

# Preserved Cognition and Functional Independence after a Large Right Posterior Cerebral Artery Infarct: Longitudinal Clinical and Neuropathological Findings

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BVR was 77 years old when he sustained a large posterior cerebral artery territory infarct. Medical, cognitive and functional data collected on four occasions over 10 years initially revealed circumscribed neurological signs, no functional or cognitive deficits. BVR became significantly impaired only after two other strokes, 3 years before death. On brain MRI, the lesions involved large portions of the right occipital and temporal cortices, the right thalamus, and the left cerebellum, as well as thinning of the corpus callosum. Postmortem investigations revealed additional recent vascular lesions in the occipital region. This case study underscores the importance of comprehensive assessment methods combining neurological, neuroimaging and cognitive tools.

## Introduction

Strokes in the posterior cerebral artery (PCA) territory account for 5–10% of all strokes (e.g., Brandt *et al.*, 2000). The severity of the infarct depends on the location of the occlusion, commonly affecting the occipital lobe but it can also affect midbrain and subcortical structures (medial and posterolateral thalamus), variable areas of the medial parietal and medial temporal lobes and the hippocampus. Almost all affected patients exhibit some visual field abnormality, with over 70% showing a homonymous hemianopia (Brandt *et al.*, 2000), not uncommonly accompanied by visual neglect (Cals *et al.*, 2002). Between 20 and 45% present with other sensory or motor deficits. Cognitive deficits are also common (20–50%) (Kumral *et al.*, 2004). In a prospective study examining the differential presentation in superficial PCA territory infarcts, Kumral and colleagues reported memory disturbance in all the patients affected by cortical and deep infarction and presenting with cognitive deficits. Others (Milandre *et al.*,

1994; Brandt *et al.*, 2000) have reported an overall prevalence of memory deficits of about 30%; deficit, which is material specific depending on the side of the infarct (Cals *et al.*, 2002). Other cognitive deficits also depend on the laterality of the lesion. In the language-dominant hemisphere (generally left), an alexic syndrome with or without dysgraphia is common, often accompanied by color dysnomia and visual agnosia (De Renzi *et al.*, 1987). Expressive dysphasic syndromes also may be observed. Infarction in the right PCA territory may result in prosopagnosia, constructional deficits and spatial disorientation (Milandre *et al.*, 1994). Risk factors associated with PCA territory stroke are those generally associated with cardiovascular and cerebrovascular disorders such as hypertension, diabetes, and cardiac disease (Kumral *et al.*, 2004).

The medial temporal lobe region plays a crucial role in declarative memory functioning in humans and monkeys (Corkin, 1984; Squire *et al.*, 2004). Lesions to the hippocampus, perirhinal and parahippocampal cortices lead to severe memory deficits due to disconnection with association cortices (Suzuki and Amaral, 1994; de Curtis and Paré, 2004; Suzuki and Amaral, 2004). In particular, Zola-Morgan and colleagues (1994) demonstrated that lesions limited to the perirhinal and parahippocampal cortices, and sparing the amygdala, hippocampus, and entorhinal cortex, produced a multimodal deficit similar to that observed after large medial temporal lobe lesions. Similar deficits occur with damage to certain thalamic territories, such as the dorsomedial nucleus, intralaminar tract and internal medullary lamina (Squire *et al.*, 1989) as observed following thalamic strokes (Winocur *et al.*, 1984). These thalamic regions are part of a circuit connecting medial temporal lobe regions with anterior association cortices.

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In summary, the topography of the PCA territory supplies oxygen to two-thirds of the hippocampus as well as other structures central to memory function; it is therefore not surprising that deficits in memory function will often follow an infarct in the PCA territory.

As detailed previously, retrospective and prospective studies of cases presenting with PCA territory infarct report variable neurological and cognitive signs (De Renzi *et al.*, 1987; Cals *et al.*, 2002; Kumral *et al.*, 2004). In these studies, the location and extent of the infarcts are generally reported in broad terms only (e.g., “superficial”, “pure cortical”, “deep”). Therefore the correlations between the lesion site and extent and clinical signs are difficult to interpret. We present longitudinal cognitive, and functional data collected over a 10-year period, as well as imaging and postmortem data on BVR, a right-handed gentleman who sustained a large right PCA territory infarct involving the occipitotemporal region and the right thalamus at the age of 77 years. This case shows remarkable preservation of cognition and functional independence following the insult.

## Methods

BVR was a participant in the Sydney Older Persons Study (SOPS). This study is a longitudinal study on ageing following a random sample of urban community dwellers from the inner west of Sydney, Australia, aged over 75 years at the time of enrollment. Background to SOPS has been presented elsewhere (Waite *et al.*, 1998). Briefly, participants were interviewed in their homes on four occasions, 3 years apart on average. Interview protocols involved a detailed past and current medical history including medication use, a medical and neurological examination, a cognitive assessment, and questionnaires of health lifestyle, social network, functional independence, and psychological wellbeing. This was complemented by an independent interview with an informant. At the time of the 6- and 10-year reviews, a subgroup of participants was invited to undergo a magnetic resonance imaging of the brain for volumetric investigations and characterization of white matter lesions. These participants took part in further cognitive testing administered at the local teaching hospital. Volumetrics and white matter lesions findings in this group have been reported elsewhere (Lye *et al.*, 2004; Piguet *et al.*, 2005). Informed consent was obtained at the time of each visit and for the postmortem examination of the brain. Each study phase was approved by the local Ethics committee.

