Risk factors for violent behaviour in psychotic disorders: Substance use and cognition

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Abstract

Background People with psychotic disorders are at increased risk of violent behaviour. One of the most robust risk factors is problematic substance use. However, the effects of pharmacologically different categories of illicit substances (e.g. stimulants, hallucinogens) and nonproblematic use on violence risk remain unclear. Impairments in executive functions and mentalizing abilities – a key feature of psychotic disorders – are hypothesized to underly violent behaviour. However, the few studies investigating this hypothesis have produced conflicting results and used composite measures of executive functions. Additionally, previous studies have been limited by reliance on selective samples of male inpatients or prisoners and criminal records for the measurement of violence.

Methods Data came from Genetic Risk and Outcome of Psychosis, a multi-centre project in the Netherlands. Patients with psychotic disorders (*N* = 891) were recruited at various care settings (e.g. psychiatric hospitals, outpatient clinics) in geographically representative areas of the country. Problematic and nonproblematic use of alcohol, cannabis, stimulants, depressants and hallucinogens at any point in life were ascertained using the Composite International Diagnostic Interview-Substance Abuse

Module. Neuropsychological tests were used to measure inhibition (Continuous Performance Test-HQ), cognitive flexibility (Response Shifting Task), fluid intelligence (Wechsler Adult Intelligence Scale-Third Edition [WAIS-III] Block Design subtest), planning (Neuropsychological Assessment Battery Mazes Test) and cognitive (Hinting Task) and affective (Degraded Facial Affect Recognition Task) mentalization. Lifetime violent behaviour was recorded with the Life Chart Schedule based on patient and parent interviews and case notes. In two studies, I investigated the associations of violence with: (i) problematic and nonproblematic use of each substance category using logistic regression; and (ii) performance on each neuropsychological test using analysis of covariance. All analyses were adjusted for age and gender.

Results Problematic and nonproblematic use increased the odds of violent behaviour between 20% and 100% across substance categories. The increases were significant for problematic use of alcohol (adjusted odds ratio [aOR] 1.7, 95% confidence interval [CI] [1.0, 1.3]), stimulants (aOR 2.0, 95% CI [1.3, 3.0]) and depressants (aOR 2.0, 95% CI [1.0, 3.9]), and nonproblematic use of hallucinogens (aOR 2.0, 95% CI [1.3, 3.1]). Violence accounted for 1% or less of the variance in performance across neuropsychological tests. Violent patients performed significantly worse than non-violent patients on the WAIS-III Block Design subtest (F [1, 847] = 5.1, p = .024) and Hinting Task (F [1, 839] = 9.4, p = .002).

Conclusions Problematic and nonproblematic use of all substance categories increase violence risk, which needs consideration in risk assessment and prevention. The small effect sizes suggest that deficits in fluid intelligence and cognitive mentalizing ability mainly have theoretical relevance. Future studies may improve our understanding of causal mechanisms with prospective designs and tests of additional possible confounders (e.g. genetics, childhood maltreatment) and mediators (e.g. treatment nonadherence, unemployment).

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1 Introduction

As described in the Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-5; American Psychiatric Association [APA], 2013), psychotic disorders (e.g. schizophrenia, schizoaffective disorder, delusional disorder) are characterized by delusions, hallucinations, disorganized thinking and motor behaviour, and negative symptoms (e.g. diminished emotional expression, avolition, anhedonia). Although not fully understood, pathogenesis likely involves both biological (e.g. genetics, neurobiological abnormalities) and environmental (e.g. stressful life events, premorbid substance use) factors (Mäki et al., 2005). Despite a lifetime prevalence of just under 1% (Moreno-Küstner, Martín & Pastor, 2018), psychotic disorders are among the most debilitating (Rosenheck et al., 2006) and expensive (Korver et al., 2012) mental disorders.

Epidemiological studies conducted since the 1990s have established that psychotic disorders increase risk of violent behaviour (e.g. Appelbaum, Robbins & Monahan, 2000; Brennan, Mednick & Hodgins, 2000; Fazel, Grann, Carlström, Lichtenstein &

Långström, 2009; Swanson et al., 2006; Tiihonen, Isohanni, Räsänen, Koiranen & Moring, 1997; Van Dorn, Volavka & Johnson, 2012). Lifetime prevalence estimates of violence in patients range between 11% and 22% (Corrigan & Watson, 2005; Fazel, Grann et al., 2009; Fazel, Wolf, Palm & Lichtenstein, 2014; Mullen, Burgess, Wallace, Palmer & Ruschena, 2000; Tiihonen et al., 1997). In a study using a large population-based sample of patients with psychotic disorders (*N* = 24,297), the lifetime prevalence of violent crime was estimated at 23% in men and 5% in women (Fazel et al., 2014). Risk estimates differ widely, with studies reporting up to 7-fold increases in violent behaviour in patients compared with unaffected controls (Bo, Abu-Akel, Kongerslev, Haahr & Simonsen, 2014; Douglas, Guy & Hart, 2009; Fazel, Gulati, Linsell, Geddes & Grann, 2009). A meta-analysis of 20 studies with a total of 18,423 cases found that psychotic disorders were associated with an odds ratio (OR) for violence of 4.0 (95% confidence interval [CI] [3.0, 5.3]) in men and 7.9 (95% CI [4.0, 15.4]) in women (Fazel, Gulati et al., 2009). Estimates of population attributable risk vary from 3% to 10% (Fazel, Gulati et al., 2009; Walsh, Buchanan & Fahy, 2002).

