Deficit Schizophrenia

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Abstract

Schizophrenia patients show symptoms in the framework of negative, positive, affective, disorganized, and cognitive dimensions. In particular, a relationship between neurocognitive impairment, negative symptoms, and disorganization has been detected, featuring the so-called deficit schizophrenia. In this context, we here present a clinical case of severe schizophrenia characterized by neurocognitive dysfunction, altered functionality, negative symptoms, and imaging abnormalities.

Keywords

Negative symptoms · Deficit subtypes · Disorganizative dimension · Neurocognitive impairment · Functional neuroimaging · Poor outcome

2.1 Introduction

The concept of schizophrenia was introduced by Eugen Bleuler in 1908. He coined the term "schizophrenia", or more precisely "the group of schizophrenias," because in his opinion "the breaking up or splitting of psychic functioning is an excellent symptom of the whole group" [1]. Moreover, Bleuler identified avolition (i.e., lack of motivation or initiative) as central to schizophrenia. As is known, the term schizophrenia is still used, but throughout the seven DSM (*Diagnostic and Statistical Manual of Mental Disorders*) editions, the definition of schizophrenia evolved, sometimes to encompass the undeniable heterogeneity of schizophrenia symptoms.

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The previous DSM-IV indeed specified five schizophrenia subtypes (paranoid, disorganized, catatonic, undifferentiated, and residual type). This notwithstanding, traditional schizophrenia subtypes have been demonstrated as not being stable over time and not responsive to specific treatments. In the DSM-5, these subtypes have been removed because of their low reliability and poor validity but also because of the growing tendency to focus on a dimensional rather than a categorical perspective [2]. Nevertheless, patients suffering from schizophrenia show differences in terms of clinical symptoms, daily-life difficulties, illness course, cognitive impairment, treatment response, and biological and neuroimaging features. Sometimes the clinical picture of schizophrenia may be associated with a specific medical condition or substance abuse. For this reason, clinicians should also ask about recent head injury or trauma, seizures, cerebrovascular disease, and headaches. They should also exclude oncologic causes, thyrotoxicosis, encephalitis, and porphyria. Testing for human immunodeficiency virus infection and syphilis should also be considered [3].

Beyond these aspects of differential diagnosis, regarding the dismissal of categorical subtypes of schizophrenia with the DSM-5, the diagnostic dimensional approach is also partially implied by the conceptualization of the negative, positive, disorganized, and affective dimension [4]. These symptomatological clusters have been related in various degrees to cognitive impairment, unsatisfactory functioning, treatment response, and outcome of the disease, allowing the identification of worsening subtypes of schizophrenia [5] that are hypothesized as deficit subtypes of schizophrenia [6].

While positive dimension has been less related to neurocognitive impairment [7], more than a year's persistence of negative symptoms (affective flattening, alogia, avolition-apathy, asociality, attentional impairment), in spite of an adequate pharmacologic treatment, has been stated as the core of a supposed separate disease, with its specific risk factors and its specific biological features. In the past, Carpenter et al. [8] defined this syndrome as deficit schizophrenia, empathizing the persistence of decrease in emotional range, poverty of speech, loss of interest, and the loss of drive with, compared to schizophrenia, positive anamnesis for worsening premorbid functioning, poor insight, long-term disability, and bad prognosis [9]. To this purpose, Kirkpatrick et al. [10] strengthened the diagnostic importance of distinguishing primary enduring negative symptoms (clinical core of deficit schizophrenia) from secondary ones, which often occur in the context, or as a consequence, of concurrent positive, depressive, and/or extrapyramidal symptoms.

This negative enduring and unremitting schizophrenia was also mentioned as "Kraepelinian schizophrenia" [11]. In his manuscripts, Kraepelin indeed described how some schizophrenic patients exhibit "failure of mental activities," "weakening of volition," "loss of mastery over volition," and "loss of ability for independent action" [12]. Underlining that schizophrenia is a processual progressive disease that leads to neurocognitive defects, Kraepelin used the term "dementia praecox," in order to remark the putative neuropathological aspects of this syndrome. We now know that some forms of schizophrenia are associated with progressive structural brain abnormalities, affecting both gray and white matter [13, 14]. Other schizophrenic patients exhibited a progressive reduction in frontal lobe white matter volume, with a concomitant increase in frontal lobe cerebrospinal fluid volume. As

partially predicted by Kraepelin, schizophrenic patients with poor outcome had a greater lateral ventricular enlargement over time, while enlargement in frontal lobe cerebrospinal fluid volume has been associated with greater negative symptoms severity [15].

Most studies have hinted that deficit schizophrenia is related to a more severe neurocognitive impairment [16] [17], which may also sustain a group of signs and symptoms, named as psychomotor slowing and emphasized as characterizing enduring negative schizophrenia [18]. During psychomotor tasks the behavior is governed by a number of neurocognitive processes (not only based on motor skill learning ideas and cognitive control of actions) which, if impaired, may cause psychomotor slowing, proved to be related to the patients' social, clinical, and functional outcome. Selecting writing tasks that were able to generate measurements for different subprocesses of psychomotor functioning (planning, initiation, and execution), Bervoets et al. [19] sought to explain the relationship between psychomotor slowing and neurocognition and predominant symptoms in deficit schizophrenia. Interestingly, they found that negative symptoms were found to be mainly associated with difficulties in the initiation of fine motor movements, whereas planning and execution deficit were independent of the symptomatology. Compared to non-deficit patients, deficit ones performed significantly worse on social and global cognition and language [20]. Yu et al. also compared clinical deficit schizophrenia to non-deficit types [21]: both schizophrenia subgroups had overall more severe cognitive impairments than the controls, while patients with deficit schizophrenia performed worse on every neuropsychological measure except the Stroop interference, during the homonymous test in which the patient must say the color of a word (on PC monitor) but not the name of the word. The authors speculated that reduced sustained attention might be the key impaired cognitive domain for negative subtype of deficit schizophrenia.

