient 1		Patient 2	
	11 d	4.5 mo	4 d	18 d
Verbal anterograde memory Rey auditory verbal learning test				
Trials 1 through 5	7,10,13,13,14	6,11,13,12,14	8,11,14,15,14	NA
Delay	13	14	12	NA
Wechsler memory scale logical memory Immediate/delay	NA	12, 8/13, 8	NA	8,11/11,NA
Wechsler memory scale paired associates Immediate/delay	NA	12, 14, 14/14	NA	6,12,12,/12
Release from proactive inhibition	NA	Present	NA	Present
Nonverbal anterograde memory Wechsler memory scale visual reproduction Immediate/delay	NA	13/12	NA	NA
Benton visual retention test Number correct/errors	8/2	NA	8/3	NA
Complex figure Copy/delay	34/16.5	31/20	NA	34/21
Kimura recurring figures T score	NA	61	NA	NA

*NA indicates not administered. All delay trials were 20 minutes.

†All scores were normal; remote memory was also normal (see text).

the posterior commissure was marked at the superior point of the midbrain aqueduct. The anterior commissure-posterior commissure (AC-PC) line was then drawn. Another line, perpendicular to the AC-PC line, was drawn through point O. The intersection of these lines was point M. The distances from O to M and from PC to M

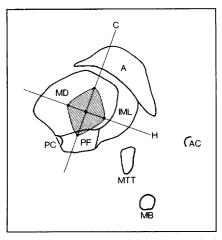


Fig 2.—Lesion of patient 1 plotted on sagittal atlas plate 5 mm from midline. Lesion involved 29% of area of right dorsomedial nucleus in this plate. It did not extend to mamillothalamic tract or anterior nucleus. MD indicates dorsomedial nucleus; PF, parafascicular nucleus; A, anterior nucleus; IML, internal medullary lamina; MTT, mamillothalamic tract; and MB, mamillary body. (Adapted from Schaltenbrand and Wahren atlas.¹⁶)

were measured. The angle between lines C and AC-PC was measured.

2. On the coronal and horizontal MR cuts, which contained the lesion, the medial and lateral limits of the infarct were measured. These distances were multiplied by a conversion factor (CF) to account for the different size of the atlas and patient brains. The CF equals the length in millimeters of the AC-PC line in the atlas, divided by the length in millimeters of the AC-PC line on the scan. The distances from the midline of the sagittal plates of the Schaltenbrand and Wahren atlas¹⁶ were then reviewed. Three plates were chosen to correspond as nearly as possible to the medial aspect, midline, and lateral aspect of the lesion. Returning to the MR cuts, the anterior, posterior, superior, and inferior limits of the infarct were measured at the distances corresponding to the three atlas plates chosen.

3. The following procedure was used for each of the three sagittal atlas plates determined above (Fig 2). After tracing paper was placed over the plate, the AC-PC line was drawn. Points M and O were then marked using the distances calculated in the first section (multiplied by CF and by the atlas magnification factor of 4). The coronal and horizontal planes, lines C and H, were drawn using the angle between lines C and AC-PC as measured in the first section. The anterior, posterior, inferior, and superior limits of the lesion were marked using the distances calculated in the second section (multiplied by CF and by the atlas magnification factor of 4). A line was drawn through these points and taken to represent the extent of the lesion.

4. For each sagittal plane, a digitizer was used to calculate the area of each thalamic nucleus and the area of the nucleus involved by the lesion. By comparing the ratio of these areas for the three sagittal planes, a good estimate of the volume of

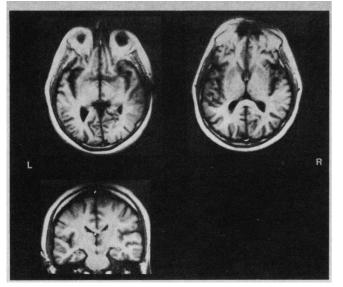


Fig 3.—Coronal magnetic resonance and axial cuts from patient 1. The lesion involved right medial thalamus.

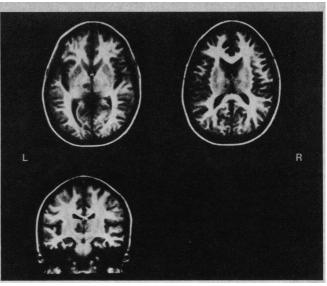


Fig 4.—Coronal magnetic resonance and axial cuts from patient 2. Lesion involved bilateral medial thalamus.

the nucleus involved by the infarction was obtained.

