Spontaneous improvement in severe, chronic schizophrenia and its neuropsychological correlates

G. K. MURRAY, V. LEESON and P. J. McKENNA

Summary Cognitive impairment is well established in schizophrenia but its relationship to the course of the illness remains incompletely understood. Here we document two patients with schizophrenia who underwent neuropsychological testing while chronically unwell, and this was repeated after improvement took place. Both patients showed significant recovery of general intellectual function, accompanied by improvements in some but not all areas of neuropsychological function: executive function remained particularly impaired.

Declaration of interest None.

For Kraepelin and Bleuler, schizophrenia was a disorder leading inexorably to a state of permanent deterioration. Bleuler's son, Manfred Bleuler, however, argued that this was an oversimplification; he found that a quarter of 208 patients followed up for 25 years showed improvement late in the course of illness (Bleuler, 1978). A contemporary example is the Nobel Prize-winning mathematician John Nash who developed schizophrenia at around the age of 30 years. After nearly 30 years of illness he began to improve at a time when he was taking no antipsychotic medication, and he now teaches and lectures again, although he continues to experience some symptoms.

It is now accepted that schizophrenia is associated with cognitive impairment, but the course of this remains controversial. Birth cohort studies (Jones & Done, 1997) and studies of armed forces recruits (David *et al*, 1997) have established that at least some of the impairment is neurodevelopmental, i.e. present as a lifelong trait that pre-dates the onset of symptoms. The fact that cognitive impairment can approach the levels seen in dementia in some patients (Owens & Johnstone, 1980) suggests that there might be an additional neurodegenerative component. However, attempts to demonstrate direct evidence of cognitive decline in schizophrenia have been unsuccessful. In these circumstances the cognitive correlates of spontaneous improvement in schizophrenia are of considerable interest.

METHOD

Here we report neuropsychological findings on two patients who had experienced several years of stable, severe illness but who have both undergone considerable clinical improvement unrelated to treatment. For details of the neuropsychological instruments used, see Lezak (1995).

RESULTS

Case 1

Case 1 is a 46-year-old man who first became ill at the age of 17 years, exhibiting first-rank symptoms (passivity and running commentary hallucinations) together with grandiose and persecutory delusions. By the age of 30 years he had become chronically hospitalised and was continuously

Table 1 Neuropsychological test performance before and after clinical improvement

	Case 1		Case 2	
	1990/95	2001/2	1995	2002
General intellectual function				
Estimated premorbid IQ (NART)	113		105	
WAIS FSIQ	68	82	66	77
MMSE	23/25	28	24	29
Visual/visuospatial function				
VOSP Incomplete letters (20)	18	20	19	19
VOSP Object decision (20)	12*	15	12*	18
VOSP Silhouettes (30)	13*	15*	19	20
VOSP Dot counting (10)	9	10	7*	9
VOSP Position discrimination (20)	17*	20	16*	19
VOSP Cube analysis (10)	–	10	4*	4*
Rey figure copy (36)	25.5*	35	–	–
Language				
Graded Naming Test (30)	14*	17	2*	4*
Modified Token Test (36)	32	32.5	–	–
Memory				
RBMT screening score (12)	1*	4*	9	7
Forward span	6	6	4*	5
Reverse span	3*	5	3*	4
RBMT prose recall (21)	0*	8	0*	0*
Executive function				
Modified WCST (categories achieved) (6)	1*	2*	6	5
Verbal fluency (animals/1 min)	12*	12*	10*	17
Verbal fluency (letter S/1 min)	19	7*	–	–
Cognitive Estimates Test (error score)	15*	10	22*	16*

Maximum scores are given in parentheses and an asterisk indicates performance below the 5th percentile cut-off. WAIS, Weschler Adult Intelligence Scale; FSIQ, full-scale IQ; MMSE, Mini-Mental State Examination; VOSP, Visual Object and Space Perception battery; RBMT, Rivermead Behavioural Memory Test; WCST, Wisconsin Card Sorting Test.

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symptomatic with incoherence of speech, fragmentary delusions and hallucinations and poor self-care. Treatment with clozapine, started 13 years ago and augmented with sulpiride 6 years ago, resulted in only minimal improvement.

Spontaneous clinical improvement was first noticed around 3 years ago. He became less isolated and began to spend more time doing activities. His self-care has improved but he still needs encouragement to bathe and change his clothes. Having previously shown severe formal thought disorder, he now speaks rationally, although poverty of content of speech is evident.

Neuropsychological testing was carried out between 1990 and 1996 and revealed marked impairment in all areas (see Table 1). With clinical improvement his MMSE score and his IQ increased. His original patchy performance on tests of visual and visuospatial function became normal on all but one test. Language, however, showed little change. He showed improvement from severely impaired levels on a number of long-term memory measures but he remained in the impaired range on most of these. He was impaired on three of four tests of executive function at initial testing and remained impaired on three of four measures on retesting.