During the past decades, a relationship between neurocognitive impairment and disorganization was also detected. Considering schizophrenia and DSM-5 classification [22], international experts emphasized five key symptoms of schizophrenia: (1) delusions, (2) hallucinations, (3) disorganized speech, (4) disorganized or catatonic behavior, and (5) negative symptoms. As noted, the adjective "disorganized" recurs: a disorganized behavior means casual sequence of activities, formal thought disorder, loosened thought associations, and schizophasia. Schizophrenia has indeed been linked to the disorganized dimension since 1881 when Ewald Hecker, a German psychiatrist, described a specific syndrome, hebephrenia, characterized by an early-onset and severe disorganized symptoms, quickly progressing to functional and cognitive impairment. Several features of hebephrenia led to the diagnosis of the disorganized subtype (DSM-IV TR) [23], consisting in disorganized speech, disorganized behavior (distortion of idea production, distortion of language, and activities), and inappropriate affectivity. In their meta-analysis [24], Ventura et al. examined the strength of the relationship of neurocognition with schizophrenic symptom clusters across a range of neurocognitive domains (attention, reasoning, speed of processing, verbal and visual memory, working memory). The extent of the relationship between neurocognition and disorganization was significantly larger than the correlation between neurocognition and reality distortion. Disorganized

patients also showed deficits in theory of mind [25] and in the ability of integration of contextual stimuli [26] with low-level visual integration processes and impaired visual closure task [27]. Disorganized patients have also been found to exhibit reduced spatial working memory performances [28] with, on Multiple Errands Test and Hotel Task (an ecological test) [29], a greater number of errors compared to the other diagnostic groups [5].

The clinical case we are going to describe aims to show how in serious schizophrenia specific symptomatological dimensions join in different ways with neurocognitive deficits, involving at different level executive functions, working memory, attention span, and sensory-motor coordination, and all together seemingly related to the increase over the years of functional neuroimaging alterations.

2.2 Case Presentation

Mr. B. is 24 years old. He graduated from middle school; he was never been employed, and he lives with his parents. He was brought to the emergency room by his parents, who were worried about the fact that he had begun talking to the television. They also revealed his poor functioning during the previous months: he didn't attend the local religious voluntary organization, he lost all his friends, and he spent his days at home.

During the interview at the emergency room, the patient is evasive: he speaks in monosyllables, he shows poor interest in his psychic conditions, and he also looks scarcely interested in his parents' worries. He looks untidy and bizarre: his long hair is dirty, and he is wearing an orange hat which he pulls over his eyes. He says he can't take it off; he says "saints" talk to him through that hat. He speaks with a low voice, and sometimes he stops talking, exclaiming "not now!". He watches a laptop monitor, and then he falls into silence and begins staring at it. After that, he starts touching the tip of his shoes by alternating his right hand on his left foot and vice versa. He keeps doing this for half an hour, refusing to provide any explanation. His mother says he has recently taken to making that sequence of movements. She made him come to the hospital that day because he'd gotten into a physical fight with his father just because he turned on the television. The patient burst into tears exclaiming that in that way the "saints" couldn't contact him.

The patient displayed a variety of signs: delusions, hallucinations, disorganization, as well as a recent increase in aggressive behavior. He also showed a significant decline in his functioning. Despite having a caregiver motivated to put him on treatment, Mr. B. exhibited no insight into his psychic conditions, being also poorly collaborative about undergoing therapies, stating he would take only orange pills. Furthermore, a substantial part of the interview was impaired by his lack of attention, as he appeared disturbed by acoustic hallucinations. So, considering all these aspects, the patient was hospitalized in the psychiatry unit.

Family anamnesis was positive for schizophrenia (uncle, maternal line), but negative for substance abuse. The patient is a smoker (30 cigarettes/day); negative findings for alcohol and substance use were collected. His personal history revealed

eutocic delivery, with a birth weight of 3.7 kg and a normal psychomotor development. Family members described Mr. B. as quite a shy child. They reported that he hadn't difficulties in studying, and he had an intermediate academic performance at first. He didn't develop an outgoing character, but he had a few close friends among his schoolmates. Things worsened after graduation. Without a scheduled scholastic routine, the patient used to spend a lot of time at home, showing little interest in responding to calls or emails from his mates. After a month, he quit his job at the supermarket, because his mind wandered easily, not allowing him to focus on his activities. Worried about his social isolation, Mr. B.'s mother forced him to participate in her voluntary religious activities, although unsuccessfully. At home, he began exhibiting strange behaviors, such as wearing the hat (only the orange one), speaking about "saints," not eating certain foods because "he didn't like their colors," and turning around the TV and PC screens. He cared less about his appearance, and surprisingly, on one occasion, he shaved only half of his beard, without giving any reasonable explanation.

At the first psychic examination after admission to the ward, he appeared to be time and space oriented, though perplexed. He was restless, getting up uninterruptedly from the chair, running away, and then returning to the room. His speech was fragmentary, with partially loose associations and occasional neologisms. He was partly reticent to elaborate his contents during the interview. Nevertheless, he admitted he was hearing voices of "saints," who were accustomed to communicating with him through television and other monitors.

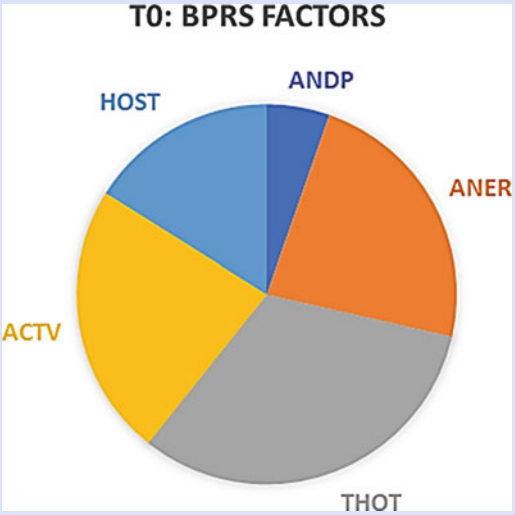
2.2.1 Physical Examination

The patient was alert and oriented. His vital parameters were collected: blood pressure 130/80 mmHg, respiration rate 22, and heart rate 90 bpm. Head was normocephalic, pupils were equal and reactive, and nostrils were pervious. Neck was without lymphadenopathy. The cardiac rate and rhythm were regular; at the auscultation, normal breathing sounds, with no crackles or wheezes. The abdomen was mildly adipose, with bowel sounds heard. Extremities were without cyanosis, clubbing, or edema; the skin was warm and dry. Blood count, renal, and hepatic function were on limits. TSH reflex was average. HBV, HCV, HIV, and *Treponema pallidum* antibodies were negative. At the EKG, sinus rhythm and QTC $<$ 430 milliseconds.

