Simple Schizophrenia Revisited: A Clinical, Neuropsychological, and Neuroimaging Analysis of Nine Cases

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Abstract

Simple schizophrenia is widely considered to be a controversial or even discredited entity. However, cases showing typical clinical features continue to be identified in surveys of schizophrenia patients. This article reports on nine patients who met proposed diagnostic criteria for simple schizophrenia. The patients all showed the classical features of social and occupational decline, as well as negative symptoms in the absence of clear-cut positive symptoms. A range of other symptoms, which were either nonspecific or fell short of psychotic phenomena, was also seen. Neuropsychological testing revealed evidence of general intellectual impairment plus deficits in executive function and memory. Computed tomography scans were normal or showed only minor abnormalities. All patients, however, showed abnormalities on single photon emission computerized tomography (SPECT), mainly affecting frontal and temporal regions. It is concluded that cases conforming to the original descriptions of simple schizophrenia continue to be seen and are still best understood as representing a form of schizophrenia.

Keywords: Schizophrenia, subtypes, simple, neuropsychology, neuroimaging.

***Schizophrenia Bulletin*, 26(2):479–493, 2000.**

The idea that schizophrenia could present solely with deterioration was introduced by Diem at the turn of the century (Diem 1903). He described what he considered to be a form of dementia praecox, the onset of which was "simple, indolent, without special prodrome" and which progressed insidiously "without acute episodes and remissions...and without illusions and hallucinations" (p. 33). Bleuler (1911) and subsequently Kraepelin (1913) agreed, and added the category of simple schizophrenia to the existing subtypes of paranoid, hebephrenic, and catatonic schizophrenia. Common to the accounts of all three authors were personality change, narrowing of interests, falloff in functional capacity, and impoverishment of mental life; these changes could be accompanied by altered temperament with irritability or depression but active psychotic symptoms never supervened. The disorder typically began in early adulthood, although Kraepelin (1913) considered that it could sometimes be traced back even earlier, and in Diem's (1903) series of cases the age of onset ranged up to 50 years. Ultimately, as in other forms of schizophrenia, there was progression to a stable end state characterized by indifference, inactivity, and avolition. According to Diem and Kraepelin this was never profound, but Bleuler described patients who became completely apathetic and required institutional care.

From the outset, simple schizophrenia was a controversial concept, with Bleuler (1911) observing: "In spite of serious attempts of some very competent investigators, the concept...is still not generally accepted" (p. 236). Later reviewers were uniformly critical. Lewis (1936) concluded that patients who were diagnosed as having simple schizophrenia were heterogeneous to the extent that the disorder was a diagnostic wastebasket. Kant (1948) reviewed 64 chronically hospitalized patients who had been given the diagnosis and found that most showed delusions or hallucinations at examination or had these phenomena recorded in their case notes. After examining eight cases, Stone et al. (1968) found that a number eventually developed positive symptoms, while others were not developmentally normal or had a history of alcoholism, and argued that simple schizophrenia "is no longer a viable psychiatric diagnosis" (p. 305).

Despite these criticisms, several surveys of schizophrenia patients have found a small number who seem to fulfill the requirements for a simple subtype diagnosis. Levit (1977) noted that an unspecified proportion of 200 "sluggish" schizophrenia patients in the USSR resembled simple schizophrenia in course and outcome. In the

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International Pilot Study of Schizophrenia (World Health Organization 1979) the diagnosis of simple schizophrenia was made in 31 (4%) of 811 patients. Dworkin (1992) identified 18 typical cases (9%) among 202 previously published twin pairs who had schizophrenia. Most recently, in an epidemiological survey of schizophrenia in Ireland, Kendler et al. (1994) made the diagnosis of simple schizophrenia in 11 (4%) of 285 patients.

Simple schizophrenia occupies an ambiguous position in current diagnostic systems. The American Psychiatric Association has omitted the category from *DSM–III* and subsequent revisions. ICD–10, on the other hand, continues to recognize it, but the accompanying guidelines suggest that the diagnosis is difficult to make with confidence. Based on a review of all the available descriptions of simple schizophrenia, Black and Boffeli (1989) developed a set of provisional diagnostic criteria for the disorder. These criteria included core features such as insidious onset, avolition, blunted affect, and deteriorating course, but also permitted the presence of a variety of abnormal experiential and behavioral phenomena that fall short of those seen in schizophrenia proper. A series of exclusions were also incorporated into the criteria, including mood disorder, personality disorder, organic brain disease, and pervasive developmental disorder. The full set of criteria is shown in table 1.

This article describes a series of patients who conform to a strict, as opposed to the previously sometimes loose, clinical definition of simple schizophrenia, namely that meeting Black and Boffeli's (1989) criteria. Schizophrenia is now accepted as being associated with cognitive impairment (McKenna 1994; Goldberg and Gold 1995), so neuropsychological testing was also carried out to see if the patients showed a typical pattern of deficits. Structural and functional imaging were also performed, both for diagnostic purposes and to allow comparison with neuroimaging abnormalities established (or claimed) for schizophrenia as a whole.