### Cognitive Examination

The Mini-Mental State Examination (MMSE) (Folstein *et al.*, 1975) was administered as a screening test. In addition, the cognitive examination comprised measures of: (1) memory: Reid Memory Test (Reid *et al.*, 1996), Wechsler Memory Scale – Revised, Logical Memory and Visual Reproduction subtests (Wechsler, 1987), the Recognition Memory Test for

faces (Warrington, 1984) (session 3 only); (2) language: Boston Naming Test (Kaplan *et al.*, 1983), semantic fluency (animal category) (Spreen and Strauss, 1991); (3) visuosperceptive and spatial skills: copy of simple designs (cube, coil, infinity loop, interlocking infinity loops), drawing of a clock to command (Reid *et al.*, 1996; Waite *et al.*, 1998), Judgment of Line Orientation Test (Benton *et al.*, 1983), Visual Object and Space Perception battery (Warrington and James, 1991) (session 4 only); (4) executive functions and working memory: Oral trail making test-part B (Oral Trails) (Kaye *et al.*, 1990), Phonemic fluency (FAS) (Benton and Hamsher, 1983), Wechsler Adult Intelligence Scale-Revised (WAIS-R) Similarities subtest (Wechsler, 1981), WAIS-R-Digit span subtest (Wechsler, 1981) (sessions 3 and 4).

### Neuropathological Methods

The brain was removed at autopsy (postmortem delay 2.5 hours), weighed and the entire brain was fixed by suspension in 15% buffered formalin for two weeks. The brain was then reweighed, the antero-posterior dimensions recorded and the brainstem and cerebellum separated from the cerebrum at the level of the superior colliculus. The cerebrum was embedded in agar and cut into 3mm thick coronal slices using a rotary slicer. The brainstem was embedded in agar and similarly cut into 3mm thick slices in the transverse plane, as previously described (Kril *et al.*, 1997). Each slice was photographed for future detailed assessments. Tissue samples were prepared for routine neuropathological examination. Briefly, samples were taken from the frontal (Brodmann area 9), temporal (area 20), parietal (area 39), occipital (areas 17 & 18) and anterior cingulate (area 24) cortices, as well as from the hippocampus at the level of the lateral geniculate nucleus, amygdala, anterior and posterior basal ganglia (including the basal forebrain), thalamus, hypothalamus, midbrain, pons, medulla oblongata, cerebellum and from areas of infarction. These were embedded in paraffin and sectioned at 10 micrometers. Sections from all regions were stained for routine screening using currently recommended diagnostic protocols for common dementia syndromes (Halliday *et al.*, 2002). Standard stains used included haematoxylin and eosin, Congo red and the modified Bielschowsky silver stain; while immunohistochemistry was performed using antibodies against ubiquitin (Z0458, Dako, Glostrup, Denmark, diluted 1:200), tau (T5530, Sigma, St Louis, MO, USA, diluted 1:10,000), and  $\alpha$ -synuclein (18–0215, Zymed Laboratories Inc., San Francisco, CA, USA, diluted 1:200).

## Results

### Case Background and Personal History

BVR was born in 1913 and was the last of three children. His developmental milestones and early medical history were unremarkable apart from an operation for a right clubfoot at

the age of 3 years. He completed 16 years of education and obtained a university degree. During the Second World War, he was posted in New Guinea and the Middle East. After the war, BVR worked for a scientific publication before becoming its editor until he retired from full-time employment at the age of 64 years. During this time, he was also a board member of several international scientific groups and traveled overseas on numerous occasions. He continued writing scientific papers until the age of 77 years and was working on his autobiography until he was 85 years old. BVR never married and had no children. He always had an active social network, was meeting friends and attended his local church regularly. BVR died at the age of 90 years 11 months following a short illness (bronchopneumonia) and a recent stroke (7 weeks).

**Longitudinal Medical Investigations**

At the initial investigation, BVR was 79 years old. He was right-handed, a non-smoker and a non-drinker. He was not involved in any physical activity or gardening and had never been involved in sports but went for walks several times a week. At the age of 77, he underwent an emergency double coronary artery bypass grafting after being admitted to hospital with severe angina. He apparently had two heart attacks during that time. During the same year, he sustained an “occipital CVA”; however, it remains uncertain whether this

incident was directly related to the bypass surgery. The CVA left him with a left homonymous hemianopia. The same year, he also underwent a laparotomy for diverticulitis. Medical history also revealed a left eye retinal artery thrombosis and glaucoma. BVR had a cataract operation on his right eye and an intraocular lens inserted when he was in his early 70s. There is a possible family history of heart disease on his father’s side. A summary of BVR’s neurological status at each assessment is presented in Table 1. Between the age of 79 and 85 years, BVR experienced at least three transient ischaemic attacks (TIA) accompanied by unsteadiness and vertigo. At the initial assessment, the visual deficit and a gait abnormality were the only abnormal neurological signs. Over the next 6 years (i.e., until the third review), positive neurological signs became progressively more prevalent.

