

## Case Report

Cognitive function fifty-six years after surgical treatment of temporal lobe epilepsy: A case study <sup>☆</sup>Sarah Jane Banks <sup>\*</sup>, William Feindel <sup>1</sup>, Brenda Milner <sup>1</sup>, Marilyn Jones-Gotman <sup>1</sup>

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## ABSTRACT

We report a long-term follow-up investigation of a patient who was operated in 1954 to relieve intractable temporal lobe seizures characterized by automatism and amnesia. Neuropsychological review at 16 months after surgery showed a slight residual impairment of verbal comprehension and verbal recall and good nonverbal skills. Seizure-free since the operation except for two attacks in the early postoperative years, the patient has been off medication for 25 years and has pursued a successful career as an artist.

Our investigation at 56 postoperative years focused on cognitive skills, with some emphasis on learning and memory; a clinical examination was also performed, and the anatomical extent of the resection was determined on 3-Tesla magnetic resonance imaging. Four age- and IQ-appropriate women were tested as healthy control subjects. The patient showed material-specific impairments in language and verbal memory compared with the control subjects and also compared with her own earlier performance, but her performance on other cognitive tasks did not differ from that of the control subjects. Thus, her specific deficits had worsened over time, and she was also impaired compared with healthy individuals of her age, but her deficits remained confined to the verbal sphere, consistent with her temporal lobe seizure focus and surgery.

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## 1. Introduction

Hughlings Jackson first related seizures with automatism and amnesia to focal pathology in the uncinate region of the temporal lobe [1,2]. In the 1950s, Penfield and his team developed the surgical treatment for such attacks by subtotal temporal lobectomy that included the temporal cortex and medial structures, mainly the amygdala and hippocampus [3,4]. This procedure, based on experimental electrographic and surgical evidence [5], became adopted in neurosurgical centers worldwide [6].

The existence of memory dysfunction in the pattern of temporal lobe seizures was noted by Jackson [7]. Later, surgical studies showed that seizure discharge localized in the amygdala was clearly associated with an arrest of memory input that resembled attacks in which there was a period of automatic amnesic behavior [8]. Further evidence for the importance of the temporal lobes in memory came from systematic pre- and postoperative neuropsychological studies of patients with temporal lobe resections. Much of the earliest work was carried out by Brenda Milner and her students and colleagues, showing a

material-specific role in verbal learning and memory for the left temporal lobe and in nonverbal material for the right (e.g., [9–13]). This work rapidly extended to findings showing an importance of the medial temporal lobe structures in this material-specific learning and memory (e.g., [14–16]).

Surgical resection of an epileptic focus in the temporal lobe continues to be an effective treatment for seizures, with 3000 surgical procedures per year noted by 1993 and with over 100 neurosurgical centers adopting this surgical approach [6,17]. Patients who underwent surgery early in the history of this treatment now face the cognitive challenges inherent to aging. Given that they already have specific deficits related to their surgery, these patients might be expected to show greater cognitive losses than those attributable to aging or surgery alone. However, there is a paucity of evidence on the long-term cognitive outcome of surgical treatment of epilepsy in general and of temporal lobe surgery in particular. Most studies report follow-up periods no greater than about 10 years [18,19].

In this context, we report here on a patient who is particularly remarkable for her age and the length of her follow-up. She is also interesting from a historical perspective, as she was one of the early patients operated upon by Penfield and studied neuropsychologically before and after operation by Milner.

## 1.1. Case study

The patient, MP, an 82-year-old, right-handed woman, was seen in follow-up 56 years after surgical treatment of her temporal lobe

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epilepsy. Assessment included neurological examination, testing of visual fields, structural 3-Tesla MRI, and neuropsychological evaluation. Her hospital records and neuropsychology files were reviewed.

#### 1.1.1. History

MP's early history was notable for two febrile seizures as an infant, a complaint of pain in her left ear as a child, and daily, low-grade, dull headaches across her forehead bilaterally since her teens. Her first seizure occurred when she was 20 years old, but after that episode she experienced no further events until a year later, while she was in her fourth year of college; she had 10–20 episodes involving unconsciousness each day for two days. The frequency then reduced to once or twice per day for several days, followed by a few months with none. Thereafter, she began to have 1–4 episodes a day for 3–5 days at a time.

MP was very disturbed by her seizures, with an early report suggesting that she did not consider life worth living if her seizures would continue. She became socially withdrawn and did not want to have a family in case she should not be strong enough either to have or to raise a child, and she also feared passing on her seizure disorder to the next generation.