Violent behaviour in psychotic disorders is a costly phenomenon. It increases costs of mental health care as a cause of involuntary commitment, extended hospital stays and disproportionate consumption of staff time (Volavka, 2013). Additional costs are imposed on the criminal justice system (e.g. pretrial investigation, adjudication, jail and prison). For example, the annual costs of violent crime committed by people with schizophrenia in the U.S. are approximately $3.5 billion (Wyatt, Henter, Leary & Taylor, 1995). Another study estimated that the costs of criminal justice involvement

for assault, robbery, rape and homicide constitutes almost half of the total healthcare costs incurred by schizophrenia patients each year (Ascher-Svanum, Nyhuis, Faries, Ball & Kinon, 2010). The issue of costs is underlined by studies showing that prisoners with mental disorders are incarcerated longer and pose more management problems than other prisoners (e.g. Adams & Ferrandino, 2008; Torrey, Kennard, Eslinger, Lamb & Pavle, 2010) and rates of mental disorders in prisoners are higher than in the general population (e.g. Dudeck, Kopp & Kuwert, 2009; Falissard, Loze, Gasquet, Duburc & de Beaurepaire, 2006). In a meta-analysis, which contained information from 74 studies and 30,635 prisoners, the 6-month prevalence of psychotic disorders was nearly 4% (Fazel & Seewald, 2012).

Numerous factors have been proposed to account for the increased risk of violent behaviour in psychotic disorders. These predominantly relate to sociodemographic (e.g. male gender, young age, low socioeconomic status) and clinical (e.g. delusions and hallucinations, deficient insight, problematic substance use) features (Lamsma & Harte, 2015). However, studies examining potential risk factors have produced conflicting results. In a meta-analysis of a total of 110 studies and 45,533 individuals with psychotic disorders, the following factors were significantly associated with violence: a criminal history, positive symptoms (e.g. delusions, hallucinations, conceptual disorganization), treatment nonadherence, lack of insight, impulsivity and problematic substance use (Witt, Van Dorn & Fazel, 2013).

Problematic substance use is perhaps the most robust risk factor for violent behaviour in psychotic disorders (Elbogen & Johnson, 2009; Fazel, Långström, Hjern,

Grann & Lichtenstein, 2009; Volavka & Swanson, 2010). This may be unsurprising given the high rates of problematic substance use in patients (Winklbaur, Ebner, Sachs, Thau & Fischer, 2006) and that problematic substance use has been shown to increase violence risk in the general population (Tomlinson, Brown & Hoaken, 2016). However, the effects of pharmacologically different substance categories (e.g. stimulants, depressants, hallucinogens) and nonproblematic use on violence risk in psychotic disorders remain unclear. These are relevant avenues of inquiry, as the pharmacological effects of substances may modify associations with violent behaviour (Miles et al., 2003; Smith, Homish, Leonard & Cornelius, 2012) and people with psychotic disorders are highly sensitive to the effects of substances (Gregg, Barrowclough & Haddock, 2007).

People with psychotic disorders often display impairments in executive functions (e.g. attention, planning) and mentalization (e.g. the ability to infer other people's thoughts or emotions), which are believed to underly violent behaviour (Adshead, Moore, Humphrey, Wilson & Tapp, 2013; Fabian, 2010). However, the effects of specific executive functions and mentalizing abilities on violence risk in psychotic disorders are largely unknown.

In terms of methodology, previous studies have been limited by samples drawn from psychiatric hospitals or prisons. Such samples are inappropriate for making inferences about the entire population of individuals with psychotic disorders. After all, many are never hospitalized or imprisoned (Walsh et al., 2002). Furthermore, patients who are hospitalized or imprisoned may differ in relevant aspects (e.g.

symptomatology, problematic substance use, cognition) from those who are not (Lamsma & Harte, 2015).

Another methodological limitation of earlier studies is the prevailing use of criminal records to measure violent behaviour. For various reasons, criminal records underestimate the true prevalence of violence. Many victims fail to report violent crimes because they believe the police are unable or unwilling to help, feel ashamed, fear reprisal or want to protect a known perpetrator (e.g. spouse, child) from possible legal consequences (Langton, Berzofsky, Krebs & Smiley-McDonald, 2012). In Western countries, at least one third of all violent crimes is thought to go unreported (Yoon, 2015). Even fewer reported violent crimes result in convictions. The police may not record the crime or identify a suspect and, if they do, the suspect may not be charged or found guilty in a subsequent trial (Charette & van Koppen, 2016). To illustrate, a suspect was charged in only 1 out of 10 cases of violent crime recorded by the police in England and Wales in 2017 (Home Office, 2018). Underreporting and underrecording may be particularly relevant for violent behaviour in psychotic disorders. Victims are usually family members or friends who may wish to avoid criminal action brought against their loved one (Nordström & Kullgren, 2003; Stuart, 2003). In addition, violent crimes committed by individuals with psychotic disorders may routinely be dealt with outside the criminal justice system (Hodgins, 2008). The most commonly used data sources after criminal records are patients themselves, collateral informants (e.g. family, friends) and case notes. Of course, information from each of these data sources may be incomplete or selective as well: reports of patients

are affected by social desirability and biased recall; collateral informants have conflicting interests and may be ignorant of violent incidents; and only information relevant for the patient's clinician is recorded in case notes. Therefore, it is preferable to use data sources in combination (Lamsma & Harte, 2015).

The identification of risk factors for violent behaviour in psychotic disorders facilitates the development and improvement of: (i) interventions to prevent violence in patients in regular and forensic mental healthcare; (ii) risk assessment tools for targeting at-risk patients for interventions and informing involuntary admission, sentencing and release decisions; and (iii) evaluations by mental health professionals in civil and criminal cases concerning, among other things, the patient's degree of culpability and risk for future violent behaviour. These are essential steps to prevent violence in people with psychotic disorders and harm to future victims and their families, and decrease its financial burden on society.

