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Impulsivity in schizophrenia: A comprehensive update

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ABSTRACT

Impulsivity has been repeatedly identified as a major problem in schizophrenia. The literature revealed several ways of defining and conceptualizing impulsivity as well as a variety of measures and an analysis of the consequences of impulsivity. Thus, we review the lack of agreement in the conceptualization and measurement of impulsivity. We also review the latest evidence that impulsivity may have an important role in the etiology of substance use, aggression, violence, and suicide in schizophrenia. In addition, we outline the recent findings in neuroimaging research to elucidating the neurobiological deficits underlying pathological impulsivity in schizophrenia.

Contents

1. Introduction

Impulsivity is generally considered a multidimensional construct that may be defined as ‘a predisposition toward rapid unplanned reactions to internal or external stimuli without regard to the negative consequences of these reactions to themselves or others’ (Moeller, Barratt, Dougherty, Schmitz, & Swann, 2001).

Pathological impulsivity is often thought of as a core feature of schizophrenia (Heerey, Robinson, McMahon, & Gold, 2007; Kester et al., 2006). Several studies found that people with schizophrenia were more impulsive than healthy subjects (Dursun, Szemis, Andrews, Whitaker, & Reveley, 2000; Enticott, Ogloff, & Bradshaw, 2008; Kaladjian, Jeanningros, Azorin, Anton, & Mazzola-Pomietto, 2011). This pathological impulsivity has been reported by both self-report and behavioral assessments of impulsivity including response inhibition (e.g., Nolan, D'Angelo, & Hoptman, 2011) novelty seeking (e.g., Zuckerman, 1993), and choice impulsivity or delay discounting (e.g., Heerey et al., 2007). However, psychometric and behavioral impulsivity measures do not correlate well with each other (Barratt & Patton, 1983; Barratt, Stanford, Kent, & Felthous, 1997), and suggests that impulsivity is a construct with multiple facets. An extensive literature in the general population and in schizophrenia patients considers that impulsivity increases the risk for aggression and violence (Barratt, 1991; Barratt & Felthous, 2003; Quanbeck et al., 2007; Volavka & Citrome, 2008), suicidal behavior (Mann, Waternaux, Haas, & Malone, 1999; Gut-Fayand et al., 2001; Iancu et al., 2010) and plays a key role in the development and maintenance of drug addiction (Bickel, Odum, & Madden, 1999; Dervaux et al., 2001; Krishnan-Sarin et al., 2007). In this review, we aim to give a coherent view on the conceptualization and assessment of impulsivity, as well as its relationship with some behavioral outcomes (substance use, violence, aggression, and suicidality).

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In addition, we provide an overview of the current knowledge of neural disturbance of pathological impulsivity by summarizing a wide and sparse body of literature.

2. Conceptualization of impulsivity

Impulsivity is an important and a multidimensional construct that covers a wide range of behavioral, motivational, and emotional phenomena. However, the literature reflects numerous inconsistencies in the conceptualization of impulsivity that may be due in large part to the heterogeneity of the construct. In this context, Eysenck and McGurk (1980) suggest that impulsivity may involve an inability to assess the risk associated to behaviors or decisions, or a tendency to choose risky options despite an accurate assessment of risk associated to them. From this theoretical framework, Eysenck and Eysenck (1985) considered that impulsivity consists of two components: 'venturesomeness' that corresponds to extraversion, and 'impulsiveness', that corresponds to psychoticism. Dickman (1990) proposed two fundamental aspects of this trait: 'dysfunctional' and 'functional' impulsivity. Functional impulsivity is related to a tendency to make quick decisions when they are required by the situation for personal gain, and dysfunctional impulsivity is related to speedy and irreflexive decisions according. Some definitions considered impulsivity as behavior that is performed with little or inadequate forethought (Evenden, 1999), as a personality trait characterized by novelty seeking behavior, rapid processing of information, person's inability to delay gratification or act with regard for consequences of their behavior (Barratt, 1993; Cloninger, Przybeck, & Švrakić, 1991; Zuckerman, 1993).