2.2.2 Psychometric Evaluation

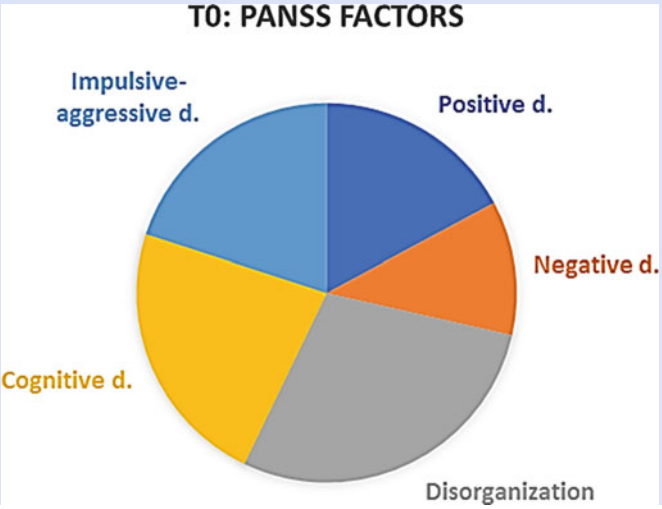
The patient underwent the Brief Psychiatric Rating Scale (BPRS), with a total score of 58 (Box 2.1). BPRS can be divided into five factors: hostility (HOST), anxiety depression (ANDP), anergy (ANER), thought disorder (THOT), and activity (ACTV). As can be seen, the patient got higher scores on items related to thought alterations and disorganized activities.

Box 2.1 As can Be Seen, THOT Is the Most Detected Factor



The Positive and Negative Syndrome Scale (PANSS) was also administered (Box 2.2), with a score of 95 and prevalence of disorganized dimension: Mr. B. lost his train of thought during conversations, beginning to talk to "saints." Tangentially jumping from one argument to another, apparently at random, he made loose associations of topics too, gave answers to unrelated questions, and made ritual movements like begging the "saints" to absolve him.

Box 2.2 PANSS Can Be Subdivided into Five Dimensions

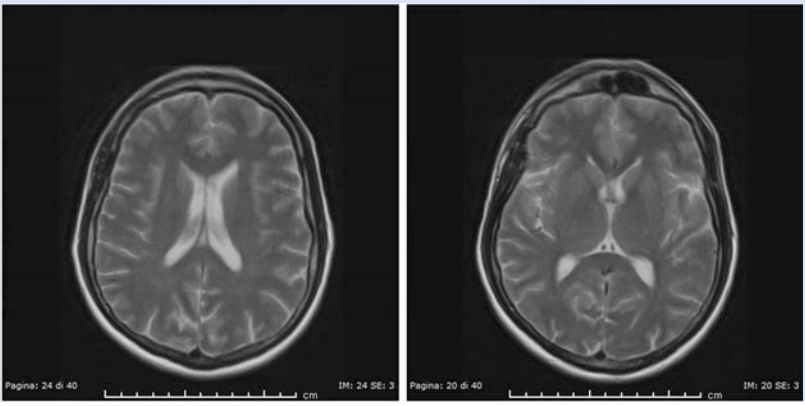


2.2.3 Neuroimaging Assessment

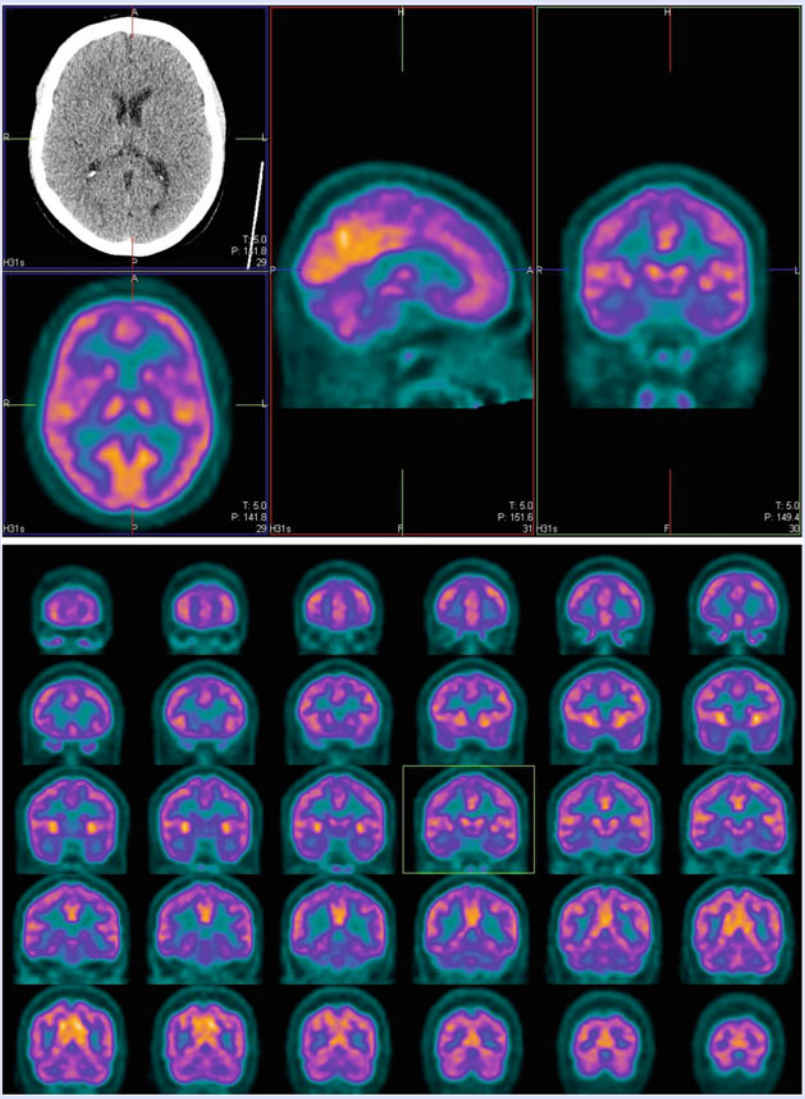
The patient had not been previously scanned with magnetic resonance imaging (MRI) of the brain. At MRI, T1-weighted, T2-weighted, TSE (Turbo Spin Echo), FLAIR (fluid-attenuated inversion recovery), and DWI (diffusion-weighted imaging) scans were acquired. Images were reported as normal (no midline shift, no intracerebral or extra-axial areas of abnormal signal, no evidence of posterior fossa abnormalities, no ventricular enlargements). Liquor and ventricular spaces resulted within the normal age limits (Box 2.3).