#### 1.1.2. Preoperative evaluation

In light of the intractability of her seizures, at the age of 25, MP was investigated at the Montreal Neurological Institute to determine whether she might be helped by surgery. Investigation at that time (1954) included neurological and visual-field exams, skull X-rays, pneumoencephalogram, EEG, and neuropsychology. A “long-standing smallness of the left cerebral hemisphere, probably more marked in the temporal lobe than elsewhere, and ... a slight generalized enlargement of the left lateral ventricle” were found. An ictal EEG recorded during a spontaneous seizure was also in keeping with abnormality in the left temporal region; furthermore, MP was aphasic for about 30 s following the recorded seizure and did not remember the attack. This amnesia for her attacks or aspects of her attacks was typical of her seizures.

The neuropsychological evaluation revealed a full-scale IQ in the high average range. Milner also reported a “slight, but consistent” language difficulty that was clear anecdotally but not significantly evident from the formal tests used at that time. MP's verbal memory was described as “worse than would be expected for someone of her age and education level,” while her visual memory was good. Milner considered MP's verbal memory inefficiency to be secondary to a more general language difficulty. No other cognitive deficits were found; thus, MP showed a material-specific deficit on verbal tasks, consistent with the likelihood of a seizure focus in the dominant temporal lobe.

Given the concordant findings pointing to a left temporal lobe seizure focus, MP was deemed a suitable candidate for resective surgery. Penfield performed the operation later that year.

#### 1.1.3. Surgery

A left anterior temporal lobe resection was carried out, reported to measure 5 cm along the Sylvian fissure and 6.5 cm along the incisura. Herniation of the parahippocampal gyrus inside the incisura of the tentorium was noted. In his summary, Penfield stated: “It was impossible to produce the patient's aura or to produce her attacks. Prognosis must be guarded.”

#### 1.1.4. Outcome

Following surgery, there was “a marked right homonymous hemianopic field defect” (not present before surgery) “and some postoperative aphasia.” MP's neuropsychological evaluation two weeks after operation was notable primarily for dysphasia.

She had one major seizure in the first year following her surgery, and a minor attack near the end of her first pregnancy six years later.

Since then, she has had no further seizures. During the first year after operation, she took phenobarbital at a dosage of 300 mg a day. She reduced this over the next 8 years to 30 mg a day, which she then took irregularly for another 10 years, usually when she was tired or ill. She has taken no anticonvulsant medication for the past 25 years.

After surgery, MP completed college (where she was studying art), married, and had two children. She divorced her husband in the 1980s.

#### 1.1.5. Career

MP has been a lifelong artist. Her interest in art began when she was a young child. At nine years of age, a picture that she had drawn on the blackboard was photographed and shown in a local exhibition. She later received the only full scholarship awarded at her college of fine art. She continues to collect and immerse herself in art, volunteering at a museum where she introduces children to the collections. When asked if her art changed since surgery, she reported that she became less precise due to her visual problem. She continues to paint, despite her restricted eyesight, and gets great enjoyment from her own art and that of her colleagues. In addition, she volunteers at an art gallery, sharing her passion for art with others.

## 2. Material and methods

### 2.1. Follow-up 54 years later

MP currently lives in her own apartment within an assisted living facility. She has not had any major illnesses since surgery, with high blood pressure and swelling on her foot as her only medical conditions. She does not complain of any new or recent changes in her cognition or, notably, in her memory; she stated that she has always had trouble recalling names. Of note, she commented that she has been unable to sing since her surgery.

### 2.2. Visual fields

In MP's early postoperative examination, a right homonymous upper quadrant field defect that also extended slightly into the lower quadrant was noted. This finding remained evident in subsequent examinations of her vision (1965, 1974, 1978, 1999) and was seen again in the current one. However, the methodology for measuring visual fields has changed, and the 2010 exam appears to show a more extensive field loss than previous exams. Whereas all previous exams used manual perimetry, the latest one used automated perimetry (Humphrey Field Analyzer), which provides more sensitive detection than was possible manually. Whether MP's apparent loss reflects deterioration since the last examination or is simply related to the change in measurement approach is unknown. Behaviorally, after her surgery, MP reported the appearance of visual problems, but she has not reported additional changes in her vision since then.