In order to capture a "pure" form of impulsivity, Patton, Stanford, and Barratt (1995) separated impulsivity into three components: acting on the spur of the moment (motor impulsiveness), not focusing on the task at hand (attentional impulsiveness), and a tendency to act on the spur of the moment and not planning and thinking carefully (non-planning impulsiveness). Thus, the Barratt Impulsiveness Scale suggests that greater motor activation, less attention, or decreased planning are key factors of impulsivity. Alternatively, impulsivity may be related to an underlying mechanism of behavioral inhibition (Enticott, Ogloff, & Bradshaw, 2006; Logan, Schachar, & Tannock, 1997).

Moreover, Whiteside and Lynam (2001) have suggested that impulsive behaviors can be divided into four distinct personality traits which served as the basis for the Urgency, Premeditation (lack of), Perseverance (lack of), and Sensation seeking (UPPS) Impulsive Behavior Scale. Urgency is defined as the tendency to experience strong impulses, frequently under conditions of negative affect. Premeditation (lack of) is defined as the tendency to think and reflect on the consequences of an act before engaging in the act. Perseverance (lack of) reflects the ability to remain focused on a task that may be boring or difficult. Sensation seeking reflects a tendency to enjoy and pursue activities that are exciting, and an openness for new experiences. For instance, the International Society for Research on Impulsivity (ISRI) defines impulsivity as human behavior without adequate thought, the tendency to act with less forethought than do most individuals of equal ability and knowledge, or a predisposition toward rapid, unplanned reactions to internal or external stimuli with diminished regard to the negative consequences of these reactions (http://impulsivity.org/).

3. Assessment of impulsivity

Several instruments have been used for the evaluation of impulsivity in schizophrenia. These can be classified based on the type of test used, that is, self report and laboratory–behavioral tasks. A variety of questionnaires has been used to provide operational definitions of impulsivity in schizophrenia. These questionnaires recognize the multifaceted nature of impulsivity. As evident in Table 1, five self-report measures have been frequently used in schizophrenia. The Barratt Impulsiveness Scale (BIS; Patton et al., 1995), one of the most common self-report measures, represents the latest effort by Barratt et al. to measure impulsivity construct that is orthogonal to anxiety and is related to similar personality traits, such as extraversion and sensation seeking. This scale has 30 items grouped into three subscales of factors: three subscales: attentional impulsiveness (e.g., I get easily bored when solving thought problems), motor impulsiveness (e.g., I do things without thinking), and non-planning impulsiveness (e.g., I am more interested in the present than the future). The Impulsiveness–Venturesomeness–Empathy questionnaire (IVE-7), a 54-item questionnaire in a yes/no format, has also been developed to identify three dimensions of personality: Impulsiveness (19 items; e.g., I generally do and say things without stopping to think), Venturesomeness (16 items; e.g. I quite enjoy taking risks), and Empathy (19 items) (Eysenck & Eysenck, 1985). Some scales have separated impulsivity into four components. For example, the Sensation Seeking Scale (SSS, Zuckerman, 1978), a 40-item self-report (scores from 0 to 40), includes four components: désinhibition, thrill and adventure seeking, experience seeking and boredom susceptibility. Indeed, the Impulsivity Control Scale (ICS) that consists of 15 Likert-scale items was developed to measure the tendency to engage in impulsive, spur-of-the-moment behavior and lack of patience, all of which reflecting possible loss of control (Plutchik & Van Praag, 1989). Lecrubier, Braconnier, Said, and Payan (1995) developed

Table 1
Evaluation of impulsivity in schizophrenia.

Type of scale	Measure of impulsivity	Number of items	Features of scale	Authors
Self-report	Barratt Impulsiveness Scale (BIS)	30	Evaluates tree factors: Motor (Acting without thinking) Cognitive (Making quick cognitive decisions) and Non-planning impulsivity (Present orientation or lack of "futuring")	Patton et al. (1995)
	Impulsivity Control Scale (ICS)	15	Assesses the tendency to engage in impulsive, spur-of-the-moment behavior and about lack of patience.	Plutchik and Van Praag (1989)
	Impulsivity Rating Scale (IRS)	7	Evaluates time needed for decision, capacity to pursue an activity, aggressivity, irritability, impatience, ability to delay and control of response.	Lecrubier et al. (1995)
	Sensation Seeker Scale (SSS)	40	Assesses the thrill and adventure, disinhibition, experience seeking and boredom susceptibility.	Zuckerman (1978)
	Impulsiveness–Venturesomeness–Empathy questionnaire (IVE–7)	54	Assesses unconscious risk taking and conscious sensation seeking.	Eysenck and Eysenck (1985)
	Kirby Delay Discounting Task (KDDT)	27	Delay discounting	Kirby et al. (1999)
Behavioral approaches	Go/No-Go task	–	Measures inhibition and motor impulsivity	Newman et al. (1985)
	Iowa Gambling Test (IGT)	–	Measures emotional decision-making and non-planning impulsivity	Bechara et al. (1994)
	Wisconsin Card Sorting Test (WCST)	–	Assesses attentional impulsivity.	Heaton et al. (1993)
	Stroop Color–Word Test	–	Measures cognitive impulsivity and resistance to distraction.	MacLeod (1991)
	Continuous Performance Task (CPT)		Measure of sustained attention (vigilance) and impulsive behavior.	Roswold et al. (1956)