The joint purpose of the two studies undertaken for this MRes is to address the substantive and methodological limitations of previous studies mentioned above. To that end, I have used a nationally representative sample of patients with psychotic disorders to investigate the associations of a sensitive marker of violent behaviour with: (i) problematic and nonproblematic use of substances categorized by their pharmacological properties (study I); and (ii) performance on an extensive set of neuropsychological tests measuring specific executive functions and mentalizing abilities (study II).

2 | Research setting, definition and measurement of violent behaviour and sample characteristics

2.1. Research setting

Data were collected as part of a larger research project, called Genetic Risk and Outcome of Psychosis (GROUP). Started in 2004, the main aims of GROUP are the elucidation of the interaction between biological, psychological and environmental risk factors and description of courses and outcomes in psychotic disorders. GROUP is conducted by the psychiatry departments of 4 university medical centres and their affiliated mental health centres (k = 36) in the Netherlands. These institutions are located in representative geographical areas of the country and provide mental health care in a variety of settings (e.g. psychiatric hospitals, residential facilities, outpatient clinics) to approximately 75% of the population. Assessments took place at baseline, and after 3 and 6 years of follow-up.

Eligible patients were identified by screening clinicians' caseloads for the following criteria: (i) age between 16 and 50; (ii) good command of the Dutch language; and (iii)

a DSM-IV (APA, 2000) diagnosis of schizophrenia or other psychotic disorder. In accordance with standard local practice, diagnoses were made with the Comprehensive Assessment of Symptoms and History (Andreasen, Flaum & Arndt, 1992) or Schedules for Clinical Assessment for Neuropsychiatry 2.1 (Wing et al., 1990). The DSM-IV category of "schizophrenia and other psychotic disorders" encompasses all mental disorders with psychotic symptoms as the defining feature (e.g. schizophrenia, schizoaffective disorder, psychotic disorder due to a general medical condition). Hence, patients diagnosed with mental disorders that may present with psychotic symptoms but not as the defining feature (e.g. dementia of the Alzheimer's type, substance use-induced delirium, bipolar disorder with psychotic features) were excluded (APA, 2000). For the sake of brevity, I will refer to "schizophrenia and other psychotic disorders" as "psychotic disorders" throughout.

The protocol was approved centrally by the ethics committee of the university medical centre Utrecht. All patients gave written informed consent before the first assessment.

2.2. Definition and measurement of violent behaviour

Violent behaviour was measured with the Life Chart Schedule (Susser et al., 2000). Designed to record the long-term development of symptoms and health care needs and consumption in patients with schizophrenia, the LCS contains the following

question regarding violence: "Did the patient physically attack or abuse someone else?" Responses were coded as "yes" or "no", making violent behaviour a dichotomous variable. The LCS covered the lifetime at baseline and the previous 3 years at each follow-up. Statistical power was deemed too low to perform meaningful prospective analyses because of: (i) the small number of patients with violent behaviour at follow-up; (ii) division of patients by substance categories in study I; and (iii) the small effect sizes observed in study II. The LCS was filled out based on an interview with the patient, collateral sources of information (i.e. one or both parents) and review of case notes. The interrater reliability of the LCS is fair to excellent (Susser et al., 2000).

2.3. Sample characteristics

Demographic and clinical characteristics of patients at baseline (*N* = 891) are presented in Table 1. Most patients were male (*n* = 688, 77%), had received a primary diagnosis of schizophrenia (*n* = 615, 69%) and had been admitted to a psychiatric hospital at least once in their lives (*n* = 683, 79%).

Lifetime prevalence of violent behaviour was 21% (*n* = 183). This estimate is higher than those reported in most previous studies and likely reflects the combined use of patient interviews, collateral information and case notes instead of criminal records for data collection (see Introduction).

3 Study I: Substance use and violent behaviour in psychotic disorders

3.1. Introduction

3.1.1. Psychoactive substances

The term "psychoactive substance" refers to any substance that affects mental processes (e.g. cognition, affect) when ingested (World Health Organization [WHO], 2018). For the sake of brevity, I will use the term "substance" instead of "psychoactive substance" henceforth.

Depending on their primary pharmacological effects, substances can be classified as stimulants, depressants or hallucinogens. Stimulants increase the activity of the central nervous system by releasing or inhibiting the reuptake or metabolism of catecholamines (e.g. epinephrine, norepinephrine, dopamine) or serotonin (Hill & Thomas, 2016). Examples of stimulants are cocaine, amphetamine and methamphetamine (Hill & Thomas, 2016). Depressants decrease central nervous

system activity (WHO, 2009). Many depressants act as agonists or positive allosteric modulators of γ-aminobutyric acid type A receptors (Christian et al., 2013; Davies, 2003; Rudolph & Knoflach, 2011). Examples of depressants are alcohol, benzodiazepines (e.g. diazepam, temazepam, alprazolam), barbiturates (e.g. phenobarbital, amobarbital, aprobarbital) and opioids (e.g. heroin, morphine, methadone) (Hill & Thomas, 2016). Hallucinogens alter thought, perception and mood (López-Giménez & González-Maeso, 2018). The pharmacological property shared by most hallucinogens is binding affinity or agonist activity at serotonin 5-HT_2 receptors (Canal & Murnane, 2017). Examples of hallucinogens are lysergic acid diethylamide, mescaline and phencyclidine (PCP) (Hill & Tomas, 2016).

Many substances have pharmacological properties in more than one category. A notable example is cannabis, which can produce stimulant, depressant and hallucinogenic effects (Zeiger et al., 2010). The primary psychoactive component of cannabis is Δ^9-tetrahydrocannabinol, an agonist that binds to cannabinoid receptors (Hill & Thomas, 2016).