### 2.3. MRI

Magnetic resonance imaging using the Siemen's 3-Tesla unit showed that the left temporal lobe excision was large, as was common at the time of her operation. Removal of the temporal neocortex measured 3.5 cm at the level of the Sylvian fissure (along T1), 4.3 cm along T3, and 5.0 cm along the inferior aspect of the temporal lobe. The amygdala was radically excised, as were the parahippocampal gyrus and the entorhinal cortex. The head and body of the hippocampus were completely removed, with only a small portion of the tail of the hippocampus remaining. Some cerebellar degeneration was evident but not to a greater extent than expected for her age, and overall, aside from the resection, the hemisphere looked good.

The structures in the medial temporal region of the right side appeared normal on the MRI, and indeed, measurements of right hippocampal volume, mean diffusivity, and fractional anisotropy of

the uncinate and stria of the fornix (using Freesurfer software; <http://surfer.nmr.mgh.harvard.edu/>) [20] showed results within plus or minus one standard deviation of healthy subjects.

Magnetic resonance images of MP's resection in the coronal, sagittal, and horizontal planes are shown in Fig. 1, together with comparative images from one of the control subjects (S3, described below).

#### 2.4. Healthy comparison subjects

We recruited four neurologically and psychiatrically healthy right-handed women similar in age and education level to MP and administered to them the same tests that had been given to her. Subject 1 (S1) was a 77-year-old salesperson whose only health issues were some osteoarthritis, hypertension, and glaucoma. Subject 2 (S2) was a 78-year-old retired nurse with hypertension and hypercholesterolemia. Subject 3 (S3) was a retired accounting clerk with type II diabetes (controlled) and osteoarthritis. Subject 4 (S4) was a 79-year-old retired bookkeeper with type II diabetes and osteoarthritis in the knees. Their years of education were 12, 13, 14, and 11, respectively. Thus, their ages were comparable to that of MP, but education level was slightly lower as it is difficult to find college-educated women of their age. Informed consent was obtained from all subjects; this protocol was approved by the Montreal Neurological Institute's Research Ethics Board.

#### 2.5. Neuropsychological findings

##### 2.5.1. Preoperative

Prior to surgery, MP earned scores on the Wechsler–Bellevue Intelligence Scale [21] in the high average range, with higher scores on nonverbal than on verbal subtests. Her memory was tested using the Wechsler Memory Scale (WMS [22]). She was grossly within normal limits (using the Hulicka normative data [23]) on tests of verbal (paired-associate learning and logical memory) and nonverbal (visual reproduction) immediate memory. In the original version of the WMS, memory was tested only once, immediately following stimulus presentation. However, to obtain a more sensitive test of verbal memory, Milner included an additional recall test of the paired associates and

stories following a 90-minute delay. This demonstrated losses for MP of 62% and 66% for the two stories and 25% for the paired associates. Milner remarked in her report that those verbal scores were lower than would be expected from a college graduate. Immediate memory was good for the designs of the visual reproduction test; it was not retested after a delay.