Method

Patients with a clinical diagnosis of schizophrenia under the care of a psychiatric rehabilitation service were informally screened to see if any showed the characteristics of

Table 1. Black and Boffeli's (1989) proposed criteria for simple schizophrenia

A.	Presence of four or more of the following symptoms:
	1. Marked social isolation and withdrawal.
	2. Marked impairment in role functioning as wage earner, student, or homemaker.
	3. Markedly peculiar behavior (e.g., collecting garbage, talking to self in public, hoarding food).
	4. Marked impairment of personal hygiene or grooming.
	5. Blunted or inappropriate affect.
	6. Digressive, vague, overly elaborate, or circumstantial speech, or poverty of content of speech.
	7. Odd beliefs or magical thinking, influencing behavior and inconsistent with cultural norms (e.g., superstitiousness, belief in clairvoyance, telepathy, "sixth sense," overvalued ideas, ideas of reference).
	8. Unusual perceptual experiences (e.g., recurrent illusions, sensing the presence of a force or person not actually present).
	9. Marked lack of initiative, interest, or energy.
B.	Continuous signs of the disturbance for at least 6 months.
C.	During the course of the disturbance, functioning in areas such as work, social relations, and self-care is markedly below the highest level achieved before the onset of the disturbance (or, when the onset is in childhood or in adolescence, failure to reach the expected level of social development).
D.	Has never met criterion A for schizophrenia during the course of the disturbance.
E.	Schizoaffective disorder and mood disorder have been ruled out.
F.	Schizotypal personality disorder has been ruled out (e.g., there is clear evidence of marked deterioration in functioning from the highest achieved in areas such as work, social relations, and self-care).
G.	It cannot be established that an organic factor initiated and maintained the disturbance.
H.	There is no history of autistic disorder.

simple schizophrenia. Further cases were recruited from out of the locality through referrals from clinicians who were aware of the authors' interest. Case notes were reviewed for all suitable patients (patients were included only if a fairly complete record of their psychiatric history was available). Where possible, patients were interviewed using a structured psychiatric interview, the Present State Examination, 9th edition (PSE; Wing et al. 1974), using a "lifetime" approach to eliciting symptoms (McGuffin et al. 1986). Relatives of patients were also interviewed to corroborate the other clinical information and to permit an assessment of premorbid personality. Finally, in order to address the possible differential diagnosis of pervasive developmental disorder, a developmental history was taken using the Autism Diagnostic Interview, 3rd edition (ADI–R; Lecouter and Rutter 1989; Rutter et al. 1994).

Black and Boffeli's (1989) criteria were applied, based on all of the above sources of information. By this means, nine patients were selected for inclusion in the study.

Neuropsychological assessment was carried out on these nine patients using a battery of widely used and mostly well-standardized tests. Tests of general intellectual function consisted of the National Adult Reading Test (NART; Nelson 1982), which gives an estimate of premorbid IQ based on ability to pronounce irregular English words, plus the Weschler Adult Intelligence Scale (WAIS), to assess current IQ. Also included was the Mini-Mental State Examination (MMSE; Folstein et al. 1975), which is widely used as a screening test for dementia.

Specific neuropsychological tests covered the standard areas of visual perception, language, memory, and executive (frontal) function. The tests were selected on the basis that they are relatively undemanding and have previously been employed by the authors in a number of studies of chronic schizophrenia patients. Testing was conducted over at least three sessions. For visual and visuospatial function, four subtests of the Visual Object and Space Perception Battery (VOSP; Warrington and James 1991) were used. The Graded Naming Test (GNT; McKenna and Warrington 1983) was used to assess language. The Rivermead Behavioural Memory Test (RBMT; Wilson et al. 1985) was used as the main memory test. The RBMT was supplemented by forward and reverse digit span for short-term memory, the prose recall subtest of the RBMT for long-term memory, and the speed of comprehension subtest of the Speed and Capacity of Language Processing Test (SCOLP; Baddeley et al. 1994), also known as the "silly sentences," for semantic memory. Three tests of executive function were employed: the Cognitive Estimates Test (Shallice and Evans 1978); verbal fluency (naming animals over 1 minute); and the modified Wisconsin Card Sorting Test (WCST; Nelson 1976). Except where otherwise stated, 5th percentiles were used as the cutoff for impairment.

Neuroimaging measures consisted of computed tomography (CT) scan and single photon emission computerized tomography (SPECT); in one case magnetic resonance imaging (MRI) examination was also carried out.

Results

Demographic and Background Information. Five of the nine patients were men. The age range was 25 to 49 (mean 38.3) years. Eight patients were Caucasian, and one was of mixed Caucasian-Indian parentage. English was the native language in all cases. The age at onset as estimated from all sources of information ranged from early teenage years to early thirties. Details of sex, age, age at onset, marital status, and highest and lowest levels of social and occupational function are shown in table 2.

Four patients had a medical history, details of which are also shown in table 2. In all cases the physical illness was either irrelevant to the psychiatric presentation or postdated the onset of psychiatric symptomatology by several years.

Family history information was based on information in case notes, plus interview of relatives in seven cases. Case 4's father had a number of admissions to a psychiatric hospital beginning in his thirties for which he was given a diagnosis of paranoid schizophrenia, although his case notes would equally support a diagnosis of psychotic depression. Hypochondriacal delusions and low mood were the most notable symptoms, and he responded well to treatment with electroconvulsive therapy. He has remained well in the latter part of his life. The father of case 2 experienced periods of withdrawal, although no formal psychiatric diagnosis was made. The mother of case 3 suffered from an unspecified mental illness. Case 7's mother was admitted to a local psychiatric hospital with episodes of depression (no details could be traced), and his maternal grandfather had a psychiatric admission in late life—in which, however, the diagnosis was likely to have been vascular dementia.

Clinical Features. As required by Black and Boffeli's criterion A, all the patients showed at least four key symptoms of simple schizophrenia. These included in each case at least two classic negative schizophrenic symptoms. Following Black and Boffeli's (1989) terminology, the negative symptoms exhibited by the patients were as follows: marked social isolation and withdrawal, 7 patients; marked impairment in role functioning, 9 patients; marked impairment in personal hygiene/grooming, 5 patients; blunted/inappropriate affect, 8 patients; marked lack of initiative, interest, or energy, 5 patients. Four patients also showed obvious poverty of speech.