If the lesion was seen on more than one horizontal or coronal MR scan, a similar technique was used so that on each sagittal atlas plate the extent of the lesion was drawn based on six or more points.

RESULTS Neuropsychologic Findings

Patient 1 had a low average verbal IQ, consistent with his education and occupation. Performance IQ was borderline at the initial test session, but improved to a low average level at a follow-up session. Memory test results are summarized in Table 2. Results of tests of orientation, verbal and nonverbal short-term memory, recall of past presidents, and autobiographic reconstruction were normal. He had a normal performance on the Wisconsin Card Sorting Test, was easily able to repeat serial hand positions, and had normal verbal associative fluency. His performance on a test of design fluency was not examined at the first test session, but was abnormal at followup testing. His language was normal. His performance on tests of visuoperceptive and visuoconstructive abilities was impaired only for three-dimensional block construction. Visuoconstructive abilities were normal at follow-up. Dichotic listening was normal.

Patient 2 had an average performance on the revised Wechsler Adult Intelligence Scale subtests of verbal intellect (information, 12; digit span, 12; arithmetic, 10) and of nonverbal intellect (block design, 13). This was consistent with her education and occupation. Her performance on tests of orientation, short-term verbal and nonverbal memory, recall of past presidents, and autobiographic reconstruction was normal. She recognized 20 faces of the Boston famous faces test, and identified one other with cuing, a normal score for her age and background. Her performance on tests of verbal associative fluency, language, facial discrimination, and dichotic listening was also normal.

Anatomical Findings

Patient 1 had a lesion limited to the right thalamus (Fig 3). It involved about 15% of the DM nucleus, about 5% of the parafascicular nucleus, and less than 5% of the midline nuclei. The mamillothalamic tract and the anterior nucleus were spared.

Patient 2 had a bilateral lesion (Fig 4). On the left, it involved about 15% of DM, and less than 5% of the anterior, parafascicular, lateral posterior, and ventral posterior nuclei. There was also some infarction of the internal medullary lamina. The mamillothalamic tract was spared. The lesion on the right involved less than 5% of DM and less than 5% of the parafascicular nucleus.

COMMENT

Both patients had medial thalamic damage but neither had an impairment of memory. Patient 1 had no evidence of amnesia for nonverbal material, in contrast to the patient with a similar right medial thalamic lesion reported by Speedie and Heilman.⁵ Patient 2 had no evidence of amnesia for verbal or nonverbal material, unlike patients with bilateral medial thalamic lesions of Korsakoff's syndrome¹ or bilateral ischemic infarctions.^{6,8,9} Even if we only took into account her large left-sided lesion, and ignored the right thalamic damage, she was still remarkably different from patients with left medial

thalamic ischemic infarction,^{24,6} or patient NA,⁷ all of whom had verbal amnesia. The source of this discrepancy resides, in all likelihood, in the diverse anatomic placement of lesions in our cases and in those previously reported. The following discussion is aimed at clarifying such differences.

Although damage to DM has been traditionally implicated in amnesia, previously published evidence suggests that damage to DM alone might not be sufficient to cause amnesia. Thus, Mair et al¹⁷ have suggested that the amnesia of patients with Korsakoff's syndrome is caused by damage to medial thalamic structures only when there are associated lesions of the mamillary bodies. Von Cramon et al⁶ localized CT lesions stereotactically in patients with unilateral or bilateral ischemic medial thalamic infarcts. Two patients, one with a left-sided lesion and the other with bilateral lesions, had no amnesia. Their lesions were restricted to DM and the internal medullary lamina. The lesions of amnesic patients involved DM, white matter of the internal medullary lamina, and the mamillothalamic tract.

The anterior thalamic nucleus is another structure that might be related to memory. It could be damaged by an infarct extending more anteriorly in the thalamus. The very small amount of involvement seen in patient 2 was not sufficient to cause amnesia. However, more extensive damage to this nuclear complex might add to the effect of a DM lesion to produce amnesia.

Patient NA might also have damage to structures other than DM. His penetrating injury could have affected other structures important to memory including basal forebrain nuclei and pathways, anterior thalamic nucleus, fornix, mamillary bodies, and mamillothalamic tract.