When reviewed for the fourth time, BVR was 88 years old. Over the previous three years, he had sustained again two TIAs and two, possibly three, strokes. The first stroke affected his speech and vision, and his ability to walk. A second, a few months later, resulted in an increased left-sided weakness. On examination, BVR exhibited primitive reflexes such as snout, grasp and glabella tap (Table 1). He also showed increased tearfulness and emotional lability, signs consistent with pseudobulbar palsy. At that point, BVR was unable to walk unassisted and was showing reduced upper limb coordination. His vision had also declined significantly. He was legally blind because of progressing macular

**Table 1.** BVR’s longitudinal neurological status on four assessments over 10 years

|                                     | Age at time of assessment  |                            |                            |  |
|-------------------------------------|----------------------------|----------------------------|----------------------------|--|
|                                     | 79 years                   | 82 years                   | 85 years                   | 88 years   |
| Overall impression                  | –                          | –                          | –                          | Abnormal   |
| Primitive reflex release            | –                          | –                          | –                          | + glabella tap<br>+ snout<br>++ grasp bilaterally<br>+ (reduced in ankles) |
| Tendon reflexes                     | –                          | –                          | –                          |  |
| Cerebellar incoordination           | –                          | +                          | + (LL and gait)            |  |
| Speech deficits                     | –                          | –                          | + (dysarthria)             | ++ (dysarthria)  |
| Impaired ocular movements           | –                          | –                          | + (vertical gaze upward)   | + (vertical gaze upward)   |
| Gait deficit                        | +                          | + (ataxic, cerebellar)     | + (bilaterally)            | +++ Unable to walk unassisted  |
| Absent pedal pulse                  | –                          | –                          | –                          | Yes bilateral  |
| Fine finger movements deficits      | –                          | –                          | ++                         | ++   |
| Impaired hand movement coordination | –                          | –                          | ++                         | ++   |
| Impaired hand movement speed        | –                          | –                          | ++                         | ++   |
| Tremor                              | –                          | –                          | –                          | –  |
| Increased tone                      | –                          | –                          | +                          | + (all limbs)  |
| Postural instability                | –                          | +                          | +                          | +++  |
| Sensory loss (vibration sense)      | –                          | –                          | –                          | –  |
| Other signs                         |                            |                            |                            | + Left 7th nerve palsy (facial asymmetry)<br>Left homonymous hemianopia    |
|                                     | Left homonymous hemianopia | Left homonymous hemianopia | Left homonymous hemianopia |  |

Note. + mild impairment ++moderate impairment +++ severe impairment – absent (i.e., normal function).

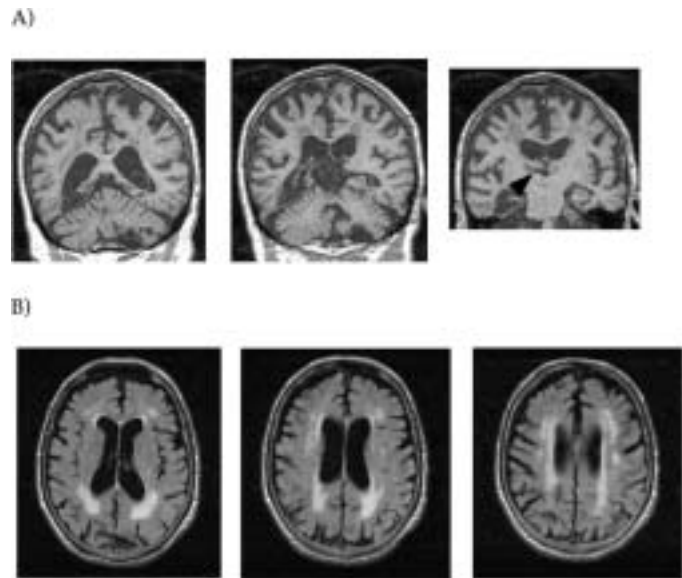
degeneration. Some hallucinations were reported by nursing staff at night (people walking around the room) and vivid, unpleasant dreams.