Case 2

Case 2 is a 39-year-old woman who became increasingly withdrawn from the age of 10–12 years. There was no history of pervasive developmental disorder. She was hospitalised at the age of 22 years, having become a virtual recluse. At that time she spent almost all of her time in bed, frequently smiled inappropriately, only spoke in monosyllables, wandered aimlessly and was occasionally incontinent of urine and faeces. She also showed minor catatonic phenomena. There was some response to neuroleptics. In 1991 she was discharged to a hostel, where she has lived ever since.

In 1995–1996 she was investigated as one of a series of nine patients who showed the clinical features of simple schizophrenia (Serra-Mestres *et al*, 2000). At that time some improvement in speech and self-care was noted, although there had been no change in her medication since discharge, and this continued. Her self-care is now normal and she does shopping, cooking and cleaning. She smiles and laughs appropriately. She talks freely but shows impoverishment of thought.

When assessed in 1995 her general intellectual function was severely impaired, but by 2002 this had improved significantly (see Table 1). On initial testing she failed four of six tests of visual/visuospatial function. After improvement her performance became essentially normal. Naming was severely impaired at initial testing and remained so on retesting. General memory was in the 'poor normal' range at initial testing and remained

at this level. She was initially impaired on two out of three executive measures. Her performance normalised on one of these tests (verbal fluency), but she remained outside the normal range on another, the Cognitive Estimates Test.

DISCUSSION

These findings suggest that cognitive impairment in schizophrenia is not immutable and can improve when, as occasionally occurs, there is spontaneous clinical improvement late in the course of the illness. The patients described in this study both had severe, chronic illness and underwent gradual clinical improvement unrelated to any changes in treatment. In both cases this was associated with IQ increases from the learning-disabled range to normal levels, and MMSE scores that rose from just above the cut-off for dementia to the upper end of the normal range.

The two patients initially showed different patterns of impairment on specific neuropsychological tests. Case 1 had a profile of impairment that is typical of severe, chronic schizophrenia: deficits in all domains of function, which were particularly marked in memory and executive function (McKenna *et al*, 2002). Case 2 showed poor performance in many areas of function but had a very conspicuous deficit in naming from pictures, a pattern that has been documented previously in chronic schizophrenia (Shallice *et al*, 1991). With clinical improvement there was a tendency for performance to improve in a non-specific way; for example, both patients showed normalisation of visual/visuospatial function, and case 1 also showed better memory performance while remaining in the impaired range. However, this did not apply to all areas of function; in particular, executive function showed little evidence of improvement in either patient.

Our findings imply that the cognitive impairment associated with schizophrenia is neither simply neurodevelopmental in nature – because this is not compatible with any postmorbid change – nor simply neurodegenerative – because this would not normally allow for any improvement. This is consistent with emerging evidence that schizophrenic cognitive impairment shows a complex trajectory over the course of the patient's life (Johnstone *et al*, 2002).

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REFERENCES

Bleuler, M. (1978) *The Schizophrenic Disorders: Long-term Patient and Family Studies* (trans. S. M Clemens). New Haven, CT: Yale University Press.

David, A. S., Malmberg, A., Brandt, L., *et al* (1997) IQ and risk for schizophrenia: a population-based cohort study. *Psychological Medicine*, **27**, 1311–1323.

Johnstone, E. C., Lawrie, S. M. & Cosway, R. (2002) What does the Edinburgh High-Risk Study tell us about schizophrenia? *American Journal of Medical Genetics*, **113**, 906–912.

Jones, P. & Done, D. J. (1997) From birth to onset; a developmental perspective of schizophrenia in two national birth cohorts. In *Neurodevelopment and Adult Psychopathology* (eds M. S. Keshavan and R. M. Murray), pp. 119–136. Cambridge: Cambridge University Press.

Lezak, M. (1995) *Neuropsychological Assessment*. Oxford: Oxford University Press.

McKenna, P., Ornstein, T. & Baddeley, A. D. (2002) Schizophrenia. In *The Handbook of Memory Disorders* (ed. B. A. Wilson). New York: John Wiley.

Owens, D. G. C. & Johnstone, E. C. (1980) The disabilities of chronic schizophrenia – their nature and the factors contributing to their development. *British Journal of Psychiatry*, **136**, 384–393.

Serra-Mestres, J., Gregory, C. A., Tandon, S., *et al* (2000) Simple schizophrenia revisited: a clinical, neuropsychological, and neuroimaging analysis of nine cases. *Schizophrenia Bulletin*, **26**, 479–493.

Shallice, T., Burgess, P. W. & Frith, C. D. (1991) Can the neuropsychological case-study approach be applied to schizophrenia? *Psychological Medicine*, **21**, 661–673.

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