Table 2. Clinical and demographic data

Case	Age	Sex	Marital status	Age at onset	Medical history	Highest function	Lowest function
1.	39	M	Married	30s	None	University graduate, working with computer company	Unemployed, living in car
2.	43	M	Single	30s	None	Painter	Unemployed, doing very little with time
3.	33	F	Single	Early teens	Crohn's disease (age 33)	Domestic work	Chronically hospitalized
4.	38	F	Married	Teens	None	Housewife	Unemployed, living in hostel
5.	49	M	Single	?30s	Hypertension (age 45)	Clerical work	Chronically hospitalized
6.	41	F	Married	20s	None	Machinist	In and out of hospital, unable to live independently
7.	46	M	Single	?20s	None	Gardener	Unemployed, living in hostel
8.	25	M	Single	20s	None	University graduate	Unemployed, living with parents
9.	31	F	Single	16	Biochemical hypothyroidism (age 25)[1]	Shop assistant	Chronically hospitalized

Note.—F = female; M = male.
[1] Raised TSH with low normal thyroxine; patient has never shown any clinical features of hypothyroidism.

Accounts of further symptoms were based on personal knowledge of the patients, most of whom had been known to two of the authors (S.T. and P.J.M.) for several years, accounts from relatives, and "lifetime" PSE examination on 7 of the 9 patients (case 1 refused PSE examination and in case 3 interview was unsatisfactory because of marked poverty of speech). This information yielded phenomena suggestive of positive schizophrenia symptoms in a number of cases, which, however, were typically minor, fleeting, or not clearly psychotic in nature, and which were in all cases permissible according to section A of Black and Boffeli's criteria. Two patients (case 4 and case 6) had experienced ideas of reference, which did not seem definitely delusional in nature. Case 4 alluded to ideas of being watched at the time of her first admission, and the relatives of case 6 remembered a period at the beginning of her illness when she complained that they were talking about her. Two patients held other abnormal beliefs. Case 1, who had worked as a teacher, felt that education should be reformed; the only elaboration he gave was that he felt the current education system was unnatural and "smothered" children. Case 8 had a dysmorphophobic belief that his cheekbones and forehead looked abnormal; this was nonbizarre and was not preoccupying (in fact it was only uncovered during the course of PSE examination). Case 4 was reported by her husband to have stated that she was a nuclear physicist and that the house was being watched just before admission, although she denied this. None of the patients described abnormal perceptions. One patient (see appendix, case 9) showed persistent abnormalities of thought form. Her speech was repetitive and lacking in content and was focused on issues of hopelessness and religion, for example: "I hope I will make it someday, make it to Heaven. I just hope the devil doesn't take me in the meantime. I have been through such degradation in the last few years. I went to...and I begged them to bring me back. I don't like the fact that I am constantly in torment or everything....I don't know what the answers are. I don't know where you're from. I don't know anything. I am quite upset."

Miscellaneous symptoms included those of case 6, who experienced disabling anxiety and obsessive compulsive symptoms. Case 7 had regular periods lasting minutes or hours during which he became agitated, seemed perplexed, and showed repetitive movements; at these times (but not at any other times) his speech made little sense. Three patients (cases 5, 6, and 7) muttered or talked to themselves but consistently denied hearing voices. Three patients (cases 2, 6, and 7) exhibited minor and infrequent catatonic phenomena such as gesticulating, grimacing, or standing with hand in mouth. Another patient's illness was ushered in by quite severe head banging (case 9). "Lifetime" PSE examination plus perusal of case notes failed to yield evidence of a mood disorder sufficient to meet criteria for *DSM–IV* (American Psychiatric Association 1994) major depressive episode in any of the patients. None of the patients had had periods of overactivity or mood elevation. Similarly, none of the patients met *DSM–IV* criteria for schizotypal disorder. Although symptoms that are included in the *DSM–IV* definition, such as ideas of reference, odd speech, abnormal affect, and odd, eccentric, or peculiar behavior, were present in some of the patients, none had the requisite five or more symptoms.

Personality and Developmental History. Information on premorbid personality was available from informants in seven of the nine cases. (Case 1's parents lived abroad and he refused permission for his ex-wife to be contacted; relevant information for case 5 had not been obtained at the time of admission some years previously and his parents had since both died.) This information is summarized in table 3. Two patients (cases 2 and 3) showed some classical schizoid traits, but neither met *DSM–IV* criteria for schizoid personality disorder. Two more (cases 7 and 8) were described as shy or solitary, but without evidence of other schizoid features. One patient (case 8) showed obsessional traits, but not to the degree that he met *DSM–IV* criteria for obsessive-compulsive personality disorder.

ADI–R interviews were carried out on the relatives of the same seven patients, either with both parents (cases 2, 4, 7, and 9), one parent and a sibling (cases 3 and 6), or one parent only (case 8). The findings are also shown in table 3. The ADI–R generates diagnoses according to the ICD–10, and none of the patients met criteria for any of the four subcategories of pervasive developmental disorder in this classification. Four patients (cases 2, 3, 4, and 9) scored zero on each of the ADI–R areas of qualitative impairments in reciprocal social interaction, communication, repetitive behaviors and stereotyped patterns, and abnormality of development at or before 36 months. In the other three cases, scores were below the suggested cutoffs for abnormality. Nevertheless, as shown in table 3, minor developmental abnormalities were evident in six of the seven cases.