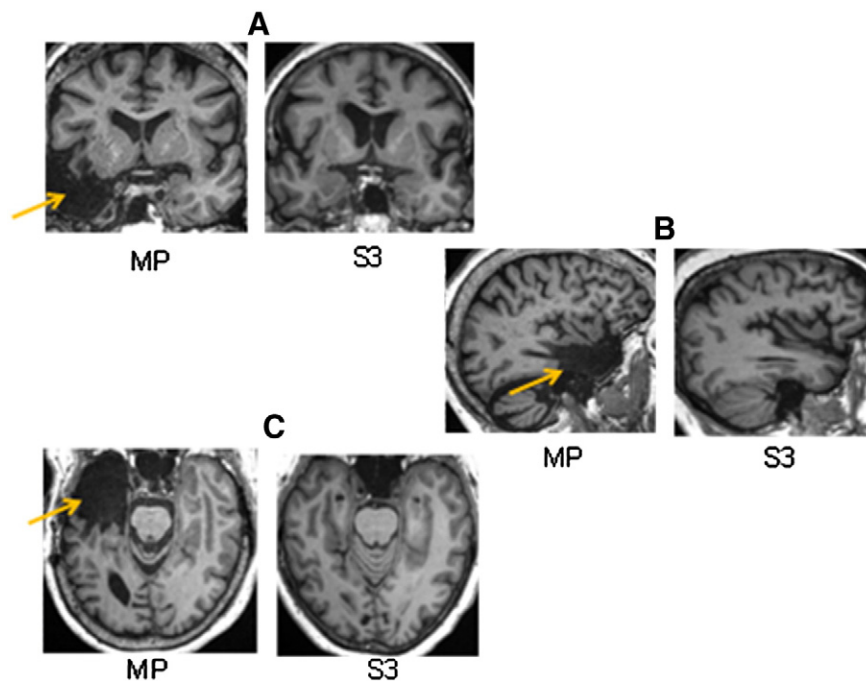
##### 2.5.2. Postoperative assessments

MP's postoperative assessment two weeks after surgery showed a drop in many test scores, including a 23-point loss in verbal IQ. Milner reported a “marked drop on all verbal tests”, with verbal memory giving “great difficulty.” However, we will focus here only on performance at the 16-month follow-up examination because losses in the early postoperative period are transient, and stability is expected by one year after surgery.

In her 16-month follow-up, MP's IQ had returned to – and surpassed – preoperative levels, with improvement in attention and concentration as seen on performance scale subtests. It should be noted that this evaluation was a retest on the same instrument, and a significant improvement can be expected, especially on the performance scale, owing to practice effects. In her report, Milner noted “a slight residual impairment of verbal comprehension and verbal recall.” Nonverbal skills continued to be good.

##### 2.5.3. Current assessment

The recent assessment was designed to address all cognitive domains but with a concentration on verbal and nonverbal memory. Overall IQ according to the WAIS-III [24] was in the average range, thus falling to a lower category compared to the previous Wechsler–Bellevue quotient. Verbal (phonemic) fluency, tested with the Chicago Word Fluency test [25], was also lower than before. In contrast, the scaled score for verbal reasoning (similarities) did not change across assessments. Confrontation naming, assessed with the Boston Naming Test [26], was impaired in keeping with Milner's preoperative qualitative evaluation of a weakness in expressive language. With respect to the two memory tasks that had been given at every evaluation, MP's performance on the visual reproduction test showed a slight decline from her previous assessments, while on the paired-associate learning



**Fig. 1.** MRI scans showing MP's surgical excision (indicated by arrows) compared with one of the healthy control subjects (S3) at the same level. A: coronal,  $x = -32$ . B: sagittal,  $y = 30$ . C: horizontal,  $z = -47$ . Coordinates in MNI space.

**Table 1**

MP's results on tests administered at all three evaluations. Significance of bold entries demonstrate a clinically significant worsening.

Test	January 1954 (before surgery)	May 1955 (16-month follow-up)	March 2011 (56-year follow-up)
Full-scale IQ <sup>a</sup>	110	117	107
Verbal scale IQ	105	111	107
Similarities (scaled score)	11	9	10
Performance scale IQ	114	124	105
Wechsler Memory Scale			
P-A learning <sup>b</sup>	13	10.5	<b>5.5</b>
P-A delayed recall	6	8	<b>5</b>
Visual reproduction	13.5	12	10
Chicago Word Fluency (9 min)	51	55	<b>32</b>

<sup>a</sup> Wechsler–Bellevue Form I in 1954 and 1955; Wechsler Adult Intelligence Scale Form III in 2011. IQ calculations are based on age-appropriate norms.

<sup>b</sup> P-A refers to the Wechsler Memory Scale Paired-Associates subtest.

test, there was a big decline in overall learning. [Table 1](#) compares MP's performance on tests that were given at all three examinations.