Positron emission tomography (PET) images (Box 2.4) revealed, instead, modest glucose cortical hypometabolism in the frontal lobe. Minor cortical metabolic perfusion irregularities were observed bilaterally in the orbitary cortices too. The fixation of the marked glucose was instead preserved in the remaining cerebral and cerebellar structures.

Box 2.3 On the Left and on the Right, Axial Images (T2)



Box 2.4 First PET



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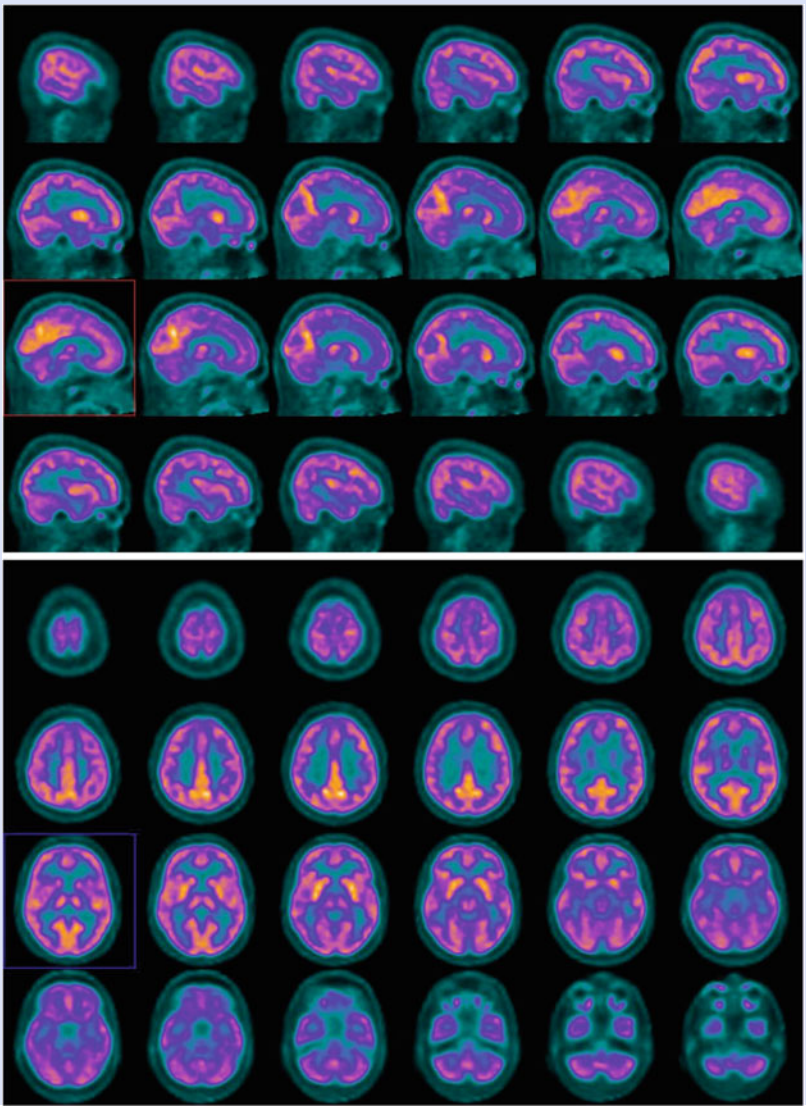


2.2.4 Pharmacological Treatment

Patient was initially treated with 15 mg of aripiprazole, which was subsequently increased (from the second week) to 20 mg/day in accordance with good clinical practice and psychiatric treatment guidelines. After a week of treatment,

Mr. B. denied hearing voices, and objectively, during the interview he appeared markedly less distressed: he showed a sufficient level of attention; he generally didn't lose his train of thought. Nevertheless, when he was in the communal spaces of the ward, in which cameras are more prominent, he used to watch them, but for less time. In such episodes, the patient denied anxiety. He stared at monitors because, he said: "I use to behave in this manner." He began taking off his hat, and he reduced the time spent in assuming bizarre postures. He could not explain why he needed to make those movements nor the relationship between the movements and the communication with "saints." Due to his extremely poor awareness of his illness, therapy with long-acting aripiprazole was chosen, and the patient began a period of rehabilitation in a psychiatric community, given the resolution of the acute clinical condition. But there was persistence of attenuated symptoms such as formal thought disturbance and disorganized sequence of actions during self-care activities. During the final phase of hospitalization, a screening neurocognitive battery of tests was administered. Then, after discharge, the patient underwent a more complete neurocognitive evaluation (Box 2.5).

Box 2.5 First Neurocognitive Evaluation

Test	Score	N.v.	Comment
MMSE (mini mental state examination)	25.60/30	>24.00	Normal
Attentional tests	19.25/60	>31.00	Deficit
Trail making test part A	95.00	<93.00	Deficit
Trail making test part B	330.00	<282.00	Deficit
Raven	23.73/60	>18.60	Normal
Token test (motor function)	24.00/36	>29	Deficit
Boston naming test	43.00/60	>43	*Low score, just above the threshold*
Verbal fluency - phonemic key	7.00	>17	Deficit
Verbal fluency - categorical key	16.00	>25	Deficit
Digit span	5.50	>3.75	Normal
Story recall test – Verbal memory	2.00	>8.00	Deficit
Learning pairs of words – Verbal memory	5.00	>6.50	Deficit
Street completion test	5.00/14	>3.25	Normal
T.O.L. (tower of London)	19.00/36	>20.00	Deficit
FAB (frontal assessment battery)	10.70/18	>13.50	Deficit
Cognitive estimation test	22.97	<18.00	Deficit
Oddity task	9.00	<4.00	Deficit

Two years after discharge, the patient had a severe relapse. He experienced imperative auditory hallucinations; he was extremely anguished and emotionally labile; he manifested aggression toward objects. He attempted suicide by swallowing a hundred pills of alprazolam, but his father, finding the empty blisters, called the emergency services while the patient went into a coma. After the intensive care unit, he was admitted to the psychiatric ward. From the family it emerged that his bizarre thoughts had worsened in the previous 3 weeks. He behaved erratically around the house, and he would talk to strangers, sometimes using neologisms. On certain occasions he also displayed the inability to perform previously learned motor activities (like washing his teeth). Regarding apraxia, at the mental examination, when asked to perform serial step commands, for example, "Take this piece of paper in your left hand, then fold it up, place it in the envelope, and put in the bag," he failed.