3.1.2. Problematic substance use in psychotic disorders

Problematic substance use is more prevalent in people with psychotic disorders than in the general population (Gregg et al., 2007). Lifetime prevalence estimates of comorbid substance use disorder in psychotic disorders range from 20% to 60%

(Lambert et al., 2005). In contrast, lifetime prevalence of substance use disorder in the general population has been estimated at 7% (Merikangas & McClair, 2012). Problematic use of alcohol and cannabis are most common (Gregg et al., 2007). However, higher rates of problematic use have been reported for other substance categories (e.g. hallucinogens [Barnett et al., 2007], amphetamine [Lambert et al., 2005], stimulants [Curran, Byrappa & McBride 2004], heroin [Farrell et al., 2002]) as well. A recent study in the United States, using a large population-based sample of patients with psychotic disorders (*n* = 9,142), reported between 3- and 5-fold increases in the odds of lifetime problematic use of alcohol (OR 4.0, 95% CI [3.6, 4.4]), cannabis (OR 3.5, 95% CI [3.2, 3.7]) and other substances (OR 4.6, 95% CI [4.3, 5.0]) in comparisons with unaffected controls (*n* = 10,194) (Hartz et al., 2014). Problematic substance use in psychotic disorders is associated with poor clinical and functional outcomes, including relapse (Olivares, Sermon, Hemels & Schreiner, 2013), frequent and long periods of psychiatric hospitalization (Manrique-Garcia et al., 2014), treatment nonadherence (Higashi et al., 2013), early mortality (Hartz et al., 2014), homelessness (Winklbaur et al., 2006), low educational attainment (Kavanagh et al., 2004) and imprisonment (Wallace, Mullen & Burgess, 2004).

3.1.3. Substance use and violent behaviour

Substance use is a well-established risk factor for violent behaviour in the general population (Boles & Miotto, 2003; Hoaken & Stewart, 2003). A recent meta-meta-analysis, which synthesized the results of a total of 20 meta-analyses of studies estimating the association between substance use and violence perpetration, found significant associations with medium effect sizes for alcohol (d = 0.39, 95% CI [0.32, 0.47]) and illicit substances (d = 0.42, 95% CI [0.32, 0.53]) (Duke, Smith, Oberleitner, Westphal & McKee, 2018).

The relationship between substance use and violent behaviour has most often been explained with the conceptual framework proposed by Goldstein (1985). According to this framework, there are three basic pathways from substance use to violence. First, certain psychopharmacological effects (e.g. hyperalgesia, disinhibition, intensification of negative emotions) of acute or chronic intoxication with or withdrawal from substances may increase the likelihood of violent behaviour. Second, violence may occur when users commit crimes (e.g. theft, robbery, burglary) to gain access to substances or the money to buy them. This mainly applies to users with an addiction. Finally, users may become involved in illegal drug markets where violent behaviour is commonplace for various reasons (e.g. territorial disputes, debt collection, enforcement of organizational rules). Violence resulting from these pathways is called "psychopharmacological violence", "economic-compulsive violence" and "systemic violence", respectively.

The causal mechanisms underlying the association between substance use and violent behaviour likely differ by substance category. The substance categories most often implicated in psychopharmacological violence – via acute and chronic intoxication and withdrawal – are cocaine, amphetamine, methamphetamine, alcohol and benzodiazepines (Boles & Miotto, 2003; Hoaken & Stewart, 2003; Tomlinson et al., 2016). Psychopharmacological violence in opioid users has usually been linked to withdrawal (Tomlinson et al., 2016). Economic-compulsive and systemic violence typically involve controlled substances with high street prices, in particular cocaine and heroin (Sarrica, 2009). There is little evidence to suggest that hallucinogens are related to violent behaviour (Hoaken & Stewart, 2003; Tomlinson et al., 2016).

Cannabis is increasingly recognised for its adverse effects on mental health and social functioning (Ramesh, Schlosburg, Wiebelhaus & Lichtman, 2011). Examples are dependency and withdrawal, an elevated risk of developing a mental illness (e.g. psychotic disorder, depressive disorder) in predisposed individuals, deficits in executive functions (e.g. attention, working memory), and educational failure (Volkow, Baler, Compton & Weiss, 2014). Correspondingly, studies have started to challenge the long-held belief that cannabis use does not increase violence risk (Tomlinson et al., 2016). In regard to psychopharmacological violence, there is tentative support for associations with acute (e.g. Haggård-Grann, Hallqvist, Långström & Möller, 2006; Howard & Menkes, 2007) and chronic (e.g. Dugré, Dellazizzo, Giguère, Potvin & Dumais, 2015; Wrege et al., 2014) cannabis intoxication. However, studies of psychopharmacological violence have been most consistent in

showing an association with withdrawal (e.g. Budney, Moore, Vandrey & Hughes, 2003; Lee et al., 2014; Smith, Homish, Leonard & Collins, 2013). Cannabis trafficking is also an important contributor to systemic violence (Kuhns & Clodfelter, 2009).

There are other explanations for the relationship between substance use and violent behaviour than those discussed above. To start, the relationship may be confounded by biological, psychological and environmental risk factors. Examples of biological factors are genetic (Dick & Agrawal, 2008) and neurobiological (e.g. hypofunction in the orbitofrontal cortex [Siever, 2008], low cerebrospinal fluid concentrations of the serotonin metabolite 5-hydroxyyindoleacetic acid [Moberg et al., 2011]) susceptibilities. Psychological factors include impairments in cognitive functions (e.g. attention, planning [Ersche et al., 2012]), and personality traits (e.g. impulsivity [Kotov, Gamez, Schmidt & Watson, 2010], sensation seeking [Hoaken & Stewart, 2003]) and disorders (e.g. antisocial personality disorder, psychopathy [Taylor & Lang, 2006]). Examples of environmental factors are childhood abuse (Moore & Stuart, 2005), low socioeconomic status (Karriker-Jaffe, 2011) and exposure to criminogenic environments (Mennis, Stahler & Mason, 2016). Some environmental factors, such as homelessness (McNiel, Binder & Robinson, 2005), difficulty finding and maintaining employment (Henkel, 2011), and erosion of social support (Moore & Stuart, 2005), may mediate the relationship between substance use and violence. It is also possible that violent behaviour precedes substance use: people with violent tendencies in childhood or adolescence have been shown to be more likely to use substances in adulthood than those without (Kuhns & Clodfelter, 2009). Finally, the

strength and nature of the association between substance use and violence may depend on other individual-level (e.g. gender, experience, body weight) and substance-level (e.g. dosage, purity, pharmacokinetic interactions) factors (Boles & Miotto, 2003; Kuhns & Clodfelter, 2009).