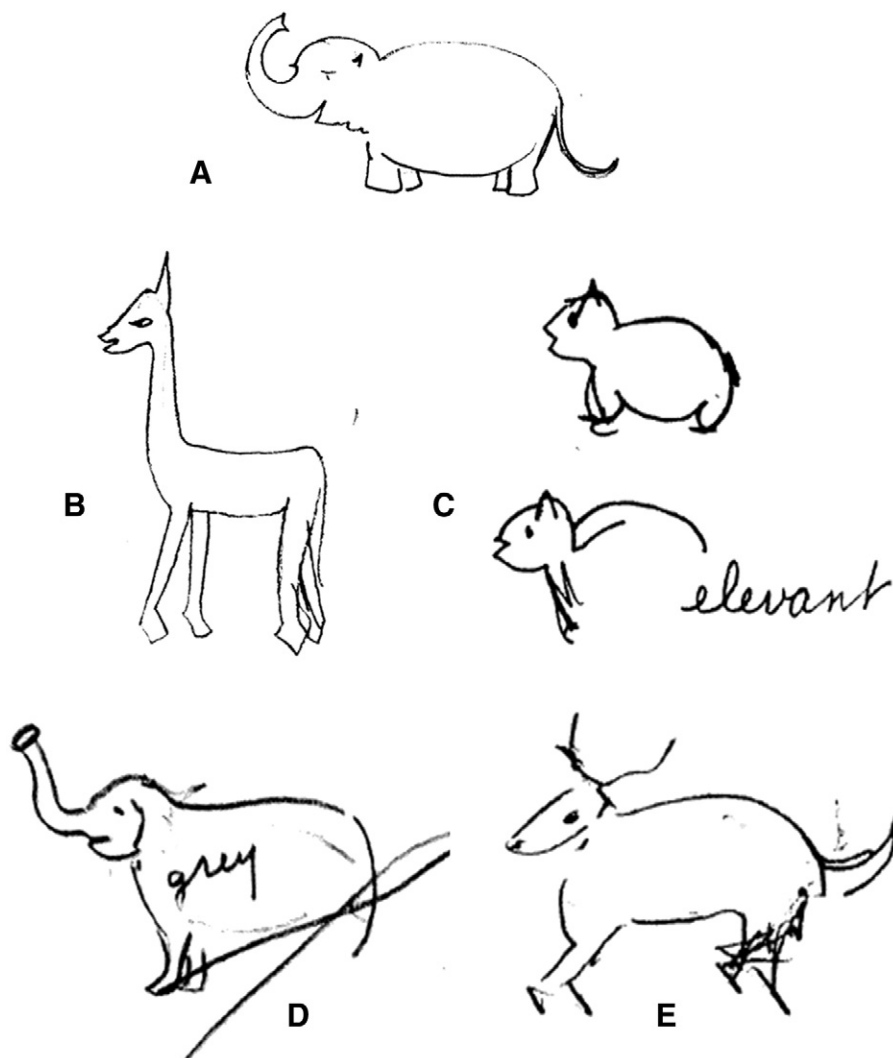
One task that was required at each examination was to draw an elephant. It is interesting, especially given that MP is an artist, that she was unable to do this in the early postoperative period, and she had great difficulty again in the current evaluation. This may reflect

semantic loss attributable to her temporal lobe lesion. Her attempts are shown in [Fig. 2](#), and here we include the several attempts she made when tested three weeks after surgery. At that time, she first drew a long-necked animal that resembled a giraffe. Two days later when asked again to draw an elephant, she produced a mammal-like animal that was quite different from her previous attempt. Her attempt in the 16-month follow-up was much better, although she did not complete it. Her current “elephant” looks like a reindeer, and her comment when asked to describe an elephant was that they are huge, but she also said that they live “up north in the bush.”

#### 2.5.4. Comparison with age-matched healthy control subjects

For a better appreciation of MP's current cognitive abilities, we compared her scores to those of four age-matched healthy control subjects. This is particularly important with respect to the newer, state-of-the-art tests that were given now but not earlier. We note first that these subjects were well matched to MP for IQ (mean FSIQ = 103.8 compared with MP's FSIQ of 107), although their education level was slightly lower than hers. We note also that to the extent that the control subjects differ from MP, it is in the direction of slightly lower IQ and slightly less education, giving the advantage to MP.

Focusing first on material-specific memory, we compared MP's performance on a design list-learning task, the Aggie Figures Learning Test (AFLT) [27], and its verbal counterpart, the Rey Auditory Verbal



**Fig. 2.** MP's drawings of elephants. A: Before surgery, January 1954. B and C: First and second attempts in postoperative evaluation, February 1954. D: In 16-month follow-up, May 1955. E: In 56-year follow-up, March 2011.

Learning Test (RAVLT) [28]. MP showed slow learning on the AFLT, but her performance on this nonverbal learning task was similar to that of her peers. On the RAVLT, both her overall learning of the word list and her recall after a short delay were well below those of the control subjects. Memory for contextual, meaningful verbal material was tested with the Story Learning and Memory test [29], which uses a trials-to-criterion paradigm. MP required one more trial to learn the story than did the control subjects, and despite having heard the story once more than they had, her recall score after a delay was lower than theirs. In addition, MP's performance on the Boston Naming Test was well below that of the healthy control subjects, as was her learning and retention on the paired-associate learning test. On the remaining tasks, she earned scores similar to those of her peers (Table 2).

Thus, she differed from them only on naming and on verbal learning and verbal memory, showing a continued material-specific deficit related to her left temporal lobe seizure focus and surgery.