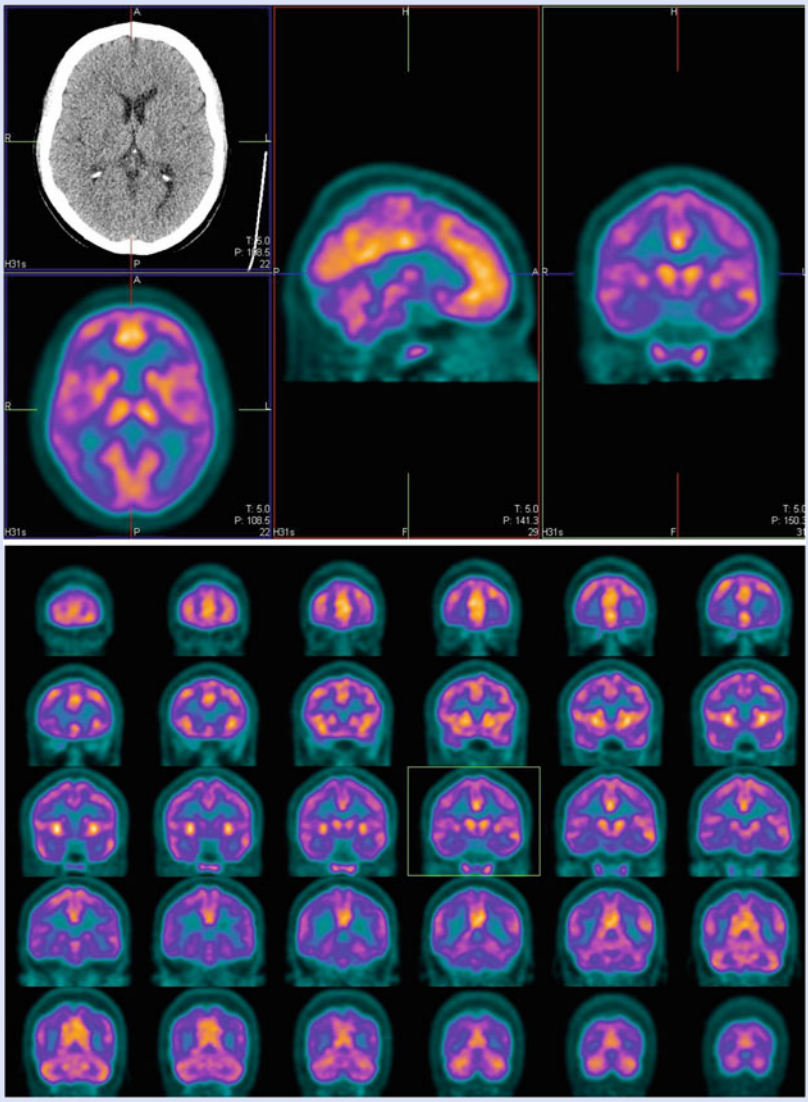
Compared with the previous hospitalization, Mr. B. appeared more aggressive. The second hospitalization lasted 3 months. The initial clinical picture consisted of severely disorganized speech. Mr. B. slipped from one topic to the next, which was vaguely connected to the first. When answering a question, the response often had nothing to do with the question at all. He also made up words. His behavior was grossly disorganized too: he would make grimaces, he brushed his teeth without water, and he wore his clothes incorrectly. During hospitalization, a second positron emission tomography was performed (Box 2.6).

He was both pharmacologically treated with atypical antipsychotics (olanzapine, previously aripiprazole) at high doses and typical antipsychotics (haloperidol and chlorpromazine) with poor effect. Of note, Mr. B. also suffered from hyperprolactinemia and gynecomastia caused by the administration of haloperidol. After these attempts, clozapine therapy was started.

After 10 days of treatment, he began showing a more organized behavior: he took the necessary self-care, and during the interview, the episodes of yelling and making strange noises markedly diminished. He also denied hearing voices and desiring to act aggressively against himself or others. He explained that he didn't know why he injured himself; his mood wasn't totally indifferent. For instance, he said he sometimes was sad to see his mother worried. He still appeared bizarre (sometimes making noises, laughing, and talking to himself in a "magic" manner), but he could answer questions, and he didn't appear anguished. He also accepted to spend another rehabilitative period in a highly protective community.

Concerning the second PET scanning (Box 2.6), the tomographic sections showed a reduction in the glucose analog fixation at the level of the posterior portions of the cortical parietal regions. No significant alterations in glucose distribution in the remaining cortical and subcortical structures emerged. In conclusion, there was evidence suggesting changes in the bilateral parietal glucose metabolism. Despite the first exam, in which frontal functional alterations were documented, the second exam exhibited reduction of the glucose analog fixation in parietal cortices.