### MRI Findings

The first structural MRI of the brain conducted at the age of 85 years revealed diffuse cerebral and cerebellar atrophy. Large areas of infarction in the distribution of the right posterior cerebral artery territory (Figure 1A), with involvement of the right parahippocampal gyrus and calcarine cortex in the right occipital lobe; in the posterior inferior left cerebellar hemisphere in keeping with the distribution of the left posterior inferior cerebellar artery territory; and small foci in the right pons were observed. Widespread deep white matter and periventricular hyperintensities in left and right cerebral hemispheres were present. These were more pronounced in the occipital than in the frontal region. In addition, one small hyperintense lesion in the right globus pallidus (Figure 1B) and three lesions (approx. 5 mm) in the thalamus bilaterally were noted. The second brain MRI conducted when BVR was 88 years old revealed additional large amounts of confluent periventricular signal hyperintensity in the corona radiata and centrum semi ovale bilaterally in keeping with a large amount of white matter ischaemia, likely reflecting the more recent strokes reported clinically. Scattered foci of ischaemic change in the cerebellar hemispheres were also noted. Thinning of the corpus callosum through its entire length was noted.

### Cognitive Examination

Test results for the four test sessions are presented in Table 2. Based on the National Adult Reading Task (Nelson, 1982), BVR's premorbid intellectual functioning was estimated to be in the high average range. No clear cognitive deficits were observed on testing at the time of the first three sessions. Cognitive functions modulated by the right hemisphere appeared well preserved. BVR's visuospatial memory was in keeping with his age group. Performance was not affected by the type of encoding required (incidental or intentional) or by the type of stimuli (diagrams or faces). In addition, BVR showed no evidence of rapid forgetting over time, as shown by a retention after delay of nearly two-thirds of the WMS-R Visual Reproduction stimuli initially presented (57% and 62%). Tests measuring visuosperceptive and constructional abilities, functions mediated by right posterior cortical areas, were also well executed. Verbal and working (immediate) memory appeared intact on testing, as were executive functions. The only change across sessions was on semantic fluency on which BVR showed an increasingly impoverished performance (Table 2). This task measures semantic knowledge within a specific category (e.g., animals, fruit and vegetables). In addition to language skills, effective performance on semantic fluency requires search strategies



**Fig. 1.** A) MRI T1-weighted images (TR: 12 ms, TE: 3.5 ms, FOV: 22 cm, matrix:  $256 \times 256$ , 1.5 mm-thick contiguous coronal slices) taken at session 3 (i.e., 8 years poststroke). Note the extent of the infarct in the temporo-occipital region with confluence with the lateral ventricle. Note also the right thalamic infarct (arrowhead) and the thinning of the corpus callosum. B) MRI FLAIR images (TR: 9000 ms, TE: 115 ms, FOV: 22 cm, matrix  $256 \times 256$ , 5 mm-thick contiguous horizontal slices) taken at session 3. Changes in the deep white matter and periventricular regions show as bright signal on this sequence. Note the extent of the changes separate from the ventricle boundaries.

and performance monitoring. On the MMSE, BVR scored close to ceiling on the first three sessions.

At the last cognitive assessment, BVR showed significant decline in most areas of cognition compared to the previous assessments (Table 2). On the MMSE, BVR was poorly oriented in time and place. A material-specific memory deficit for visuospatial information was present. In contrast, verbal memory continued to be relatively preserved. BVR further showed deficits on all timed tasks (phonemic and semantic verbal fluency, Oral Trails), and on immediate memory span. In addition, BVR showed impaired low level and high level visual processing which probably contributed to the visual memory deficit (Figure 2).

### Behavioral and Psychological Examination

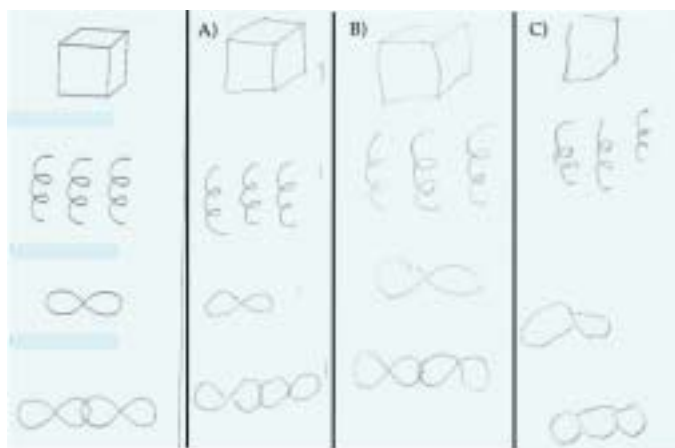
On the Life Satisfaction Index (Neugarten *et al.*, 1961), BVR rated all items very positively at the first three sessions, showing general satisfaction with his past and current life and current situation despite his visual deficits and cardiovascular/cerebrovascular problems. BVR reported no signs of depressive symptomatology on the Center for Epidemiologic Studies-Depression scale (Radloff, 1977). At the first visit, BVR's informant reported no behavioral or personality