### 3. Discussion and conclusions

In general, MP's cognitive aging appears to follow a course similar to that of her peers, but her material-specific impairments in language and verbal memory remain. Those deficits have worsened over time but not to a debilitating extent, and MP herself does not complain of severe memory problems. Indeed, given the extent of the resection from her left hippocampus, one might have expected verbal memory impairment bordering on amnesia, but that was not the case, and we might surmise that the overall healthiness of the rest of her brain, and perhaps especially the medial structures of the right temporal lobe, allow her to function as well as she does. Her verbal deficits did not stop her from pursuing her career as an artist (see Fig. 3), and she has lived a seizure-free life since surgery. This case study may provide some reassurance to patients deciding today whether or not to undergo elective surgery for the treatment of seizures. However, it also points to the need for studies of large groups of patients to determine whether MP's case is typical or whether she was particularly fortunate in her long-term outcome.

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**Table 2**

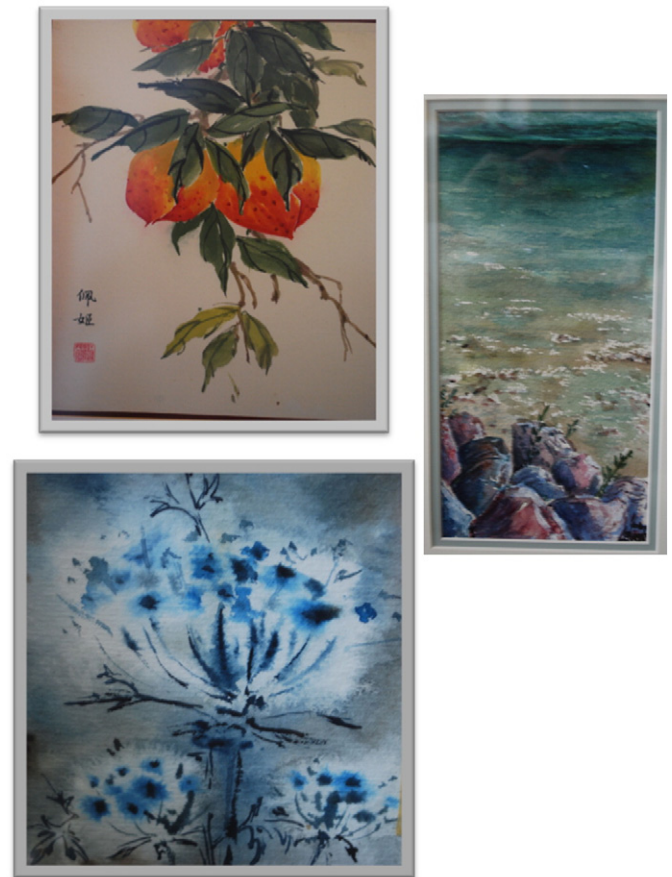
Comparison of MP to mean of control subjects on neuropsychological tests.

Test	Control subjects (mean; N = 4)	MP
Full-scale IQ (Wechsler Adult Intelligence Scale – III)	103.8	107
Verbal scale IQ	108	107
Similarities (scaled score)	13.8	10
Performance IQ	97.8	105
Wechsler Memory Scale (WMS) P-A <sup>a</sup> learning	13.1	<b>5.5</b>
WMS P-A delayed recall	7.0	<b>5</b>
RAVLT <sup>b</sup> total learning (sum of recall on 5 trials)	50.8	<b>22</b>
RAVLT delayed recall (maximum possible = 15)	10.8	<b>3</b>
Story Learning and Memory test delayed recall (%)	54.8	<b>42</b>
WMS visual reproduction immediate recall	8.9	10
WMS visual reproduction delayed recall	7.3	9
Aggie Figures Learning Test (AFLT) total learning	20.5	25
AFLT delayed recall	5.5	4
Rey–Osterrieth Complex Figure copy score	23.5	24
Rey–Osterrieth Complex Figure delayed recall (%)	31.0	37.5
Token Test of Language Comprehension (% correct)	97.2	95.2
Boston Naming Test (maximum possible = 60)	53.5	<b>39</b>
Chicago Word Fluency ("C" only, 4 min)	7.5	8
Jones–Gotman Design Fluency (4 lines only, 4 min)	9.3	<b>1</b>
Digit supraspan	5.8	6
Block-tapping supraspan	7.3	7

Scores in bold are low compared to those of control subjects.

<sup>a</sup> P-A = paired associates.

<sup>b</sup> RAVLT = Rey Auditory Verbal Learning Test.



**Fig. 3.** Three of MP's paintings, all painted in the last 30–40 years.

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