the Impulsivity Rating Scale (IRS), which consists on the description of the behavior of the patient in usual situations. It includes the following seven items rated in four degrees: Irritability, Impatience, Time needed for decision, Capacity to pursue an activity, Aggressivity, Control of response, and Ability to delay. Delay discounting is also a measure of future-oriented decision-making and impulsivity. In the laboratory, Delay discounting is often assessed using a 27-item questionnaire which assesses preferences for hypothetical rewards over different delay durations (Kirby, Petry, & Bickel, 1999).

All of these self-report measures have the advantage of allowing the researcher to gather information on a variety of types of impulsive behavior, but are unsuitable for repeated use and are difficult to relate to underlying neurobiological substrates.

In contrast, laboratory behavioral instruments provide an objective method for assessing impulsivity. According to recent evidence, two types of impulsive behavior are assessed with laboratory behavioral tasks: impulsive disinhibition and impulsive decision-making (Reynolds, Ortengren, Richards, & de Wit, 2006). Among the different experimental paradigms to measure inhibition in schizophrenia, the Go/No-Go is the action/inhibition task per excellence for motor impulsivity. The Go/No-Go task can be used with both verbal and non-verbal stimuli, and provides adequate behavioral data to examine the processes involved in inhibiting a pre-potent Go response (Newman, Widom, & Nathan, 1985). Impulsivity in this task is defined by the number of errors of commission or "false alarms" (responding when an incorrect stimulus is presented). Reaction time (RT) or the time it takes to make a response (response latency) can also be measured in this task. Another rapid response inhibition paradigm is the Continuous Performance Test (CPT) which is frequently administered to patients with schizophrenia to measures the ability to suppress dominant, automatic, or pre-potent responses (Roswold, Mirsky, Sarason, Bransome, & Beck, 1956). In this task, elevated frequency of commission errors (a response to any stimulus other than the target) represents impulsive responding (Dougherty et al., 2003).

Non-planning impulsivity may be assessed by the Iowa gambling test (IGT). In the IGT, there is a choice between a high immediate reward, but with relatively increased risk for higher future punishment, and a relatively lower immediate reward, but with relatively lower future punishment (Bechara, Damasio, Damasio, & Anderson, 1994). It is well known that normal healthy persons shift their card selection from high-risk/high-return decks to low-risk/low-return decks. Persisting in high-risk/high-return card choices is known to represent impulsivity and to relate to schizophrenia (Shurman, Horan, & Nuechterlein, 2005). In other words, it taps into non-planning impulsivity when the subject chooses smaller-sooner gains instead over a larger-later reward that comes from the overall gain (Dougherty et al., 2003).

On the other hand, attentional impulsivity may be assessed by the Wisconsin Card Sorting Test (WCST). This test tasks requiring shifting attention from one perceptual dimension to another (Heaton, Chelune, Talley, Kay, & Curtiss, 1993). Subjects are asked to correctly categorize cards based on verbal feedback. Successful completion requires the subject to shift flexibly from one sorting rule to another in response to feedback and to maintain the appropriate set while sorting to a reinforced rule. In addition, Stroop Color–Word Test is also a test of sustained attention and resistance to distraction (see a review by MacLeod, 1991). Subjects are asked to name the printed color of displayed color–words and control stimuli, even when the color of the ink and the color–word are not congruent. Naming the color of the word takes longer and is more prone to errors if the color is incongruent as compared to congruent. During incongruent trials, more interference results from the inability to inhibit the word reading. The errors on the Stroop task are considered to be a main determinant of a cognitive impulsivity (White et al., 1994).