Box 2.6 Second PET



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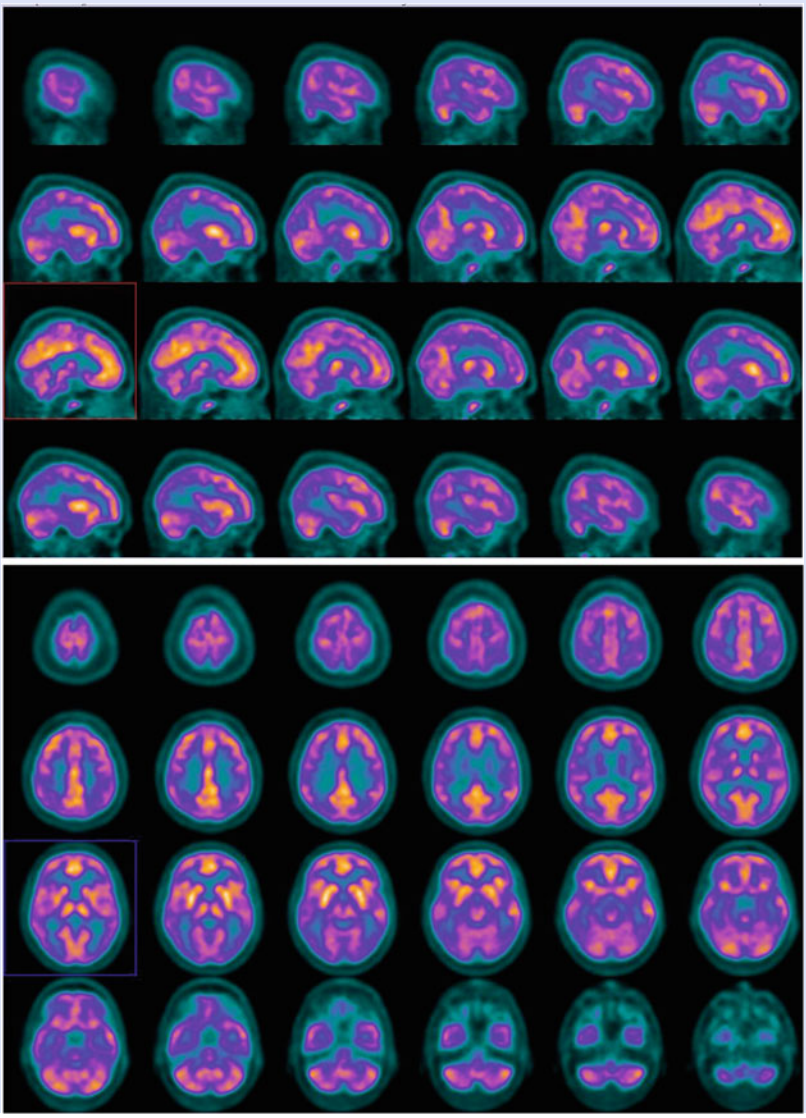


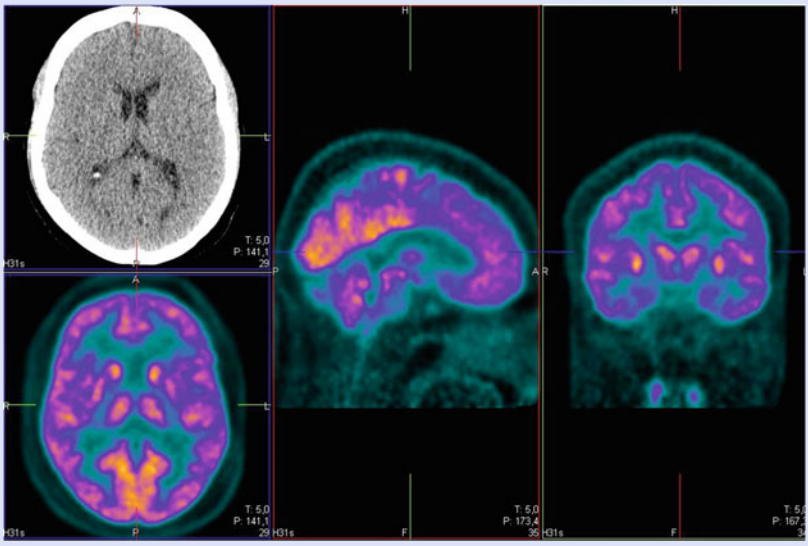
Another PET (Box 2.7) was performed when the patient was rehospitalized because he complained about tiredness, fatigue, and light-headedness; a complete blood count showed that his total WBC count was 2300/cubic mm, and his absolute neutrophil count was 1350/cubic mm, so the clozapine was stopped.

The analysis of PET images highlighted the reduction bilaterally of glucose metabolism in the frontal cortices, lower parietal lobules, and temporal and cerebellar lobes. The subcortical capture of glucose at the basal nuclei and the thalamus was preserved.

After discharge, during the psychosocial rehabilitation program at the community rehabilitation center, another neuropsychological evaluation was made, focused on core neuropsychological deficits of Schizophrenia (Box 2.8).

In November 2016, after 8 years of disease, the patient appeared as a slightly overweight young man, with an overall neat appearance and adequate hygiene. He remained alert and awake throughout the interview, with good eye contact. The orientation was intact to person, place, and time. He had difficulties in abstract thinking; he kept returning to the same limited set of ideas, which were described in a quite circumstantial manner, including some irrelevant details. There was no evidence of loosening of associations, thought blocking, hallucinations or illusions. The insight of disease was extremely poor: the patient didn't realize he was affected by schizophrenia; nonetheless he accepted to take medications. He also cooperated with the staff but had to be stimulated for the exercise of physical and cognitive activities; otherwise he sat passively with his arms crossed in a chair. He took daily therapy with quetiapine 600 mg/day and aripiprazole 5 mg/day (morning administration). He also underwent long-acting therapy with zuclopenthixol depot 300 mg every 2 weeks because of his low adherence to treatment. He has not been hospitalized for 3 years. He is attending a cognitive remediation program.