3.1.4. Substance use and violent behaviour in psychotic disorders

Problematic substance use is one of the most robust risk factors for violent behaviour in psychotic disorders (Douglas et al., 2009; Fazel, Gulati et al., 2009; Witt et al., 2013). A meta-analysis reported that a history of problematic substance use more than doubled the odds of violence (OR 2.2, 95% [CI 1.6, 2.9]) in individuals with psychotic disorders (*N* = 5,365) (Witt et al., 2013).

Debate continues on whether psychotic disorders without problematic substance use are actually associated with violent behaviour (Volavka & Swanson, 2010). This debate has largely been driven by the influential MacArthur study, which found no significant difference between the rate of violence during the first year after discharge from a psychiatric hospital in patients diagnosed with a major mental disorder (e.g. schizophrenia, bipolar disorder) without co-occurring symptoms of substance abuse or dependence (*n* = 266) and the rate of violence during the past 10 weeks in healthy controls living in the same neighbourhoods (*n* = 519) (Steadman et al., 1998). However, more recent studies with large population-based samples have consistently

reported that the association between psychotic disorders and violent behaviour remains significant after controlling for problematic substance use (e.g. Coid et al., 2006; Short, Thomas, Mullen & Ogloff, 2013; Swanson et al., 2008; Van Dorn et al., 2012). A meta-analysis also found a significant increase in the odds of violence (OR 2.1, 95% CI [1.7, 2.7]) in people with psychotic disorders without comorbid substance abuse or dependence (*N* = 2,981) compared with unaffected controls (Fazel, Gulati et al., 2009).

There are two important uncertainties regarding the relationship between substance use and violent behaviour in psychotic disorders. The first is the extent to which categories of illicit substances modify violence risk: nearly all studies have grouped illicit substances together despite their diverse pharmacological properties.

The second uncertainty regards the effect of nonproblematic use on violence risk. Owing to a combination of high stress reactivity, poor impulse control and social adversity, people with psychotic disorders are sensitive to the harmful effects of substances (Gregg et al., 2007). Thus, it may be hypothesized that nonproblematic use increases violence risk. Preliminary findings suggest that this is the case (Swanson et al., 2006; Swanson et al., 2008). Additional support for this hypothesis comes from studies reporting adverse clinical outcomes, such as treatment nonadherence (Desmarais, Van Dorn, Sellers, Young & Swartz, 2013) and rehospitalization (Cantor-Graae, Nordström & McNeil, 2001), in patients with nonproblematic use.

Problematic alcohol use has consistently been shown to increase violence risk (e.g. Coid et al., 2006; Räsänen et al., 1998; Tiihonen et al., 1997). In a meta-analysis of 19

studies, individuals with psychotic disorders (*N* = 18,549) were found to be more than twice as likely to be violent when they had a history of alcohol misuse (OR 2.3, 95% CI [1.7, 3.3]) (Witt et al., 2013). I am aware of only one study that has investigated nonproblematic use of alcohol. Using a sample of 963 patients with schizophrenia across 10 countries, this study reported a nonsignificant association between moderate alcohol use during the past year and a lifetime history of assault (risk ratio [RR] 1.02, 95% CI [0.66, 1.55]) (Volavka et al., 1997). However, the association may have been attenuated by the discrepancy in reference periods and the inclusion of patients with "occasional use" in the comparison group. The effects of other substances on violence risk are largely unknown. The few studies of cannabis (e.g. Harris et al., 2010; Koen et al., 2004; Maremmani et al., 2004) and stimulants (e.g. Bell, Greig, Gill, Whelahan & Bryson, 2002; Harris et al., 2010; Miles et al., 2003) have produced mixed results. Moreover, these studies have been limited by the use of small samples of male inpatients and proxy measures of violent behaviour (e.g. hostility, aggression). The abovementioned meta-analysis reported a nonsignificant association between a history of cannabis misuse and violence (OR 1.3, 95% CI [0.7, 2.4]) (Witt et al., 2013). However, only 4 studies with a total of 315 participants were included. To my knowledge, there have been no studies of depressants (besides alcohol) or hallucinogens.

Substances may exert different effects on violence risk in people with psychotic disorders than in the general population. Some substance categories, most notably stimulants, hallucinogens and cannabis, may induce or exacerbate delusions and

hallucinations (Bramness & Rognli, 2016; Paparelli, Di Forti, Morrison & Murray, 2011; Tang, Martin & Cotes, 2014). Cannabis deserves special attention, as it has comparatively high rates of use and has been found to increase the risk of developing a psychotic disorder and adversely affect prognosis of psychotic disorders (Manrique-Garcia et al., 2014). Furthermore, substance use may interfere with treatment in several ways. First, individuals with problematic substance use are less likely to seek and adhere to treatment than those without (Winklbaur et al., 2006). Second, substances may be used in an attempt to alleviate psychotic symptoms or side effects of antipsychotics (e.g. akathisia, dysphoria) (Gregg et al., 2007). Self-medication increases the likelihood of avoidance and discontinuation of treatment and *vice versa* (Swartz et al., 1998). Finally, substances may reduce the therapeutic activity of antipsychotics (Lindsey, Stewart & Childress, 2012). In the absence of effective treatment, delusions and hallucinations may persist or worsen.