Nonhuman primate studies are also consistent with the explanation that DM lesions must be combined with damage to another structure to produce amnesia. Aggleton and Mishkin^{11,12} studied monkeys with bilateral anterior DM lesions. Although these lesions produced amnesia, the degree of amnesia was considerably greater when the lesions were combined with damage to the mamillothalamic tract and anterior nucleus.

An alternative explanation for the lack of amnesia in our patients is that there could be a critical amount of DM damage below which amnesia does not develop. Zola-Morgan and Squire¹³ studied monkeys with bilateral posteriorly placed DM lesions involving 32% to 44% of the nucleus. They found that the monkeys had a degree of amnesia comparable to that of Aggleton and Mishkin's¹² monkeys, which had lesions of anterior DM combined with mamillothalamic tract. The effect of smaller posterior lesions has not been reported. Our patients had relatively small lesions in terms of percent of DM involved. Thus, it may be that lesions of DM which do not extend anteriorly must involve a critical amount of posterior DM to produce amnesia.

It is possible that damage to some critical part of DM is required to produce amnesia. On this point, the literature offers no help. All human and nonhuman primates with amnesia caused by medial thalamic lesions seem to have anterior lesions with associated damage to mamillothalamic tract or large posterior DM lesions.

It is unlikely that young age and lack of previous neurologic disease are the reasons for our patients' intact memory. Nonetheless, we considered that possibility and reviewed published cases of amnesia following medial thalamic ischemic infarction.^{2-6,8,9,18-28} We found that an uncommon number of these patients were young. Including the cases we have seen, 35% (9/26) of the patients with clinically diagnosed, and neuroradiologically confirmed, medial thalamic infarcts were between 20 and 40 years old. A final alternative explanation would be that our patients might have had an exceptional anatomic variation due to unusual brain development. Not only would it be unlikely to find two such cases consecutively, but there was nothing in the patients' histories or current observation to suggest unusual brain development.

Our interpretation, then, is that lesions of DM probably cause amnesia when they damage a second structure such as the mamillothalamic tract, or when they involve a critical amount of DM. Our patients failed to develop amnesia because their lesions did not meet either criteria.

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References

1. Victor M, Adams RD, Collins GH: *The Wer*nicke-Korsakoff Syndrome. Philadelphia, FA Davis Co Publishers, 1971.

2. Michel D, Laurent B, Foyatier N, et al: Infarctus thalamique paramédian gauche: Etude de la memoire et du language. *Rev Neurol* 1982;138:533-550.

3. Speedie LJ, Heilman KM: Amnestic disturbance following infarction of the left dorsomedial nucleus of the thalamus. *Neuropsychologia* 1982;20:597-604.

4. Goldenberg G, Wimmer A, Maly J: Amnesic syndrome with a unilateral thalamic lesion: A case report. J Neurol 1983;229:79-86.

5. Speedie LJ, Heilman KM: Anterograde memory deficits for visuospatial material after infarction of the right thalamus. *Arch Neurol* 1983;40:183-186.

6. Von Cramon DY, Hebel N, Schuri U: A contribution to the anatomical basis of thalamic amnesia. *Brain* 1985;108:993-1008.

7. Squire LR, Moore RY: Dorsal thalamic lesion in a noted case of human memory dysfunction. *Ann Neurol* 1979;6:503-506.

8. Guberman A, Stuss D: The syndrome of bilateral paramedial thalamic infarction. *Neurology* 1983;33:540-546.

9. Winocur G, Oxbury S, Roberts R, et al: Amnesia in a patient with bilateral lesions to the thalamus. *Neuropsychologia* 1984;22:123-143.

10. Isseroff A, Rosvold HE, Galkin TW, et al: Spatial memory impairments following damage to the mediodorsal nucleus of the thalamus in rhesus monkeys. *Brain Res* 1982;232:97-113.

11. Aggleton JP, Mishkin M: Memory impairments following restricted medial thalamic lesions in monkeys. *Exp Brain Res* 1983;52:199-209.

12. Aggleton JP, Mishkin M: Visual recognition impairment following medial thalamic lesions in monkeys. *Neuropsychologia* 1983; 21:189-197.

13. Zola-Morgan S, Squire LR: Amnesia in monkeys after lesions of the mediodorsal nucleus of the thalamus. *Ann Neurol* 1985;17:558-564.

14. Archer CR, Ilinsky IA, Goldfader PR, et al: Aphasia in thalamic stroke: CT stereotactic localization. J Comput Assist Tomogr 1981;5:427-432.