All of these behavioral measures may have the advantage of being more sensitive to transient changes in impulsivity, provide more objective assessments of impulsivity, as well as being more amenable to repeated administration (Dougherty, Bjork, Harper, et al., 2003). These behavioral measures of impulsivity do not correlate well with self-report measures, and this may be the result of their examination of more specific behaviors (Reynolds et al., 2006), and they may be more useful during both the assessment and treatment phases of disorders related to impulsivity.

4. Impulsivity and substance use

The impulsivity construct is of central importance for substance use disorders or schizophrenia–addiction comorbidity (Hollander & Rosen, 2000; Moeller et al., 2002; Whiteside & Lynam, 2001; Wing, Moss, Rabin, & George, 2012). Substance abuse disorders involve continued use of substances despite negative consequences (i.e., loss of behavioral control of drug use). In patients with schizophrenia, comorbid substance abuse is associated with an overall reduced quality of life, more frequent and longer periods of hospitalization, higher relapse rates, less treatment compliance, and a higher incidence of violent behavior (Fazel, Långström, Hjern, Grann, & Lichtenstein, 2009).

In efforts to understand underlying causes of specific problems that may be contributors to substance use, studies using the BIS-11 with people with schizophrenia and substance use disorder, including alcohol, cannabis, opiates, and cocaine use disorders, have found significant differences on future planning, motor impulsivity, and cognitive impulsivity when compared to people with schizophrenia alone (Dervaux et al., 2001; Dervaux, Laqueille, Bourdel, Olié, & Krebs, 2010). More recently, in schizophrenia patients with a positive urine drug screen (UDS) for cocaine scored higher on impulsivity measures when compared to patients with a negative UDS (Duva, Silverstein, & Spiga, 2011). In a cross-sectional study, the scores on the motor and non-planning BIS subscales were higher in the schizophrenia group with cannabis use disorders (CUD) than in the group without CUD (Dervaux et al., 2010). When compared with non-schizophrenic subjects, comorbid patients, showed significantly weaker performances for the planning domain only (Schiffer et al., 2010). More recently, However, Gut-Fayand et al. (2001) found no differences on motor impulsivity in people with schizophrenia with and without substance use disorders.

The mechanisms underpinning the association between impulsivity and substance use remain to be clarified. There are several explanations for the relationships between impulsivity and substance abuse. Gut-Fayand et al. (2001) proposed that high impulsivity might lead to substance abuse as a maladaptive behavior in response to prodromal symptoms, precipitating the onset of psychosis. However, Liraud and Verdoux (2000) suggested that impulsivity may favor substance use disorders in a non-specific way. Another possible explanation, which may complement the first, was proposed by Hogarth (2011): impulsivity confers hypersensitivity to drug reinforcement which establishes higher rates of drug-seeking/taking. Another possibility is that impulsivity does not influence drug reinforcement, but rather, facilitates automatic or habitual control of drug-seeking/taking behavior by drug-associated stimuli.

5. Impulsivity, violence and aggression

A large literature postulates that impulsivity play a significant role in more reactive violence, and criminal and antisocial behavior (Bowman, 1997; Brown et al., 1989; Dolan & Fullam, 2004; Eysenck & Gudjonsson, 1989; Hynan & Grush, 1986; Krakowski, 2005; Plutchik & Van Praag, 1989). People with major mental disorders, particularly psychosis, are associated with a greater risk of violence compared with the general population (Douglas, Guy, & Hart, 2009). Therefore, schizophrenia is consistently associated with an increased risk of violent acts compared with other psychiatric illnesses (Joyal, Dubreucq, Grendon, & Millaud, 2007) and compared with the general population in different countries and using various definitions of violence (Fazel et al., 2009). Conceptual models of violence in schizophrenia postulate that patients with schizophrenia are violent as a consequence of the psychopathologic symptoms of the disorder itself (e.g., delusions and hallucinations) (Swanson, Swartz, Van Dorn, et al., 2006). A recent review of the literature suggests that violence due to a mental condition such as schizophrenia is considered medical, but even aggression motivated by delusions or hallucinations can also be characterized as impulsive, premeditated, or compulsive (Felthous, 2008). The previous studies have shown that aggressive schizophrenia patients showed significantly more failed inhibitions on a Go/No-Go task and more impulsivity on all reaction time tests (Rasmussen, Levander, & Sletvold, 1995). Barkataki et al. (2005) provided evidence in support of this view, showing that impulsivity may be a factor in violence in schizophrenia. Further insights have come from Kumari et al. (2009). Using (IVE-7), this study found that dysfunctional impulsivity could play an important role in extreme violence in schizophrenia. However, only a single investigation has suggested that impulsivity does not seem to cause violent behavior in schizophrenic patients (Kaliski & Zabow, 1995). It is worth mentioning that Clozapine treatment induced a marked decrease in impulsiveness and aggressiveness in chronic neuroleptic-resistant schizophrenic patients (Spivak, Mester, Wittenberg, Maman, & Weizman, 1997). Taking together, evidence suggests that impulsivity can be an important consideration both forensically and clinically to the violent and an aggressive behavior of individuals with schizophrenia. However, further work is needed using heterogeneous designs and methodologies to more clearly elucidate this role.