3.2. Methods

3.2.1. Definition and measurement of substance use

The Substance Abuse Module of the Composite International Diagnostic Interview (CIDI-SAM) (WHO, 1990) was used to record the severity (i.e. problematic use, nonproblematic use, no use) and frequency (i.e. daily use, nondaily use, no use) of

lifetime substance use at baseline. The CIDI-SAM differentiates between the following categories of substances: (i) alcohol; (ii) cannabis; (iii) cocaine; (iv) stimulants; (v) sedatives (e.g. diazepam, ϒ-hydroxybutyric acid); (vi) opioids; (vii) PCP; (viii) hallucinogens; (ix) inhalants (e.g. toluene, benzene); and (x) other substances (e.g. amyl nitrite, ecstasy). Based on statistical power considerations and similarities in pharmacological properties, I combined cocaine and stimulants as "stimulants", sedatives, opioids and inhalants as "depressants", and PCP and hallucinogens as "hallucinogens" (cf. Hill & Thomas, 2016). Alcohol and cannabis were treated separately because of the high prevalence of use of these substances. I defined problematic alcohol use as an average intake of more than 18 standard drinks per week for men and more than 12 standard drinks per week for women during a minimum period of 2 weeks in the past year or 4 weeks at any other point in the past. These cutoffs were chosen based on the median of several national guidelines and a consistent 1.5:1 male to female consumption ratio (Furtwaengler & de Visser, 2013). For other substances, patients were recorded as having problematic use if they had received a DSM-IV diagnosis of abuse or dependence. These diagnoses were combined to increase statistical power and consistency with the DSM-5 diagnosis of substance use disorder. Frequency of use, which was unavailable for alcohol, referred to the most intensive period of use. The cross-cultural acceptability and interrater reliability of the CIDI-SAM have been found to be high (Cottler, Robins & Helzer, 1989).

3.2.2. Statistical analysis

I used logistic regression to estimate the lifetime associations between substance use and violent behaviour. Problematic and nonproblematic use served as the exposures of interest and violent behaviour as the outcome of interest. The analyses were stratified by substance category. For each substance category, I made three comparisons: (i) problematic use *vs* nonproblematic and no use; (ii) problematic use *vs* no use; and (iii) nonproblematic use *vs* no use. Based on theory, I included the potential confounders age (Lamsma & Harte, 2015), gender (Erkiran et al., 2006) and educational level (Hodgins, 2008) as exposures of no interest. Educational level, which indicated whether a patient had finished secondary school, was used as a proxy for socioeconomic status (Maksimović et al., 2008). A confounder was defined as a variable that: (i) is assumed to cause both the exposure of interest and the outcome; and (ii) does not lie on the causal pathway between the two (Cole & Hernán, 2002). I examined frequency of use in sensitivity analyses. To improve validity, I only included models with at least 10 observations per cell in corresponding 2x2 tables (Vittinghof & McCulloch, 2007). The level of statistical significance was set at 5%. Except where otherwise stated, analyses were carried out in SPSS (version 21.0).

Logistic regression makes the following assumptions: (i) the outcome is binary; (ii) the observations are independent; (iii) each continuous exposure has a linear relationship with the log odds of the outcome; (iv) the exposures are not linear combinations of each other (i.e. multicolinear); and (v) there are no overly influential

observations (Tabachnick & Fidell, 2007). As explained in the previous chapter, violent behaviour was a binary variable. The observations can reasonably be assumed to be independent: an independent group design was used and, although patients were recruited and assessed at different locations, the staff that administered the instruments underwent extensive training to maximize uniformity in assessments. The assumption that each continuous exposure is linearly related to the log odds of the outcome was assessed using locally weighted scatterplot smoothing (LOWESS) (bandwidth 0.8) in STATA (version 12.0). Since the linearity assumption applies to continuous exposures, this was only done for age. The LOWESS curve showed an acceptably linear relationship between age and the log odds of violent behaviour. Severe multicolinearity was said to be present if: (i) the correlation coefficient between two exposures had an absolute value of .7 or higher (Dormann et al., 2013); or (ii) the coefficient of the exposure of interest or its standard error was unstable (Vatcheva, Lee, McCormick & Rahbar 2016). The point-biserial correlation coefficient (r_{pb}) was used to calculate the correlation of the binary exposures (i.e. substance use, gender, education) with the continuous exposure (i.e. age). The correlations between the binary exposures were calculated with the phi coefficient (Φ). For all pairs of exposures, $|r_{pb}|$ and |Φ| were below .4. The coefficients for substance use and their standard errors changed negligibly after removing age, gender and educational level from the models. Hence, multicolinearity was of no concern. I used DfBeta as a measure of influence (Belsley, Kuh & Welsch, 1980). An observation was considered to exert undue influence on a coefficient for substance use if: (i) the DfBeta was

disproportionally large; or (ii) the standardized DfBeta had an absolute value higher than 1 (Verkoeijen, Polak & Bouwmeester, 2018). No such observations were found. The scatter plots of DfBeta's versus patients showed no outliers and the absolute values of the standardized DfBeta's were below 0.3.

3.3. Results

Table 2 shows the adjusted odds ratios (aORs) of violent behaviour given problematic and nonproblematic use of each substance category. Relative to patients with nonproblematic or no use, the odds of violence were significantly increased in patients with problematic use of alcohol (aOR 1.5, 95% CI [1.1, 2.1]), stimulants (aOR 1.8, 95% CI [1.2, 2.7]) and depressants (aOR 1.9, 95% CI [1.0, 3.7]). The aORs for the remaining substance categories were also increased but nonsignificant (range: 1.3–1.5). The results were similar when comparing problematic use with no use. Nonproblematic use increased the odds of violent behaviour for all categories of substances, but only significantly for hallucinogens (aOR 2.0, 95% CI [1.3, 3.1]).