Box 2.7 Third PET



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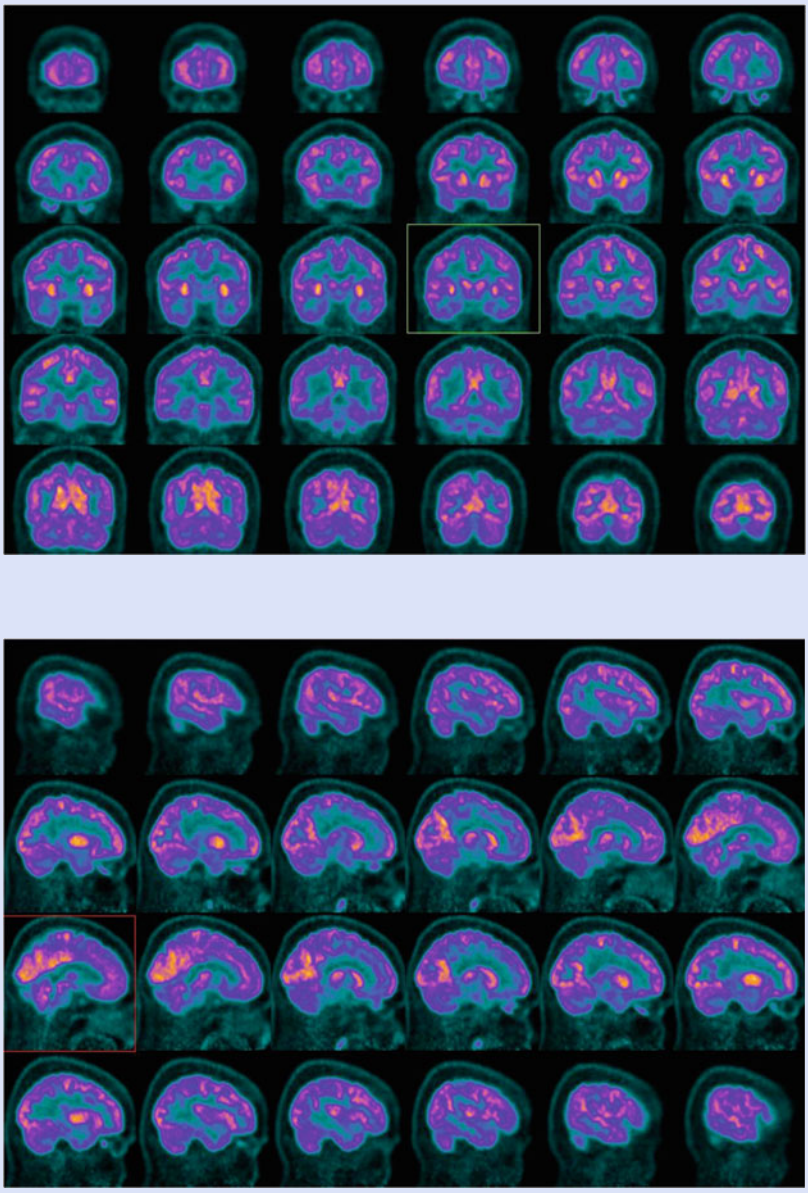

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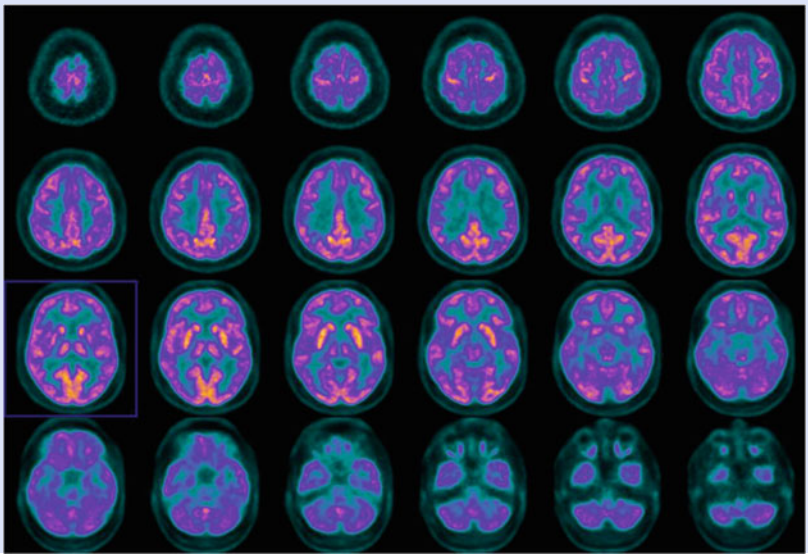

Box 2.8 Second Neurocognitive Evaluation

Test	Cutoff	Score	Comment
BACS (brief assessment cognition schizophrenia)			
Verbal memory	v.n. $\geq$ 33.01	31.00	Deficit
Working memory	v.n. $\geq$ 14.93	20.75	Normal
Token task	v.n. $\geq$ 68.77	25.25	Deficit
Symbol-coding task	v.n. $\geq$ 40.49	36.00	Deficit
Verbal fluency	v.n. $\geq$ 31.68	22.25	Deficit
Tower of London	v.n. $\geq$ 12.37	10.00	Deficit

2.3 Discussion

The diagnostic assessment and treatment of patients with deficit schizophrenia are challenging for clinicians due to the overlap of symptomatological dimensions, with concomitant impaired neurocognition and poor functioning. Consistently with the meta-analysis of Cohen et al. [6] on the psychiatric symptomatology of deficit schizophrenia, Mr. B. exhibited a wide range of psychiatric symptoms, with more

severe disorganization symptoms at the onset and, in a second phase of the disease, predominant negative manifestations, with amotivation, flattening, and reduction in speech and activities. Moreover, the fact that the patient had never achieved a minimal functioning, with the disorganized onset, the partial treatment resistance and the severely impaired cognitive evaluation posited a deficit schizophrenia. According to the multidimensional model of schizophrenia, among positive/negative/disorganized symptoms, the latter have been less studied; however, their association with an early-onset, specific neuropsychological characteristics, poor insight, and significant socio-working maladjustment has already been evidenced [30].

Firstly, the patient's neurocognitive assessment revealed deficits related both to frontal lobe function (frontal assessment battery) and executive functions (Tower of London). "Story recall test" and the task of "learning pairs of words" also scored worse, indicating a possible verbal memory dysfunction, which is a consistently reported cognitive deficit in schizophrenia [31]. The Brief Assessment of Cognition in Schizophrenia (second neurocognitive evaluation) assessed a deficit score for verbal memory too. Regarding the cognitive domain of working memory, the performance score was normal. Whereas at the first evaluation, the Trail Making Test, which also assesses spatial working memory, resulted in deficit: this neurocognitive performance difference might reflect the different extent of disorganization at clinical evaluation. The other four cognitive domain tasks (motor function, verbal fluency, speed of processing, executive function) provided a deficit evaluation. It is worth noting that in order to avoid biases from psychopathologic acute condition, the neurocognitive evaluation was made while the patient was in a period of clinical remission. In conclusion, in this case an overall neurocognitive impairment occurs in a patient who displays severe disorganization symptoms with, at the beginning, slightly less severe negative features which, however, persist and worsen.