6. Impulsivity and suicidal risk

A systematic review has estimated that suicide among people with schizophrenia is 13 times more common than in the general population (Saha, Chant, & McGrath, 2007). As in the general population and many psychiatric disorders, the mechanisms that explain elevated suicide risk in people with schizophrenia may include impulsivity and behavioral dysregulation of aggression (Allebeck, Varla, Kristjansson, & Wistedt, 1987; Baumeister, 1990; Jokinen et al., 2010; Mann et al., 1999; McGirr et al., 2008; Modestin, Zarro, & Waldvogel, 1992). Previous work by Gut-Fayand et al. (2001) and De Hert, McKenzie, and Peuskens (2001) found that impulsivity was implicated in the increased suicidal risk of schizophrenia patients. Similarly, a recent study supports the contention that high impulsivity in schizophrenia patients is significant in the etiology of suicide in schizophrenia (Iancu et al., 2010). It is important to mention that methods used in suicide attempts by persons suffering from schizophrenia were largely nonviolent with more violent methods more often associated with older men (Kerkhof, 2000). Nonetheless, in a study by McGirr et al. (2006) on 81 psychotic subjects of whom 45 died by suicide, it was found that impulsive–aggressive behaviors did not play a role in schizophrenic and chronic psychotic suicide. Even though individuals with schizophrenia are at high risk for suicidal behavior, our current understanding of its psychological determinants is insufficient. The relationship with impulsivity is not really clear because only a few studies have been performed and they have some methodological shortcomings.

7. Neuroanatomical substrates of impulsivity

As can be seen from Table 2, the response inhibition paradigm is the most common impulsivity task used in neuroimaging studies. Abnormal behavior and physiology in prefrontal and cingulate cortices during attentional processing in schizophrenia have been suggested by previous literature (Schröder et al., 1996; Siegel, Nuechterlein, Abel, Wu, & Buchsbaum, 1995; Weinberger, Berman, & Zec, 1986).

In terms of impulsivity and brain structure volume, findings suggest an association between increased impulsivity as measured by IVE-7s and reduced orbitofrontal and hippocampal volumes (Kumari et al., 2009) as well as non-planning impulsivity and reduced gray matter volumes in ACC, frontopolar and superior parietal regions in schizophrenia–addiction comorbidity (Schiffer et al., 2010). In addition, Hoptman et al. (2002) indicate that lower fractional anisotropy in right inferior frontal white matter was associated with higher motor impulsiveness in men with schizophrenia.

Studies performed with functional Magnetic Resonance Imaging (fMRI) and Positron emission tomography (PET) have shown that behavioral (motor response) inhibition is linked to activation of the cortex sites such as a prefrontal cortex (Cohen, Nordahl, Semple, Andreason, & Pickar, 1998), the right VLPFC, a region known to play a critical role in motor response inhibition (Brewer et al., 2007; Epstein, Stern, & Silbersweig, 1999; Kaladjian et al., 2007; Kaladjian et al., 2011) and the DLPFC whose activation negatively correlates with impulsivity (Barch et al., 2001; Brewer et al., 2007; Harrison et al., 2006; MacDonald & Carter, 2003; Perlstein, Dixit, Carter, Noll, & Cohen, 2003; Rubia et al., 2001; Salgado-Pineda et al., 2007; Weiss et al., 2007). However, Mathalon, Jorgensen, Roach, and Ford (2009) found patients to have significantly greater activation in the DLPFC by errors than the controls. Indeed, Nishimura et al. (2011) have stressed the absence of any change in the activity of the DLPFC during the No-Go condition compared to the Go condition in schizophrenia patients. Due to the use of small sample sizes, results of this study should be viewed with caution. In addition, six studies found evidence for right inferior frontal cortex hypoactivations in schizophrenia patients (Krabbendam, O'Daly, Morley, van Os, & Murray, 2009; MacDonald et al., 2005; Perlstein et al., 2003; Salgado-Pineda et al., 2007; Seok Jeong et al., 2005; Siegel et al., 1995).