Neuropsychology

General intellectual function. The findings are shown in table 4. Premorbid IQ as estimated by the NART ranged from 87 to 123 (mean 103.9); these estimates were in keeping with patients' educational backgrounds (secondary school in seven cases, higher education in two). Current WAIS IQ ranged from 66 to 102 (mean 82.5). All but one of the patients showed a decline in IQ of greater than 15 points, the figure commonly taken

Table 3. Personality and developmental findings

		Autism Diagnostic Interview Scores					
Case	Premorbid personality	Qualitative impairments in reciprocal social interaction (cutoff = 10)	Communication: Verbal (cutoff = 10)	Communication: Nonverbal (cutoff = 10)	Repetitive behaviors and stereotyped patterns (cutoff = 3)	Abnormality in development ≤ 36 months (cutoff = 1)	Comments
2.	Shy, solitary, few friends	0	0	0	0	0	Shy, one friend; interested in birdwatching
3.	Timid, shy, serious	0	0	0	0	0	Didn't like change
4.	"Normal," many friends, affectionate	0	0	0	0	0	—
6.	Outgoing, happy-go-lucky, friendly	4	3	3	0	0	Lack of awareness of others' feelings; some lack of pretend play; no close friends
7.	Jovial, mischievous, but somewhat solitary	0	1	1	0	0	Some lack of pretend play
8.	Shy, reserved, but had friends; fussy, tidy, hardworking	1	1	1	0	0	Some lack of pretend play with peers
9.	Friendly, outgoing	0	0	0	0	0	Never asked questions; didn't want to be cuddled; didn't want to play much; head banging as infant

Table 4. Performance on tests of general intellectual function

Case	Test: Estimated premorbid IQ (NART)	Test: Current IQ (WAIS)	Test: MMSE score
1.	123	102[1]	29
2.	99	81[1]	20[2]
3.	105	66[1]	24
4.	98	81[1]	29
5.	119	101[1]	28
6.	87	67[1]	26
7.	93	74[1]	21[2]
8.	107	89[1]	30
9.	104	91	25

Note.—MMSE = Mini-Mental State Examination; NART = National Adult Reading Test; WAIS = Weschler Adult Intelligence Scale.
[1] Significant estimated-current IQ discrepancy.
[2] Below cutoff established for mild dementia.

as indicative of significant decline from premorbid levels. Two of these patients also scored less than 24 on the MMSE (i.e., falling into the mild dementia range).

Visual and visuospatial function. Scores on subtests of the VOSP are shown in table 5. In general, poor performance was minor and scattered: two patients failed one out of the four subtests (cases 1 and 9), and one patient failed two tests (case 3). This latter patient also showed evidence of general intellectual impairment: she had a very marked IQ decline; her current IQ was in the mentally handicapped range; and her MMSE score was at the borderline for mild dementia.

Language. Scores on the naming test, the GNT, are also shown in table 5. Normative data collected by one of authors of this test (unpublished data) give a 5th percentile cutoff of 13/14. Six patients achieved scores that were in the normal range on this basis; two showed minimal poor performance, scoring 13; and one patient (case 3, who also showed evidence of marked general intellectual impairment) achieved a very low score of 7. Naming is sensitive to IQ, and this can be taken into account when interpreting low scores. Using the guidelines suggested for the GNT, the two patients (cases 6 and 7) who were

Table 5. Performance on tests of visual/visuospatial function and language

Case	Visual/Visuospatial Function: VOSP incomplete letters (normal = 17–20)	VOSP silhouettes (normal = 15–30)	VOSP dot counting (normal = 8–10)	VOSP position discrimination (normal = 18–20)	Language: Graded Naming Test (normal = 14–30)
1.	20	13[1]	10	20	23
2.	19	25	9	20	14
3.	19	19	7[1]	16[1]	7[1,2]
4.	19	21	10	20	14
5.	20	28	10	20	24
6.	18	19	10	19	13[1]
7.	20	15	10	19	13[1]
8.	20	21	10	20	17
9.	20	20	7[1]	18	20

Note.—VOSP = Visual Object and Space Perception Battery.
[1] Impaired using 5th percentile cutoff.
[2] Impaired on basis of significantly lower score than expected on basis of estimated premorbid IQ.

minimally impaired were within the normal range for their estimated premorbid IQ; however, the patient (case 3) who achieved a very low score remained in the impaired range.

Memory. RBMT screening scores for the patients are shown in table 6. Based on a 5th percentile cutoff score of 7/8, five of the nine patients showed impaired performance; most fell into the "moderately impaired" score range of 2 to 6, but one (case 8) scored at the lower end of the "poor memory" range.

Short-term memory, as assessed by forward digit span, ranged from 4 to 8. Only one patient (case 3) fell below the generally accepted limit lower normal of 5, scoring 4; this was the patient with evidence of marked general intellectual impairment. Scores on a long-term memory test, the prose recall subtest of the RBMT, ranged from 0 to 8, out of a maximum of 23 items of information for immediate recall. Using the suggested lower normal limit of 6, eight of the patients were impaired on this test.

On the test of semantic memory, SCOLP sentence processing, two patients fell below the 5th percentile for speed of processing. In addition, three patients made three or more errors of verification; the upper limit for normal individuals is two.

Executive function. Normative data on these tests has been obtained by the authors on a sample of 84 normal adults aged 18 to 65 years with a wide range of estimated IQ (unpublished data). The findings are also shown in table 6. Using 5th percentile cutoffs, four patients were impaired on the modified WCST, four patients were impaired on verbal fluency, and three were impaired on the Cognitive Estimates Test.

Neuroimaging. CT and SPECT scanning were carried out in eight of the nine patients; case 3 refused these investigations. The results are shown in table 7. Three patients (cases 1, 2, and 4) showed a minor degree of abnormality on CT. In each case, the abnormality was sulcal widening (reported as cortical atrophy) but with no consistent pattern. Followup CT scans obtained in these three patients, over a period of 1 year (case 1) or 2 years (cases 2 and 4), did not reveal any evidence of progression.