15. Graff-Radford NR, Schelper RL, Ilinsky IA, et al: Computed tomographic and postmortem study of a nonhemorrhagic thalamic infarction. Arch Neurol 1985;42:761-763.

16. Schaltenbrand G, Wahren W: Atlas for Stereotaxy of the Human Brain. Chicago, Year Book Medical Publishers Inc, 1977.

17. Mair WGP, Warrington EK, Weiskrantz L:

Memory disorder in Korsakoff's psychosis: A neuropathological and neuropsychological investigation of two cases. *Brain* 1979;102:749-783.

18. Halmagyi GM, Evans WA, Hallinan JM: Failure of downward gaze: The site and nature of the lesion. *Arch Neurol* 1978;35:22-26.

19. Mills RP, Swanson PD: Vertical oculomotor apraxia and memory loss. Ann Neurol 1978;4:149-153.

20. Von Cramon D, Eilert P: Ein Beitrag zum amnestischen Syndrom des Menschen. Nervenarzt 1979;50:643-648.

21. Schott B, Mauguière F, Laurent B, et al: L'amnésie thalamique. *Rev Neurol* 1980;136:117-130.

22. Barbizet J, Degos JD, Louarn F, et al: Amnésie par lésion ischémiquebi-thalamique. *Rev Neurol* 1981;137:415-424.

23. Petit H, Rousseaux M, Clarisse J, et al: Troubles oculo-céphalomoteurs et infarctus thalamo-sous-thalamique bilatéral. *Rev Neurol* 1981;137:709-722.

24. Pierrot-Deseilligny CH, Chain F, Gray F, et al: Parinaud's syndrome: Electro-oculographic and anatomical analyses of six vascular cases with deductions about vertical gaze organization in the premotor structures. *Brain* 1982;105:667-696.

25. Kömpf D, Oppermann J, König F et al: Vertikale Blickparese und thalamische Demenz. Nervenarzt 1984;55:625-636.

26. Karabelas G, Kalfakis N, Kasvikis I, et al: Unusual features in a case of bilateral paramedian thalamic infarction. J Neurol Neurosurg Psychiatry 1985;48:186.

27. Swanson RA, Schmidley JW: Amnestic syndrome and vertical gaze palsy: Early detection of bilateral thalamic infarction by CT and NMR. *Stroke* 1985;16:823-827.

28. Graff-Radford NR, Damasio H, Yamada T, et al: Nonhaemorrhagic thalamic infarction: Clinical, neuropsychological, and electrophysiological findings in four anatomical groups defined by computerized tomography. *Brain* 1985;108:485-516.

29. Wechsler D: Wechsler Adult Intelligence Scale-Revised. New York, Harcourt Brace Jovanovich Publishers, 1981.

30. Benton AL, Hamsher K deS, Varney NR, et al: Contributions to Neuropsychological Assessment: A Clinical Manual. New York, Oxford University Press Inc, 1983.

31. Lezak MD: Neuropsychological Assessment, ed 2. New York, Oxford University Press Inc, 1983.

32. Wechsler D: A standardized memory scale for clinical use. J Psychol 1945;19:87-95.

33. Wickins DD: Characteristics of word encoding, in Melton AW, Martin E (eds): Coding Processes in Human Memory. Washington, DC, Winston, 1972, pp 191-215.

34. Kimura D: Right temporal-lobe damage: Perception of unfamiliar stimuli after damage. Arch Neurol 1963;8:264-271.

35. Rixecker H, Hartje W: Kimura's Recurring Figures Test: A normative study. J Clin Psychol 1980;36:465-467.

36. Albert MS, Butters N, Levin J: Temporal gradients in the retrograde amnesia of patients with alcoholic Korsakoff's disease. *Arch Neurol* 1979;36:211-216.

37. Heaton RK: A Manual for the Wisconsin Card Sorting Test. Odessa, Fla, Psychological Assessment Resources Inc, 1981.

38. Luria AR: Higher Cortical Functions in Man, ed 2. New York, Basic Books Inc Publishers, 1980.

39. Benton AL, Hamsher K deS: Multilingual Aphasia Examination: Manual of Instructions. Iowa City, AJA Associates Inc, 1983.

40. Jones-Gotman M, Milner B: Design fluency: The intervention of nonsense drawings after focal cortical lesions. *Neuropsychologia* 1977;15:653-674.

41. Goodglass H, Kaplan E: The Assessment of Aphasia and Related Disorders, ed 2. Philadelphia, Lea & Febiger, 1983.