Brain functional neuroimaging studies have shown reduced error-related activation in the anterior cingulate cortex (ACC), a brain area considered to play a critical role in performance monitoring (Arce et al., 2006; Carter, MacDonald, Ross, & Stenger, 2001; Ford et al., 2004; Kerns et al., 2005; Krabbendam et al., 2009; Laurens, Ngan, Bates, Kiehl, & Liddle, 2003; Rubia et al., 2001; Seok Jeong et al., 2005; Volz et al., 1999; Weiss et al., 2007). Also, in line with these findings, PET studies provide evidence of a diminished ACC response to error commission (Carter, Mintun, Nichols, & Cohen, 1997; Epstein et al., 1999; Harrison et al., 2006; Siegel et al., 1995; Yücel et al., 2002). In contrast, it has been reported in small number of unmedicated patients with schizophrenia a greater activation in the ACC (Nordahl et al., 2001; Yücel et al., 2007) and a hypoactivation in the paracingulate cortex (Yücel et al., 2007) suggesting that patients on medication show the opposite relative to patients off medication and that there is no marked ACC hypoactivity at illness onset, but some relative reductions in paracingulate cortex activity. Besides the findings on the ACC, there was some evidence for a greater activation in patients with schizophrenia compared with healthy participants in the posterior cingulate during the Stroop task (Ungar, Nestor, Niznikiewicz, Wible, & Kubicki, 2010, Weiss et al., 2007) and in the precuneus (Arce et al., 2006; Ungar et al., 2010). Together, these three regions (ACC, posterior cingulate gyrus/précuneus) are thought to represent key nodes in a prefrontal executive attention network that supports critical cognitive functions of control and performance monitoring.

Data from fMRI studies also reveal evidence of altered response in the left thalamus during the motor response inhibition paradigm (Barakati et al., 2008; Volz et al., 1999). Additionally, evidence of the striatum's potential involvement in response inhibition emerged with the study of Barakati et al. (2008). Here, patients with and without a history of violence showed a reduced activity in the left caudate nucleus. However, Honey et al. (2005) found that the response of the thalamus bilaterally and the left caudate nucleus to the CPT task compared to baseline was abnormally high in the patient groups. It should be noted that the caudate nucleus and thalamus are known to be implicated in organizing and relaying information as well as in prepulse inhibition (Kumari et al., 2003), which is a measure of automatic inhibition; however, the inconsistency in the results makes their involvement inconclusive.

Table 2
Studies of impulsivity and brain structure.