**Table 2.** BVR’s cognitive results on four assessments over 10 years

| Cognitive task                       | Age at time of assessment |          |          |                             |
|--------------------------------------|---------------------------|----------|----------|-----------------------------|
|                                      | 79 years                  | 82 years | 85 years | 88 years                    |
| RMT total (max. 35)                  | 26                        | 29       | 29       | 12                          |
| RMT delay (max. 7)                   | 6                         | 7        | 4        | 7                           |
| WMS-R LM I (max. 50)                 |                           | 20       | 22       | 23                          |
| WMS-R LM II (max. 50)                |                           | 19       | 20       | 15                          |
| WMS-R LM % forgetting                |                           | 5        | 9        | 35                          |
| MMSE (max. 30)                       | 29                        | 30       | 27       | 25                          |
| WMS-R VR I (max. 41)                 |                           | 23       | 32       | 5                           |
| WMS-R VR II (max. 41)                |                           | 13       | 20       | 1                           |
| WMS-R VR % forgetting                |                           | 43       | 38       | 80                          |
| BNT (max. 24)                        | 7* (1 visual error)       | 17       | 21       | 13 (mostly semantic errors) |
| Phonemic Fluency (FAS)               | 54                        | 44       | 40       | 24                          |
| Semantic Fluency (Animals)           | 19                        | 16       | 14       | 6                           |
| Oral Trails (time in s; errors)      | N/A                       | 36 s; 0  | 41 s; 0  | 220 s; 3                    |
| Similarities (max. 20)               | 11*                       | 14       | 17       | 16                          |
| JLO (max. 20)                        | N/A                       | 20       | 19       | 15                          |
| Design copying                       | Normal                    | Normal   | Normal   | Fragmented                  |
| Clock                                | Normal                    | Normal   | Normal   | Distortion                  |
| Digit Span (Forward; Backward)       | N/A                       | N/A      | 8; 5     | 6; 3                        |
| Recognition test for faces (max. 50) | N/A                       | N/A      | 32       | N/A                         |
| VOSP (max. 20)                       | N/A                       | N/A      | N/A      |                             |
| Shape detection                      |                           |          |          | 15                          |
| Incomplete letters                   |                           |          |          | 1                           |
| Silhouettes                          |                           |          |          | 5                           |
| Object decision                      |                           |          |          | 5                           |

Note. N/A = Not available. BNT = Boston Naming Test; JLO = Judgment of Line Orientation; LM = Logical Memory; RMT = Reid Memory Test; VOSP = Visual Object and Space Perception; VR = Visual Reproduction; WAIS-R = Wechsler Adult Intelligence Scale – Revised; WMS-R = Wechsler Memory Scale – Revised.

\*At first assessment, maximum scores are out of 11 for the Boston Naming Test, and out of 12 for Similarities.



**Fig. 2.** BVR’s copy of simple geometric designs (left column) at session 1 (A), session 2 (B) and session 4 (C). Note the maintenance of the general shape of the designs and spatial relations despite BVR’s impaired visual perception at the last session.

change in the previous 10 years. BVR was described as being as caring and as involved in all his social and professional

activities as before. The informant also described a very positive relationship with BVR on the Intimate Bond Measure (Wilhelm and Parker, 1988). At sessions 2 and 3, BVR’s behavior and general outlook on life were unchanged and very positive; the informant reporting only a mild increase in inactivity over time. Following the strokes in 2000 and 2001, the informant reported BVR to show an increased dependency, marked physical slowness and passivity. He had become less spontaneous and less interested in social activities. No information was available from BVR on the Life Satisfaction and presence of current depressive symptomatology at that time.

**Functional Independence**

At session 1, BVR had no difficulties with all activities of daily living (ADL) or instrumental ADL (Table 3) and he was fully independent with no use of support services (e.g., meals on wheels, home help, shopping, transport, etc.). Three years later, at age 82, BVR had moved to a retirement village (two-bedroom apartment). He remained fully independent for most ADL and self-care (dressing, feeding, toileting) as well

as cooking and light housework. However, BVR took advantage of some of the services offered by the retirement village and received help with heavy housework (e.g., getting up a ladder) and grocery deliveries because of his balance. He was also getting lunches prepared and used the podiatrist/chiroprapist services. He also indicated that he had stopped working completely, although was still writing his autobiography. BVR's functional independence declined markedly at the time of the fourth assessment, paralleling the neurological deficits associated with the most recent strokes. By then, he was fully dependent for all ADL, including personal care (Table 3).

### Dementia Status

Despite his history of strokes, the extent of which was clearly visible on the first series of brain images, and the neurological signs documented at session 1, BVR did not meet any criteria for dementia until the last examination. By then, following the most recent CVAs, BVR met DSM-IV (APA, 1994) criteria for vascular dementia and NINDS-AIREN (Roman *et al.*, 1993) criteria for possible vascular dementia: with widespread cognitive deficits (memory, visuospatial, executive function), functional decline, presence of focal neurological signs of cerebrovascular disease in the absence of delirium, and evidence by brain imaging. Because of the absence of a clear temporal relation between the most recent

strokes and dementia, BVR did not meet the stricter NINDS-AIREN criteria for probable vascular dementia. The interviewer and the informant independently rated BVR's level of dementia to be of moderate severity on the Clinical Dementia Rating scale (Morris, 1993).