In this sense, because of the similarity between our results and the literature data about neurocognitive deficit in predominant negative and disorganized schizophrenic dimensions, we speculate that, in our case report, cognitive dysfunction may represent a deficit schizophrenia endophenotype, also in the sense of a measurable state-independent component whose evaluation may be reproducible [32]. A few cognitive deficits are already regarded as a core feature of schizophrenia [33], but better cognitive functioning was found in patients with positive symptoms, compared to deficit schizophrenia [34, 35].

Neuroimaging assessment was also performed. Research has highlighted how psychiatric disorders tend to show specific neuroimaging features and perfusion alterations. The MRI scan (during the first hospitalization) didn't exhibit anatomical cortical region alterations, with decreases having been found more widespread in chronic phase schizophrenia [36]. Moreover, patients with deficit schizophrenia demonstrated disruption of a few white matter tracts [37] compared with non-deficit patients. Regarding positron emission tomography in literature, a relationship emerged between decreased prefrontal cortex glucose metabolism ("hypofrontality") and severity of negative symptoms [38]. Subjects with negative symptoms were found to exhibit lower glucose metabolic rate (positron emission

tomography) in the right hemisphere, in particular the temporal and ventral prefrontal cortices [39]. The disorganization cluster was significantly correlated instead with left inferior parietal lobule hypoperfusion [40]. Patients experiencing auditory verbal hallucinations were found to have significantly higher metabolic rates in the left superior and middle temporal cortices, in the bilateral superior medial frontal cortex and in the left caudate nucleus [41]. Mr. B.'s functional neuroimaging data (PET) showed the presence of a frontal reduced uptake at the first exam. Then alterations in glucose uptake in the parietal cortical region emerged in the second exam. In the third, the areas of alteration of uptake were multiple (frontal, parietal, and temporal reduced uptake), with a time interval of about 2.5 years between one PET and the other. These peculiar changes of glucose metabolism may reflect, as already supposed by Sham et al. [42], the neurodevelopmental and, consequently, the neuropathological alterations of deficit schizophrenia.

Despite the fact that disorganization and positive symptoms are traditionally considered more responsive than other symptoms to first-generation antipsychotics, in analyzing a large dataset, Janicak et al. [43] showed that atypical antipsychotics are superior to typical in treatment of the disorganized dimension. As regards the pharmacological management of first episode psychosis, we discussed administration of aripiprazole or risperidone, both available also as long acting. We chose aripiprazole because despite a similar effect on disorganized symptoms compared with risperidone, it has fewer metabolic side effects [44]. Moreover, as demonstrated, treatment with aripiprazole has been correlated with improvement of cognitive skills in young adults with first psychotic episode [45]. Then, after the relapse, one trial with atypical antipsychotic and two trials with typical ones were made. Disorganized dimensions and negative symptoms persisted, so clozapine therapy was administered. Clozapine was discontinued after the manifestation of hematic side effects. Subsequently, the patient benefited from the association of conventional antipsychotic long-acting medication, to ensure adherence to treatment, with quetiapine at medium-high doses. He also took aripiprazole at low doses in order to combat negative symptoms.

At present the patient is attending the psychiatric rehabilitation day center on a psychiatric rehabilitation program. As is known, psychiatric rehabilitation programs for deficit schizophrenic patients involve several procedures among which family interventions, cognitive-behavior therapy, social skills training, vocational rehabilitation, cognitive remediation, and mindfulness. Considering that the proofs of efficacy are still contrasting, it is of primary importance to carry out an accurate assessment of the patient's psychopathology, neurocognition, personal motivational aspects, and social background, in order to organize a suitable rehabilitative option. There is some evidence that cognitive remediation therapy, which targets cognitive deficits with the goal of improving functional outcomes, is promising in schizophrenia [46]. Approaches vary depending on the patient's neurocognitive status and psychiatric symptomatology. Cognitive remediation includes practice exercises with the aim of restoring cognitive functions through neuroplasticity; compensatory trainings are also carried out (computerized exercises, therapist-guided instruction or combined exercises) to circumvent neurocognitive impairment, with certain

cognitive programs turning on a specific cognitive domain such as improvement of working memory or social cognition. In the most serious form of schizophrenia, it has been shown that commonly used CRT is not always efficacious [47]. Because of Mr. B.'s neurocognitive evaluation and his functional impairment, a specific cognitive remediation program for implementation of executive functions was developed. Future goals consist of starting a social skills training program to allow Mr. B. to minimize his possible neurocognitive decline and achieve some degree of recovery, especially as regards the ability to manage interpersonal relations, which are crucial in daily routine for living a more productive life.

Key Points

- Disorganized and negative symptoms seem to characterize deficit schizophrenia and tend to be more predominant and represented than psychotic and impulsive-aggressive psychopathological aspects.
- In deficit schizophrenia, a serious neurocognitive impairment has been associated with the negative and disorganized dimension. In this sense, cognitive evaluations could allow a more specific diagnostic assessment and outline targeted rehabilitative treatment. Frequently, structural neuroimaging exams are requested as part of the initial medical work-up in young patients with first-episode psychosis.
- Functional neuroimaging data, as yet to be confirmed, show a number of changes in the disease over the years, with greater anomalies such as the psychiatric picture worsening or becoming chronic. Contrariwise, some studies suggest that conventional structural neuroimaging exams may reveal few abnormalities in young patients with first-episode psychosis.

Self-Assessment Questionnaire

1. Which is the most important clinical aspect to evaluate in follow-up of the patient after clinical stabilization?
   (A) Neurocognition
   (B) Socioeconomic status
   (C) Interpersonal relationships
   (D) Subjective well-being
2. Which is the best rehabilitative option for deficit schizophrenia?
   (A) CBT
   (B) CRT
   (C) Family therapy
   (D) A, B, C
3. What supposed dimension of schizophrenia has been found linked to severe neurocognitive alterations?
   (A) Paranoid
   (B) Aggressive and hostility

(C) Negative and disorganization
(D) Affective

4. Which factors have a significant role in administering long-acting therapy?
(A) Patient prefers not to take pills
(B) Non-compliance with pharmacological treatment
(C) Stabilization of plasma levels
(D) A + B + C

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