None of the eight patients had a SPECT scan that was reported as normal. As can be seen from table 7, the reports noted patchy perfusion or hypoperfusion that was variable in distribution but which tended to involve the temporal and/or frontal lobes, usually bilaterally. Because of the high rates of apparent abnormality, the SPECT scans were independently reviewed by one of the authors (P.M.K.) who is a consultant in nuclear medicine. This review was carried out in the absence of any clinical information about the patients, and abnormalities were rated on a five-point scale from normal (1) to unequivo-

Table 6. Performance on tests of memory and executive function

	Memory	Semantic Memory		Executive Function		
Case	RBMT screening score (normal = 7–12)	SCOLP semantic processing speed (normal = 29+/31+ sentences in 2 min)	SCOLP semantic processing errors	WCST categories achieved (normal = 5–6)	Verbal fluency (normal = 14+)	CET error score (normal = 0–12)
1.	10	85	0	6	32	2
2.	4[1]	39	3[2]	2[1]	11[1]	10
3.	9	33	13[2]	6	10[1]	22[1]
4.	8	75	0	5	18	5
5.	4[1]	20[1]	0	2[1]	18	9
6.	11	39	0	5	12[1]	22[1]
7.	5[1]	30[1]	8[2]	1[1]	9[1]	16[1]
8.	7[1]	67	0	6	18	1
9.	4[1]	35	2	4[1]	22	11

Note.—CET = Cognitive Estimates Test; RBMT = Rivermead Behavioural Memory Test; SCOLP = Speed and Capacity of Language Processing Test; WCST = Wisconsin Card Sorting Test.
[1] Impaired using 5th percentile cutoff.
[2] Impaired on basis of normal 0–2 error rate.

Table 7. Structural and functional neuroimaging findings

Case	CT scan report	SPECT scan report	Areas of probable or definite abnormality on SPECT
1.	Minor degree of cortical atrophy for age, possibly affecting L hemisphere more	L fronto-temporal hypoperfusion	L temporal (probable) L parietal (probable)
2.	Bifrontal atrophic changes, more than expected for age	R frontal and L temporal hypoperfusion	R frontal (definite) L frontal (probable) L temporal (probable)
4.	Minor generalized cortical atrophy (MRI—of doubtful significance)	Bilateral fronto-temporal hypoperfusion	L frontal (definite) R frontal (probable) R temporal (probable)
5.	Normal	Generalized patchy perfusion worse in fronto-temporal regions	R frontal (probable) R temporal (probable) L temporal (probable)
6.	Normal	Bilateral frontal hypoperfusion	R frontal (definite) L frontal (definite)
7.	Normal	Hypoperfusion in inferior frontal regions bilaterally	R frontal (definite) L frontal (definite) R temporal (probable) L temporal (probable)
8.	Normal	Frontal hypoperfusion	R frontal (definite) L frontal (probable)
9.	Normal	Bilateral frontal and left parietal hypoperfusion	R frontal (definite) L frontal (definite) L parietal (probable)

Note.—CT = computed tomography; L = left; MRI = magnetic resonance imaging; R = right; SPECT = single photon emission computed tomography.

cally abnormal (5). Regions where there was probable (i.e., rating of 4) or definite (i.e., rating of 5) abnormality are also shown in table 7. These ratings further emphasize a pattern of frontal and temporal abnormality.

The two patients with both structural and functional imaging abnormalities were assessed by a neurologist. Case 1 showed minor cortical atrophy with a left-sided emphasis on CT, plus frontal and temporal lobe abnormalities on SPECT. Neuropsychological testing revealed an IQ decline of 21 points, but no specific deficits. His CT scan appearances have remained unchanged over a year. A diagnosis of fronto-temporal dementia was considered but rejected and he has been given no other neurological diagnosis. In case 4 (see also Gregory et al. 1998), a diagnosis of fronto-temporal dementia was considered on the basis of structural imaging (CT and MRI) that showed minor generalized atrophy and functional imaging that revealed bilateral fronto-temporal hypoperfusion. Although the patient showed normal performance on the WCST, Cognitive Estimates, and Verbal Fluency using animals, she performed poorly on a test of verbal fluency for words beginning with particular letters (generating only 9, 4, and 7 exemplars for F, A, and S, respectively). There was no other evidence of neuropsychological impairment apart from an IQ decline of 17 points. It remains an open question whether she has a neurological diagnosis, but she is included in the present study on the grounds that (1) her age at onset was in her teens, which would be extremely young for fronto-temporal dementia; (2) she has shown no clinical change over 2 years; and (3) there has been no change in her MRI findings over 2 years.

Discussion

If, as clinical observation suggests, the positive and negative symptoms of schizophrenia can present in endlessly varying combinations, and if there are some patients who show pictures of positive symptoms with negative symptoms remaining inapparent or very far in the background, then there seems no reason why there should not also be patients whose illnesses are characterized exclusively or

almost exclusively by negative symptoms. The nine patients described in this study had just such a presentation, undergoing a change from a previously normal or at least stable personality, deteriorating in social and occupational functioning, ultimately developing a typical schizophrenic negative symptom defect state, but never exhibiting florid psychotic symptoms.