The results of the sensitivity analyses were consistent with those of the primary analyses. Notable differences were the significant aORs for daily use of hallucinogens compared with nondaily and no use combined (aOR 1.9, 95% CI [1.3, 2.9]) and no use alone (aOR 1.9, 95% CI [1.3, 3.0]) (Table 3).

3.4. Discussion

In 891 patients with psychotic disorders, I have analysed lifetime associations of violent behaviour with problematic and nonproblematic use of different substance categories. Problematic and nonproblematic use of all substance categories increased the odds of violence. The increases were significant for problematic use of alcohol, stimulants and depressants, and nonproblematic use of hallucinogens.

Overall, the findings suggest that problematic and nonproblematic use of all categories of substances increase violence risk in psychotic disorders. A few exceptions merit discussion: nonproblematic alcohol use, problematic hallucinogen use and problematic cannabis use. High base rates may explain the nonsignificant aORs for nonproblematic alcohol use and problematic cannabis use. It is likely that the aORs for problematic hallucinogen use were rendered nonsignificant by the small number of patients with diagnoses of abuse or dependence, which are rare (Halpern, Suzuki, Huertas & Passie, 2014). The significant aORs for nonproblematic and daily use of hallucinogens support this interpretation.

As outlined in the introduction, there are at least six ways in which substance use may increase risk of violent behaviour in psychotic disorders: (i) mediation by psychopharmacological effects (e.g. hyperalgesia, disinhibition, triggering or aggravation of delusions and hallucinations) of acute or chronic intoxication with or withdrawal from substances; (ii) confounding or mediation by not receiving effective treatment; (iii) mediation by acquisitive offending to sustain an addiction; (iv)

confounding by biological factors (e.g. genetics, neurobiological abnormalities); (v) confounding by psychological factors (e.g. cognitive deficits, personality traits and disorders); and (vi) confounding or mediation by environmental factors (e.g. criminogenic exposure, childhood maltreatment, unemployment).

The current data do not support one explanation over another for any substance category. Nevertheless, a few hypotheses can be formulated. First, nonproblematic use increased violence risk for all substance categories. This suggests that violence in psychotic disorders is not entirely economic-compulsive in nature. Second, systemic violence is an unlikely explanation for alcohol because its production, sale and use are decriminalized. Finally, the finding that hallucinogen use increases violence risk contrasts with those of general population studies and points towards possible mediation by delusions and hallucinations.

3.4.1. Limitations

There are several limitations to this study. First, there has been a large increase in the use of novel psychoactive substances (NPS) in the years following data collection (Tracy, Wood & Baumeister, 2017). NPS are synthetic compounds designed to mimic the pharmacological effects of traditional substances (Miliano et al., 2016). Based on this and the assumption that the same causal mechanisms apply to NPS as traditional substances, I hypothesize that NPS increase violence risk. Second, I included patients

who used substances belonging to different categories. This may have affected some risk estimates. However, exclusion would have made cell counts too low for meaningful analyses of most substance categories. Finally, it is not possible to draw causal inferences, because the temporality of substance use and violent behaviour is unknown and I did not control for possible confounders other than age, gender and educational level.

3.4.2. Implications for clinical practice and recommendations for future studies

A practical implication of the findings is that use of any substance category, whether problematic or nonproblematic, deserves consideration in risk assessment. This contrasts with risk assessment tools commonly used to predict violence in people with psychotic disorders, such as the Historical Clinical Risk Management-20 (HCR-20) (Douglas, Hart, Webster & Belfrage, 2013), Violence Risk Appraisal Guide (VRAG) (Quinsey, Harris, Rice & Cormier, 2006) and UK700 (Wootton et al., 2008), which contain items for problematic use of selected substance categories. At the same time, it is unclear whether separate items for problematic and nonproblematic use of different substance categories add incremental validity to risk assessment tools with a single item for problematic use of any substance. Similarly, interventions often focus on problematic use and the findings indicate that interventions for both problematic

and nonproblematic use may be effective in preventing violent behaviour in people with psychotic disorders.

For future studies, I recommend even larger samples to isolate the effects of different substance categories on violence risk. Additionally, studies may improve our understanding of causal mechanisms by using prospective designs with short time frames between substance use and violent behaviour, and testing additional potential confounders (e.g. genetics, exposure to a criminogenic environment) and mediators (e.g. acquisitive offending, lack of effective treatment).

4 Study II: Cognition and violent behaviour in psychotic disorders

4.1. Introduction

4.1.1. Cognition

The construct of cognition encompasses all actions performed with the mind (i.e. mental operations) to acquire, store, transform, retrieve and use knowledge. Examples are perception, memory and reasoning (Brandimonte, Bruno & Collina, 2006). Two important domains of cognition are executive functions and social cognition. Executive functions are defined as mental operations needed to direct behaviour toward the realisation of goals (Miller & Wallis, 2009). In general, three elementary executive functions are distinguished: inhibition, working memory and cognitive flexibility (Diamond, 2013). Inhibition is the deliberate control of attention, thoughts, emotions and behaviour in overriding a prepotent response in favour of one that is more appropriate or effective (Bender, Filmer, Garner, Naughtin & Dux, 2016;

Diamond, 2013). Working memory allows the temporary storage and manipulation of information that is not perceptually present (Baddeley, 2003). Cognitive flexibility is the ability to change perspectives (Kloo, Perner, Aichhorn & Schmidhuber, 2010). It requires inhibition and working memory, as one perspective is kept in mind (i.e. working memory) and others are suppressed (i.e. inhibition) (Diamond, 2013). Inhibition, working memory and cognitive flexibility combine to build the higher order executive functions of fluid intelligence (i.e. the ability to solve novel problems independent of acquired knowledge) and planning (Diamond, 2013).