### Neuropathological Findings

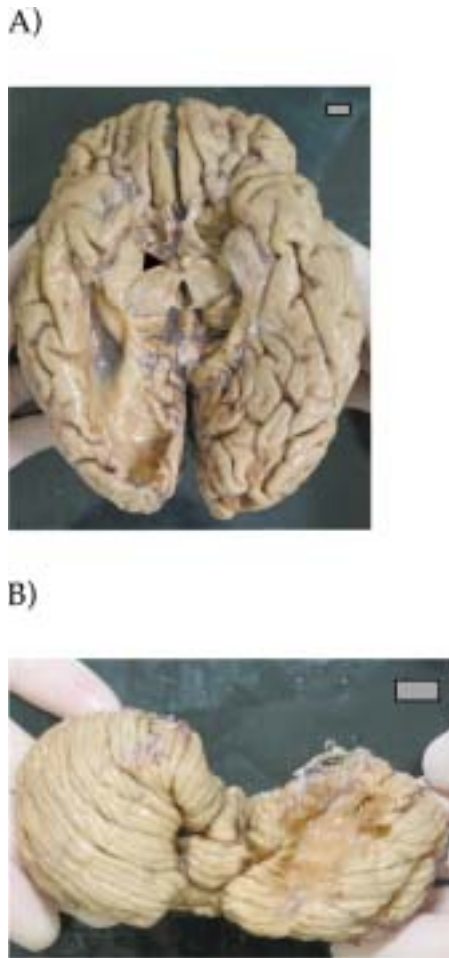
After fixation for at least 2 weeks, the brain weighed 992 g. External inspection revealed a large (8.5 × 2.5 cm) old cavitated lesion on the right inferior surface, which involved the entire grey and white matter, being contiguous with the lateral ventricle, but sparing the anterior hippocampus (Figure 3A). There was another large (2.5 × 1.0 cm) infarct in the left occipital pole. There was mild generalized atrophy over the convexities of the frontal lobe and a large (3.5 × 2.0 cm) old cavitated lesion in the left cerebellum extending to the white matter (Figure 3B). The left cerebellar flocculus was resorbed. The right mammillary body was smaller than the left and the brainstem was asymmetric. The left optic nerve was brown and atrophic but the other cranial nerves were normal. The vessels at the base of the brain show ectasia and numerous atherosclerotic plaques, some of which were calcified.

Three-mm thick coronal sections reveal the complete destruction of the grey and white matter in the right inferior

**Table 3.** BVR's functional status on four assessments over 10 years

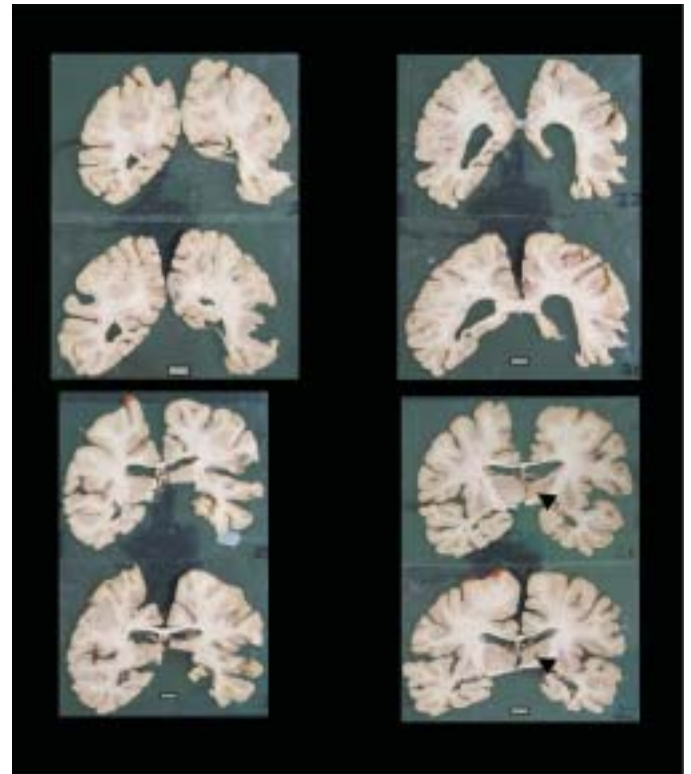
|                                   | Age at time of assessment |          |          |          |
|-----------------------------------|---------------------------|----------|----------|----------|
|                                   | 79 years                  | 82 years | 85 years | 88 years |
| <b>Instrumental ADL</b>           |                           |          |          |          |
| Private transport                 | –                         | –        | +        |          |
| Shopping/Errands                  | –                         | +        | +        | +++      |
| Meals preparation                 | –                         | –        | +        | +++      |
| Heavy housework (e.g., vacuuming) | –                         | +        | +        | +++      |
| Light housework (e.g., dishes)    | –                         | –        | +        | +++      |
| Laundry, Linen                    | –                         | –        | +        | +++      |
| Gardening/lawnmowing              | –                         | NA       | NA       | NA       |
| Home repairs                      | –                         | ++       | ++       | +++      |
| Financial management              | –                         | –        | ??       | ??       |
| <b>Self-care tasks</b>            |                           |          |          |          |
| Showering/bathing                 | –                         | –        | –        | +        |
| Dressing (incl. shoelaces)        | –                         | –        | –        | +++      |
| Eating/feeding                    | –                         | –        | –        | +        |
| Foot care                         | –                         | +        | ++       | +++      |
| Incontinence management           | –                         | –        | –        | +        |
| <b>Mobility</b>                   |                           |          |          |          |
| Using public transport            | –                         | +        | ++       | +++      |
| Going to places away from home    | –                         | –        | +        | +++      |
| Moving about the house            | –                         | –        | –        | ++       |
| Getting in or out of bed or chair | –                         | –        | –        | +        |