These nine patients had a presentation dominated by the negative symptoms of schizophrenia, but their clinical picture was not wholly restricted to these symptoms. Some of their additional symptoms, such as anxiety, obsessional symptoms, or disturbed behavior, were nonspecific. Others, such as minor catatonic phenomena or talking to oneself, are commonly associated with schizophrenia without being diagnostic of it. For example, catatonic symptoms are known to occur in affective disorder, organic states, mental handicap, and autism (Wing and Attwood 1987; Rogers 1992), and the phenomenon of talking to oneself has also been described in autism (Rumsey et al. 1985). Abnormal beliefs were present in a few of the patients, but these were either occasional and/or fleeting, or not convincingly psychotic in nature. Thus, the dysmorphophobic belief in one patient was uncovered only during a structured mental state examination and seemed to lack a delusional quality (Andreasen and Bardach 1977). The speech of two patients was difficult to follow. In one this was also a fleeting phenomenon seen only in periods of disturbed behavior, and in the other it would probably be regarded by most clinicians as showing only poverty of content of speech.

The clinical features shown by the patients in this study may be consistent with simple schizophrenia, but it is obviously necessary to exclude alternative diagnoses before concluding that this is what they suffer from. One realistic differential diagnosis is pervasive developmental disorder. Patients with autism sometimes undergo a catastrophic decline in function in adolescence or early adult life (Gillberg and Coleman 1992). Various psychiatric syndromes, both neurotic and psychotic, are also associated with Asperger's syndrome, where they may take unusual forms and be difficult to diagnose (Tantam 1991). It could therefore be argued that some or all of the patients in this study were suffering from one or other of these disorders, which went undiagnosed during childhood. Such a possibility is, however, contradicted by the failure of detailed developmental questioning to reveal any major abnormalities in the realms of reciprocal social interaction, communication, or repetitive and stereotyped behaviors. Minor and scattered developmental abnormalities were certainly picked up in the patients in the course of the ADI–R interviews, but these of course are also features of children with preschizophrenia (Done et al. 1994; Jones et al. 1994*a*).

Schizotypal personality disorder also requires consideration as a differential diagnosis. Some of the patients had experienced ideas of reference and others held odd beliefs. However, these symptoms were invariably minor features of the presentation and were not associated with any evidence of the superstitiousness, magical thinking, paranormal beliefs, or sensation of presence that are prominent features of schizotypal personality disorder. There was more evidence of the objective mental state abnormalities associated with schizotypal personality, including odd speech; abnormal affect; and odd, eccentric, or peculiar behavior. These features, however, are equally characteristic of schizophrenia and so cannot be used to support one diagnosis over the other. Other arguments against a diagnosis of schizotypal personality disorder are first the fact that none of the patients met *DSM–IV* criteria for the disorder, and second the clear evidence of change from a previous level of functioning in the patients. In fact, prior to this most had shown evidence of only minor personality deviations.

A third possibility is that that some of the patients in the study were suffering from undiagnosed organic brain disease. This would fit with the finding of functional imaging abnormalities in all of the patients examined and the CT scan abnormalities in a minority. Against this possibility, however, is the lack of any suitable candidate neurological disorder. In particular, fronto-temporal dementia (Gregory and Hodges 1993; Brun et al. 1994) seems unlikely given the patients' long histories and lack of progressive deterioration. Furthermore, some of the patients have shown long-term trends to improvement with treatment and rehabilitation. For example, case 5 was regularly incontinent of urine when first admitted to hospital, but over the years this has largely stopped, although his self-care remains otherwise poor. Case 1, one of the two patients who were investigated by a neurologist, showed no response to conventional neuroleptics, but went on to improve steadily on treatment with clozapine to the point that he was able to leave hospital. Similar improvement on clozapine was also seen in case 9 (see appendix). Organic neurological disease, in the shape of dementia of frontal type, appears to be a credible alternative diagnosis in only one patient (case 4). This case is discussed in detail by Gregory et al. (1998); however, as noted above, several features of her case argue against such a diagnosis, including the fact that her structural imaging abnormalities showed no progression over 2 years.

It is now widely accepted that schizophrenia is associated with impaired cognitive function that takes the form of general intellectual impairment plus disproportionate deficits in executive function and memory (McKenna 1994; Goldberg and Gold 1995). This provides an important means of corroborating the diagnosis of simple schizophrenia. A large majority (eight) of the patients in this study showed

evidence of impaired general intellectual function, which ranged from mild (i.e., IQ decline) to severe (i.e., MMSE scores below the cutoff for dementia). In addition, whereas only minor and scattered impairments were found on tests of visual and visuospatial function, deficits in executive function and memory were prevalent and at times marked. Impairment on tests of linguistic function is also found in schizophrenia (Thomas and Fraser 1994), but it is not clear if such deficits are marked or present over and above the general tendency to poor performance. This impairment is also consistent with the findings in the present study: three of the nine patients had low scores on a naming test, but those were only definitely abnormal in the one patient who also showed marked general intellectual impairment.

These neuropsychological findings also help counter the possibility that some or all of the patients in this study could be suffering from schizotypal personality disorder. Schizotypal personality disorder has been found to be accompanied by poor neuropsychological test performance that affects memory and executive function particularly (Voglmaier et al. 1997), but the deficits are modest and comparable to the subtle deficits found in the first degree relatives of schizophrenia patients rather than those seen in schizophrenia itself (Keefe et al. 1993).

A closer examination of the pattern of memory impairment displayed by the patients in this study reinforces the relationship with schizophrenia further still. In a sample of 60 mixed acute and chronic schizophrenia patients, Tamlyn et al. (1992) found a pattern of preservation of short-term memory coupled with impaired long-term memory—only 14 percent scored less than 5 on forward digit span compared with 80 percent who were impaired on prose recall. These levels of impairment are similar to the ones found in this study, where, using the same tests, only one of the nine patients was impaired on digit span but eight were impaired on prose recall. An even more striking similarity concerns the poor performance found on the test of semantic memory, with a third of the patients making multiple errors on a simple sentence verification task. Semantic memory has repeatedly been found to be impaired in schizophrenia (Tamlyn et al. 1992; Duffy and O'Carroll 1994; McKay et al. 1996), but remains intact in depressed patients (Ilsley et al. 1995) and is spared in neurological patients with amnesia, at least for information acquired prior to onset (Squire 1987; Baddeley 1990).