Authors	Participants	Impulsivity measure	Neuroimaging	Main findings
Kaladjian et al. (2011)	26 patients with schizophrenia 30 healthy subjects	BIS-11 Go/No-Go task	fMRI	Greater BIS-11 scores are associated with greater activation within the right VLPFC during response inhibition.
Nishimura et al. (2011)	14 patients with schizophrenia 40 healthy controls	Go/No-Go task	fMRI	Deactivation in the DLPFC during the No-Go condition compared to the Go condition in the healthy controls, and such changes were not shown in patients with schizophrenia.
Schiffer et al. (2010)	12 patients with paranoid schizophrenia and 12 with additional comorbid substance use disorders 27 healthy subjects	BIS-11 WCST Go/No-Go task	VBM	Increased non-planning impulsivity was negatively related to gray matter volumes in anterior cingulate, frontopolar and superior parietal regions in schizophrenia–addiction comorbidity.
Kumari et al. (2009)	24 male schizophrenia patients 14 healthy male controls	IVE-7	MRI	Impulsivity is associated with reduced orbitofrontal and hippocampal volumes.
Mathalon et al. (2009)	11 patients with schizophrenia 10 healthy controls	Go/No-Go task	fMRI and ERP	DLPFC was more activated by errors in patients than controls.
Barakati et al. (2008)	12 men with schizophrenia with a history of violence 12 men with schizophrenia without a history of violence 14 healthy control	Go/No-Go task	fMRI	Patients with a history of violence showed a reduced activity in the left caudate nucleus and in the left thalamus. Patients without a history of violence demonstrated reduced activity in the left caudate nucleus.
Kaladjian et al. (2007)	21 schizophrenic patients 21 healthy subjects	Go/No-Go task	fMRI	A significant decrease in activation during motor response inhibition in the right VLPFC.
Salgado-Pineda et al. (2007)	14 patients with schizophrenia 14 healthy subjects	CPT	fMRI	Reduced connectivity between the DLPFC and other brain areas, particularly posterior brain regions.
Arce et al. (2006)	17 individuals with chronic schizophrenia 17 healthy comparison subjects	Go/No-Go task	fMRI	Hypoactivation in the DLPFC and dorsal ACC during inhibition but greater activation in the inferior frontal gyrus and left precuneus during cues and cued inhibition.
Honey et al. (2005)	22 patients with schizophrenia 12 healthy subjects	CPT	fMRI	A task-specific relationship between the medial superior frontal gyrus, ACC and the cerebellum was disrupted in patient groups in comparison with controls.
MacDonald et al. (2005)	18 never-medicated, first-episode schizophrenia patients 12 never-medicated patients with first-episode psychosis 28 healthy subjects	CPT	fMRI	Lower levels of activation in the left inferior frontal cortex, in the right inferior frontal cortex and in right middle frontal gyrus.
Ford et al. (2004)	11 patients with schizophrenia 11 healthy subjects	Go/No-Go task	ERP and fMRI	No-Go P300 was modestly related to activations in the ACC.
Perlstein et al. (2003)	16 patients with schizophrenia 15 healthy subjects	CPT	fMRI	Decreased right DLPFC activity related to prepotent response.
Laurens et al. (2003)	10 patients with schizophrenia 16 healthy subjects	Go/No-Go task	fMRI	Relative under-activity in the rostral ACC.
MacDonald and Carter (2003)	17 medicated patients with schizophrenia 17 healthy subjects	CPT	fMRI	Decreased left DLPFC activity unrelated to performance.
Barch et al. (2001)	14 first-episode, medication-naive patients with schizophrenia 12 healthy subjects	CPT	fMRI	Deficits in DLPFC activation in task conditions requiring context processing.
Carter et al. (2001)	17 patients with schizophrenia 16 healthy subjects	CPT	fMRI	Lower activity in the ACC correlate with task performance.
Rubia et al. (2001)	6 male schizophrenia patients 7 healthy male controls	Go/No-Go task Stop tasks	fMRI	Reduced activity in the ACC and left DLPFC during inhibition.
Volz et al. (1999)	14 patients with schizophrenia 20 healthy volunteers	CPT	fMRI	Decreased activation in the right mesial prefrontal cortex, the right ACC and the left thalamus.
Cohen et al. (1998)	19 male medication-withdrawn schizophrenic patients 41 healthy males	CPT	PET	Poor performance associated with lower prefrontal cortex metabolic and high posterior putamen metabolic.
Schröder et al. (1996)	79 patients with schizophrenia 47 healthy controls	CPT	PET	Hyperactivity of parietal cortex and motor area are related to disorganized thinking. Hippocampal and lateral temporal dysfunction are related to delusional symptoms. Hypofrontality is associated with negative symptoms.
Siegel et al. (1995)	25 schizophrenic patients 20 healthy subjects	CPT	PET	Reduced activity in medial frontal, right inferior temporal gyrus and anterior cingulate correlate with task performance.
Ungar et al. (2010)	15 patients with schizophrenia 15 healthy comparison subjects	Stroop task	fMRI	Greater activation in medial parietal regions (posterior cingulate gyrus/precuneus).
Krabbendam et al. (2009)	11 patients with schizophrenia 9 healthy volunteers	Stroop task	fMRI	Attenuated activation within the anterior cingulate gyrus, left pre-/post-central gyrus and inferior frontal junction. A significant correlation between the increased activation in the inferior frontal junction and the reduction in positive symptoms.
Yücel et al. (2007)	8 antipsychotic-naïve first-episode schizophrenia 8 healthy volunteers	Stroop task	PET	A relative under-activation of the left paracingulate cortex and a greater activation in the ACC.
Brewer et al. (2007)	8 antipsychotic-naïve first-episode schizophrenia 8 healthy volunteers	Stroop task	PET	Attenuated activation in R-DLPFC and R-VLPFC.