*Note.* ADL = activities of daily living; NA = not applicable; ?? = no information available; + mild impairment; ++ moderate impairment; +++ severe impairment; – absent (i.e., normal function).



**Fig. 3.** A) Ventral view of the BVR's brain surface showing the right PCA territory infarct. It involves the entire grey and white matter along the occipitotemporal region and merges with the lateral ventricle. Note the shrunken mammillary body (arrowhead). B) Ventral view of the cerebellum showing the left posterior inferior cerebellar artery infarct. The grey bars represent 1 cm.

temporal lobe, involving the hippocampus medially, the entorhinal, fusiform, inferior temporal cortices and inferomedial aspect of Brodmann areas 37 and 17–19 (Figure 4). Left and right occipital infarctions involved the destruction of the visual cortical grey matter and underlying white matter. The infarct in the left occipital cortex was contiguous with the lateral ventricle. The right occipital infarct was soft, discolored and cavitated, and passed through 10 three-mm thick slices. There was a large slit infarct in the inferior aspect of the right thalamus from the anterior inferior thalamus through to the ventrolateral thalamus. It involved the mamillothalamic tract and the intralaminar nuclei (Figure 4). There were multiple small lacunes in the right superior caudate nucleus and the right and left putamen. In the cerebellum, in addition to the infarction described previously, sections revealed several small white matter infarcts adjacent to the left dentate nucleus. There was also mild atrophy of the superior cerebellar vermis.



**Fig. 4.** Three-mm thick coronal sections showing the large PCA territory infarct in the rostro-caudal axis. Note the slit infarct in the right thalamus (arrow heads) and, when present, the atrophy of the right hippocampus. Note also the thinning of the corpus callosum throughout. The grey bars represent 1 cm.

Microscopic examination revealed rare neuritic plaques (<1 per 100 × magnification field) but a moderate density of diffuse plaques (up to 20/100 × magnification field). Neurofibrillary tangles were present in the pre-alpha layer of the entorhinal cortex and the CA1 region of the hippocampus, but none were seen on silver staining of the temporal neocortex. Occasional ubiquitin-positive,  $\alpha$ -synuclein-negative neurons were seen in neocortical areas. This degree of Alzheimer-type pathology was consistent with the age of the subject and insufficient to reach any criteria for Alzheimer's disease. The substantia nigra was well pigmented and symmetrical.

## Discussion

BVR was a 79-year old gentleman when he enrolled in a longitudinal study on ageing of community dwellers. At that time, his medical history revealed that he had sustained two significant CVAs 2 years before entering the study. Over the next 10 years, he received four medical and cognitive examinations and two brain MRIs. Despite these brain insults, BVR showed remarkably preserved cognitive functioning and functional

independence. On initial examination, the only clinical signs were a mild impairment of gait and a left homonymous hemianopia. On cognitive testing, most aspects of cognition were maintained across the first three assessments. Semantic fluency was the only performance to decline over time. Similarly, BVR showed preserved ADL and instrumental ADL. Mild increase in apathy over time, reported by the informant, accompanied BVR's general behavior. It is only in the last 3 years of his life (i.e., 2 years prior to the last examination and the year after), and following at least two other strokes, that BVR's level of independence and cognitive functioning became compromised. Neuroimaging data and brain postmortem examination revealed a large right PCA territory infarct, which destroyed a large portion of his medial temporal and occipital regions, a portion of the thalamus, and a left posterior inferior cerebellar artery territory infarct.

Infarcts in the PCA territory are uncommon in the general population (<10% of all strokes) (Brandt *et al.*, 2000). Of those, about 30% represent a combined cortical and deep PCA infarct (Kumral, 2004). Thus, such a vascular event is rare and, apart from the visual defect, BVR showed almost none of the deficits generally associated with a lesion in the right PCA territory. We discuss some of these deficits in the context of BVR's performance and test results.