Structural imaging of the brain revealed only minor abnormality in the patients. None were reported as showing lateral ventricular enlargement, the most robust CT scan finding in schizophrenia. This result is unsurprising as the degree of enlargement in schizophrenia is small (Andreasen et al. 1990; Jones et al. 1994*b*) and clinically detectable in only about 10 percent of cases (Weinberger et al. 1979). Perhaps more surprising is the sulcal widening reported in three patients. Although documented in several series of schizophrenia patients, this is a considerably less well replicated finding than lateral ventricular enlargement (Lewis 1990). It may be relevant that in all three patients the radiologists' reports were qualified by statements such as "minor," "more than expected for age," or "of doubtful significance." Functional imaging, in contrast, was abnormal in all the patients examined, with a pattern of predominant frontal and/or temporal perfusion deficits. This was an unexpected finding, particularly as doubt has recently been cast on hypofrontality as a general phenomenon in schizophrenia (see Chua and McKenna 1995; Gur and Gur 1995). The frontal perfusion deficits could be considered to be in keeping with the more consistently found association of hypofrontality with aspects of the clinical picture of schizophrenia such as chronicity, negative symptoms, and cognitive impairment (Liddle et al. 1992; Wolkin et al. 1992; see also Chua and McKenna 1995). However, there was also a high rate of temporal lobe perfusion deficits in the present study, a finding that does not fit well with the functional imaging literature on schizophrenia.

Within the limitations inherent in a case series—for example, that numbers are small and ascertainment may be biased (in this study to more severely ill hospitalized and treated patients)—it can be concluded that there are present-day patients who conform quite closely to the classic accounts of simple schizophrenia and who resist diagnosis as anything else. Such patients insidiously develop typical negative schizophrenic symptoms and progress to a state of unexceptional schizophrenic deterioration. Close scrutiny also reveals the presence of other symptoms in most cases, such as ideas of reference, other abnormal beliefs, talking to oneself, catatonic phenomena, and poverty of content of speech. However, these symptoms make only a minor contribution to the overall clinical picture and are not by themselves sufficient to make a diagnosis of schizophrenia. What the presence of such symptoms does emphasize is the continuity of simple schizophrenia with the other subtypes of the disorder, which are themselves on a continuum with each other and not always stable over time (Carpenter and Stephens 1979). In fact, the present study originally reported on a series of ten cases, but one patient had to be withdrawn at a late stage when, after 25 years, he developed clear-cut delusions of reference and auditory hallucinations that persisted for several months. The onset of these symptoms supports the view expressed by Kraepelin (1913) that "a dementia simplex which lasts for many years, even for decades, forms often enough the introduction to one of the [other] forms of dementia praecox" (p. 93). Although the other findings of this study have to be treated with caution because of the small numbers and/or lack of control data, they suggest that patients with simple schizophrenia show a typical "schizophrenic" pattern of neuropsychological deficits and there are hints of a high rate of functional imaging abnormality.

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Acknowledgments

The authors wish to thank Dr. G.E. Berrios for locating relevant articles. They are also grateful to Dr. D. Bermingham and Dr. R. Goddard for referring patients. The authors are also indebted to Dr. P. Wraight for facilitating SPECT scanning.

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Appendix. Representative cases

Case 6—Typical Illness. This 41-year-old divorced woman was first admitted to hospital at the age of 36. She complained of low mood but was found to be "cheerful" during her brief stay. Two years later she was re-admitted via a general medical ward, where she presented with severe leg ulcers thought to have been caused by neglect. At this time her relatives provided an account of a personality change that dated back to her twenties, plus at least 10 years of self-neglect. Some time after the birth of her second child she began exhibiting bizarre behavior such as standing aimlessly in the kitchen, serving the family only plates of gravy, and making growling noises. She also became increasingly sexually disinhibited and took to disappearing for several days at a time. For several years she had not washed her hair or changed her clothes with any regularity.

The patient's birth and early development were unremarkable. As a child she was described as outgoing and cheerful. She worked in a factory before marrying at the age of 18 and having two children. In the early years of her marriage she was described as being an excellent mother who worked hard, for instance single-handedly renovating her and her husband's house.

On admission the patient was dirty and disheveled but denied any problems. She required a great deal of encouragement to look after her grooming and hygiene, and at times her behavior was grossly disinhibited (e.g., masturbating openly). On occasion she grimaced and put her hand in her mouth in a stereotyped way. Her subjective mood varied between feeling "fine" and vague complaints of depression and anxiety. Objectively, she showed obvious flattening of affect and her manner was facile. She showed a minor degree of poverty of speech, typically giving only brief replies to questions, and more obvious impoverishment of thought. She complained of having to check many things, which seemed to have a genuinely obsessional quality. However, she would also repeat phrases over and over again and walk in and out of shops after purchasing an item without being able to give any explanation of why she did so. Although she was distracted and self-absorbed at times, there was no evidence of delusions or hallucinations. Questioning of the patient's relatives also failed to reveal any evidence of psychotic symptoms over the previous 20 years, apart from a brief period when she complained that they were talking about her. They also remembered sometimes hearing her talking to herself in her bedroom.

Treatment with neuroleptics has brought about some general improvement, but she remains handicapped by anxiousness and obsessional and ritualistic behavior. At present, she remains an inpatient on a rehabilitation ward.