(continued on next page)

Table 2 (*continued*)

Authors	Participants	Impulsivity measure	Neuroimaging	Main findings
Weiss et al. (2007)	8 unmedicated patients during an acute episode of schizophrenia 8 healthy volunteers	Stroop task	fMRI	Reduced activation in DLPFC, ACC and parietal regions and a higher activation in temporal regions and posterior cingulate.
Harrison et al. (2006)	8 young male patients with first-episode schizophreniform 8 healthy volunteers	Stroop task	PET	Under-activation of the left middle-frontal gyr with significant task-related activation of the DLPFC.
Kerns et al. (2005)	13 schizophrenia patients 13 healthy subjects	Stroop task	fMRI	Decreased conflict- and error-related activity in the same region of the ACC.
Seok Jeong et al. (2005)	10 patients with schizophrenia 10 healthy controls	Stroop task	fMRI	Activation of right inferior frontal and the right frontal precentral gyri.
Yücel et al. (2002)	6 patients with schizophrenia 5 healthy subjects	Stroop task	PET and MRI	Hypoactivation in the ACC.
Nordahl et al. (2001)	9 unmedicated patients with paranoid schizophrenia 10 healthy subjects	Stroop task	PET	Increased metabolic activity in the right ACC correlated positively with the total incongruent trial errors.
Epstein et al. (1999)	11 patients with schizophrenia (6 paranoid and 5 unmedicated patients). 6 healthy subjects	Stroop task	PET	A decrease in dorsal ACC and VLPFC activity and a greater activation parahippocampus in paranoid schizophrenia.
Carter et al. (1997)	14 patients with schizophrenia 15 healthy subjects	Stroop task	PET	Lower anterior cingulate gyrus activation.
Weinberger et al. (1986)	20 medication-free patients with chronic schizophrenia 25 healthy subjects	WCST	133-xenon rCBF	Deficits in DLPFC activation.
Hoptman et al. (2002)	14 male inpatients with schizophrenia	BIS-11	DTI	Right inferior frontal white matter microstructure of was associated with impulsivity.

ACC: anterior cingulate cortex; BIS-11: Barratt Impulsiveness Scale-Version 11; CPT: Continuous performance test (another version of the Go/No-Go task); DLPFC: dorsolateral prefrontal cortex; DTI: Axial Diffusion Tensor Images; ERP: Event-related potential; PET: positron emission tomography; VBM: voxel-based morphometry; VLPFC: ventrolateral prefrontal cortex; WCST: Wisconsin Card Sorting Test.

8. Conclusion

In recent years, there have been several investigations supporting the notion that impulsivity may play a central role in the pathogenesis of schizophrenia. Researchers have differed in their definitions and conceptualizations of impulsivity as well as in their tools of assessment. The vast majority of studies so far support the view that impulsivity is a multi-faceted behavioral trait and that proper measurement of impulsivity in schizophrenia can be critical for treatment planning and patient management. Clearly, impulsivity has important effects on a patient's behavior. The association among impulsivity, substance use, aggression, and violence is well documented. However, more research is required to evaluate the association between impulsivity and suicide. Therefore, the amelioration of impulsivity is an important factor in the treatment of these conditions.

In terms of neurological deficits, experimental paradigms integrating neuropsychological testing with data from neuroimaging techniques (e.g., PET, 133-xenon rCBF, structural MRI and fMRI), provide evidence of the relationship between the deficits in DLPFC, VLPFC and ACC activation and impulsivity. There is also preliminary evidence to suggest deficits in the thalamic and striatum nuclei and hippocampus. Despite recent advances in neuroimaging, continued progress will require targeted a combination of neuroimaging techniques and neuropsychological task to deliver many insights into our understanding of impulsivity in schizophrenia and consider their potential application in clinical practice. Taking together, these results suggest that patients with schizophrenia benefit from a multidisciplinary approach to managing their problem of impulsivity.

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