### **Memory Impairment**

Deficit in memory functioning is reported in about a third of patients overall and in up to 50% of patients with left-sided lesion. BVR did not show evidence of memory deficit until the last examination and this was probably compounded by the occipital strokes sustained more recently and the peripheral visual deficits (glaucoma and right retinal artery thrombosis). Surprisingly, however, his visuospatial memory functioning was preserved despite the additional right thalamic stroke. In other words, BVR was able to encode, retain and spontaneously recall novel visual stimuli even with lesions in parahippocampal, entorhinal and perirhinal cortices, posterior hippocampus and thalamus, structures known to be closely involved in memory function (Squire *et al.*, 2004). This would suggest that the anterior portion of the hippocampus is crucial for the processing of visual information. Compensation strategies using verbal encoding cannot be entirely ruled out but appear unlikely: First, BVR's performance was unimpaired on Visual Reproduction, a task incorporating stimuli which are not easily verbalised. Second, his very thinned corpus callosum, possibly secondary to the thalamic lesion, would suggest that inter-hemispheric transfer of information might have been impaired.

### **Visual Neglect**

Visual neglect is uncommon and has been reported in less than 5% of series. Although this was not formally tested, apart from the simple design drawing task, BVR did not

display signs of neglect at any point. In addition, neither he nor his informant signaled functional impairments (e.g., dressing difficulty, geographical disorientation, inattention to his left hemispace) that would suggest the presence of visual neglect. Interestingly, Cals *et al.* (2002) reported visual neglect in 20% of patients with right hemisphere infarction and that, among these, 80% had a lesion involving the parietal or temporal lobe in addition to the right occipital lesion as was the case with BVR.

### **Prosopagnosia and Spatial Disorientation**

Difficulty recognizing familiar faces (prosopagnosia) and spatial disorientation are seen predominantly after lesions in the right occipitotemporal region (e.g., De Renzi *et al.*, 1994; Vuilleumier, 2001) or with bilateral lesions (e.g., Mesulam, 2000). Recent functional neuroimaging studies have underlined the importance of the right fusiform gyrus in face recognition (Kanwisher *et al.*, 1997) and that of the parahippocampal region in place and geographical perception (Epstein and Kanwisher, 1998). Face recognition was not directly tested. Functionally, however, neither BVR nor his informant reported a difficulty in recognizing family members or friends. On the Recognition Memory Test for faces (Warrington, 1984), a task that requires the encoding and recognition of novel faces, BVR performed within normal limits for his age, supporting the view that his ability to use facial features to discriminate among different faces remained intact.

### **Poststroke Depression**

Data available for the first three sessions show that BVR maintained a positive outlook on life. Despite his strokes and TIAs, he always scored high on the Life Satisfaction Index (Neugarten *et al.*, 1961) and denied the presence of any depressive symptoms. The role of the location and severity of the stroke in the onset of poststroke depression remains under debate (Carson *et al.*, 2000; Narushima *et al.*, 2003). Poststroke depression has been reported in about 30% of cases (e.g., Vataja *et al.*, 2004). These studies, however, have generally investigated the presence of depressive symptomatology in the few months following the stroke. In our case, this information was not available as the initial interview was conducted 2 years after BVR's stroke. The initial informant interview investigated behavioral changes covering the 10-year period prior to the initial visit. The absence of depressive symptoms reported by the informant for that time period would suggest that it is not likely that BVR exhibited signs of depression during the time following his CVA.

### **Strengths and Limitations of the Study**

The extensive longitudinal cognitive and functional data accompanied by neuroimaging and postmortem data are

undoubtedly the strength of this study. Postmortem examination allowed us to establish precisely the site and extent of BVR's cortical and subcortical lesions and to relate these findings to the test results and psychological measures. In addition, repeated collection of data from an independent informant who had been in regular contact with BVR strengthened the validity and reliability of the functional capacity data. A possible limitation to our findings is the non-specific nature of the cognitive testing: BVR was enrolled in an epidemiological study which investigated aspects of successful ageing. Therefore, the cognitive assessment was not aimed primarily at detecting and mapping existing cognitive deficits with precision. It is possible that additional tests designed specifically to assess visuoconstructive abilities and face recognition would have detected subtle deficits in BVR. The same cannot be said for the memory tests, however. These tests are widely used in clinical practice and have good validity and reliability. This strongly suggests that BVR did not sustain a significant visuospatial memory deficit in association with his PCA infarct. Performance during the last session is more difficult to interpret, given the coexisting visual deficits.

In summary, BVR showed preserved cognition and functional independence despite a large right PCA territory infarct at the age of 77 years. This case study demonstrates the difficulty in determining the presence of underlying brain damage in the post acute phase of stroke by cognitive tests and functional assessment only, in the absence of a careful neurological examination or neuroimaging investigation. The absence of clear cognitive deficits further suggests that cognitive reserve contributes in a very important fashion towards neuroprotection following cerebral insult (see for example Whalley *et al.*, 2004). Interestingly, in this previously high functioning individual, high-level pragmatic measures of functional ability (e.g., independent ADL) may reflect the underlying brain pathology better than selective cognitive tests. Our longitudinal data also demonstrate that, even in the event of an extensive PCA stroke, such lesions do not lead necessarily to apparent long-term impairments or further degeneration.

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