Case 5—Severe Illness. This 49-year-old single man was first admitted to hospital at the age of 40 after he became angry and abusive following a minor surgical procedure. At this time he had not washed, cut his hair, or changed his clothes for several years, and he was spending all day and night sitting in a chair. The only activity he engaged in was watching TV. His parents took meals, which he ate erratically, to his room.

The patient's early life and childhood were, according to his parents, unremarkable. He left school at age 16 with average academic qualifications and went on to work for some years as a clerk in the local hospital. He lived with his parents until the time of admission. Information about his personal life was not recorded in much detail at admission and his parents had since both died; however, he was reported to have had few friends and to never have had any sexual relationships.

At the time of his admission he was filthy with long hair, an unkempt beard, and uncut fingernails. His movements were slow. At times he was doubly incontinent. He showed poverty of speech, answering most questions monosyllabically; on occasion, however, he would speak at length, for example about minor medical problems. His affect was flat and blunted, and was one of unvarying bland unconcern. There was no evidence of formal thought disorder and he denied delusions and hallucinations (and has ever since). He sometimes shouted without apparent reason and could be observed talking to himself (e.g., in the bathroom).

The patient was treated with neuroleptics and showed gradual improvement, becoming less slow and having fewer aggressive outbursts. After transfer to a rehabilitation service, his self-care also improved and his incontinence became only occasional. After 2 years he was resettled in a 24-hour staffed hostel, where he has lived ever since. He remains vacuous in manner and requires considerable supervision to maintain minimal standards of personal hygiene.

Case 3—Illness Developing Against a Background of Preexisting Abnormalities. This 22-year-old single woman was referred to the psychiatry service with a 3-year history of "turning into a recluse." Over the previous year she had not been going out at all and replying only yes and no in response to questions. Immediately prior to admission she had taken to her room and was spending all

day in bed; she had to be coaxed to eat and drink and was defecating on the floor.

The patient was described as a quiet, serious, and timid child, who, however, was responsible and "quite popular." She had a tragic and disturbed childhood. Her mother had a breakdown (no further details were available) and shortly afterward developed leukemia, dying when the patient was 9 years old. Her father then neglected her and her two siblings, made them take on most of the house chores, probably left them alone in the evenings, and spent long periods away from home. As a consequence, much of her later childhood was spent in various forms of residential care.

Psychological assessment at age 10 suggested language deprivation and withdrawal resulting from emotional difficulties. According to her sister, the patient underwent a definite change between the ages of 10 and 12 during a period when the two of them were living abroad in a convent. Psychiatric assessment was carried out at the age of 12 but no diagnosis was made. During a period in care in her teens she was reported as looking sad and not mixing with the other children at first, but later joining in group games and talking readily enough if approached. Stereotyped behavior and qualitative impairments in communication and reciprocal interaction were never noted.

By the age of 15 the patient was noted to be stealing and showing other evidence of disturbed behavior. She also showed a refusal to talk "to the point of rudeness at times." After leaving school at 16 her only employment was working as a housekeeper in an old people's home, which she did for only a few months.

At examination, she smiled inappropriately and replied to some but not all questions, and then only in monosyllables. She frequently wandered aimlessly and was occasionally incontinent of urine and feces. At one point she was noted to be walking in circles, but no other catatonic phenomena were described. At no time has there been any evidence of hallucinations or delusions.

After treatment with neuroleptics the patient showed modest overall improvement. She spent 6 years in hospital and was then discharged to a 24-hour staffed hostel. She remains very socially isolated, but now talks a little, although only to people she knows. Her self-care has improved and she recently developed an interest in her appearance. She cooks and takes part in house chores and attends various day activities. Her speech remains largely monosyllabic and her affect is grossly abnormal with frequent causeless smiles. She is no longer incontinent.

Case 9—Illness Associated With Considerable Diagnostic Difficulty. At the age of 16 this 31-year-old single woman started having outbursts of irritability and childishness and also took to head banging, which she had previously done as a young child. She then began to drink heavily and became promiscuous. Later, she converted to Christianity. She had her first psychiatric admission at the age of 20 and went on to have numerous subsequent hospitalizations, in between living in hostels or sometimes at home with her parents. Lately she has spent months at a time on locked wards because of numerous instances of quite serious aggressive behavior triggered by trivial provocation. She has also made a number of suicide attempts, become pregnant from casual sexual encounters, and engaged in behavior such as walking naked in public.

According to her parents, the patient was a normal, outgoing girl until the age of 16, and questioning revealed no evidence of developmental abnormality or abnormal personality traits.

The patient's mental state has appeared much the same over the entire course of her illness. Typically, when approached she begins reciting a range of religious and other preoccupations in a monotonous voice, becoming increasingly agitated and eventually walking away shouting. Despite her subjective distress, her affect is typically flat and unconcerned. Her talk has repeatedly struck clinicians as abnormal, but not in a way suggestive of schizophrenic formal thought disorder (see Results section). She is always overwhelmingly concerned with complaints she can describe only vaguely, such as "pressures" and "inability to cope." She has never been considered to be deluded and has always denied hallucinations, but has held the belief that she is possessed by the devil. She has also had unusual fears, such as of being stabbed in her sleep. At one point she stated that she felt a previously aborted fetus was controlling her; on questioning this appeared to reflect only a belief that this baby's soul was in Heaven and looking out for her interests.

With regard to her diagnosis, a typical pattern has been followed: When admitted under a new psychiatrist a diagnosis of schizophrenia has usually been given, only to be changed to personality disorder after a few weeks. However, in view of the clear history of change at the age of 16, together with the finding of bilateral frontal and left parietal hypoperfusion on SPECT scan, the diagnosis of simple schizophrenia was ultimately made by the authors. Treatment with neuroleptics, sometimes in high doses, has had no discernible effect, but clozapine has had favorable results sustained over 2 years.