Social cognition refers to mental operations that underlie social behaviour (Couture, Penn & Roberts, 2006). One of the most oft-studied social cognitive functions is mentalization (Penn, Sanna & Roberts, 2008). Mentalization is the ability to infer mental states in oneself and others (Fonagy & Allison, 2012). Two forms of mentalization can be distinguished based on whether the mental state being inferred is cognitive (e.g. motivation, belief) or affective (e.g. feeling, mood) in nature: cognitive mentalization and affective mentalization, respectively (Shamay-Tsoory, Harari, Aharon-Peretz & Levkovitz, 2010).

4.1.2. Cognition in psychotic disorders

Although not included in the diagnostic criteria of the DSM-5 (APA, 2013) or the International Classification of Diseases (10th ed.; ICD-10; WHO, 1992), cognitive

impairment is considered a core feature of psychotic disorders (Kahn & Keefe, 2013). This applies to all executive functions and cognitive and affective aspects of mentalization (Brüne, 2005; Neuechterlein et al., 2004). In an umbrella review of 10 meta-analyses, individuals with schizophrenia were found to perform between 0.5 and 1.5 standard deviations below unaffected controls on neuropsychological tests of executive functions (Reichenberg & Harvey, 2007). Meta-analyses of mentalizing abilities have reported similar effect sizes (Bora, Yucel & Pantelis, 2009; Chung, Barch & Strube, 2014; Sprong, Schothorst, Vos, Hox & van Engeland, 2007).

Cognitive impairment is largely present before onset (Chung et al., 2014; Kahn & Keefe, 2013), independent of psychotic symptoms (Nieuwenstein, Aleman & de Haan, 2001; Sprong et al., 2007) and treatment with antipsychotic medication (Mishara & Goldberg, 2004; Reichenberg, 2011), and stable over time (Reichenberg, 2011). Furthermore, it is associated with adverse clinical and functional outcomes such as rehospitalization (Harvey, Loewenstein & Czaja, 2013), treatment nonadherence (Haddad, Brain & Scott, 2014), interpersonal difficulties (Zanello, Perrig & Huguelet, 2006), lack of independent living skills (Lepage, Bodnar & Bowie, 2014) and unemployment (Keefe, 2008).

4.1.3. Cognition and violent behaviour

General population studies have repeatedly found that people with violent behaviour perform worse on neuropsychological tests of executive functions (e.g. Baker & Ireland, 2007; Barker et al., 2007; De Brito, Viding, Kumari, Blackwood & Hodgins, 2013; Miura, 2009; Zhang, Wang, Liu, Song & Yang, 2017) and mentalizing abilities (e.g. Hoaken, Allaby & Earle, 2007; Nyline, Softas-Nall, Peterson, Peake & Woods, 2018; Schönenberg, Mayer, Christian, Louis & Jusyte, 2016) than those without. A meta-analysis of 126 studies involving 14,786 participants reported a significant inverse association between neuropsychological test performance and antisocial behaviour (including violence) across executive functions. This association had a medium effect size (d = .44, 95% CI [.41, .47]) (Ogilvie, Stewart, Chan & Shum, 2011). Further evidence comes from studies reporting increased rates of violence in mental disorders characterized by impairments in mentalization, namely autism spectrum disorder (Chung et al., 2014; Fitzpatrick, Srivorakiat, Wink, Pedapati & Erickson, 2006) and borderline personality disorder (Fonagy & Luyten, 2009; Leichsenring, Leibing, Kruse, New & Leweke, 2011). Impaired affective mentalization has been observed in two mental disorders associated with violent behaviour: antisocial personality disorder (Bateman, Bolton & Fonagy, 2013) and psychopathy (Blair, 2005).

Since executive functions and mentalizing abilities are essential for social adaptation, impairments in these cognitive functions are considered risk factors for violent behaviour (Adshead et al., 2013; Fabian, 2010). However, causal mechanisms

likely differ by executive function and mentalizing ability. Disinhibition may engender difficulty withholding a violent response that is inappropriate to the situation or jeopardizes long-term goals (Raine, 2008). Cognitive flexibility subserves the ability to adequately adjust one's behaviour in response to changes in the environment (Dajani & Uddin, 2015). When this ability is impaired, violent behaviour may persist despite repeated negative consequences (Fabian, 2010; Vilà-Balló et al., 2015). People with relatively low fluid intelligence may resort to violence as a maladaptive solution to difficult situations (Weiss, 2012). They may also experience a disproportionate amount of stress in such situations, which increases the likelihood of a violent response (Sandi & Haller, 2015). Planning deficiencies may give rise to violence by negatively affecting a person's ability to assess the possible consequences of his or her actions (Meijers, Harte, Meynen & Cuijpers, 2017). The relationship between working memory and violent behaviour is likely mediated by other executive functions (Diamond, 2013).

There are at least four ways in which impairments in mentalization may elicit violence. First, mentalization is necessary to understand and predict other people's behaviour (Baron-Cohen, Golan, Chakrabarti & Belmonte, 2008). Accordingly, people with poor mentalizing abilities may become violent by misinterpreting social cues. For example, they may incorrectly perceive a comment as threatening and strike out pre-emptively, fail to identify a high-risk situation or insufficiently recognise emotions in victims (Adshead et al., 2013; Weiss, 2012). Second, mentalization is important for affect regulation (Fonagy & Luyten, 2009). Underregulation of negative emotions,

such as anger and anxiety, lowers the threshold for violent behaviour (Roberton, Daffern & Bucks, 2012). Third, mentalization enables people to differentiate their own mental states from those of others (Fonagy & Luyten, 2009). People with impairments in mentalizing abilities may consequently experience blurring of self-other boundaries (Debbané et al., 2013). Such experiences may cause severe anxiety, increasing the likelihood of violence (Adshead et al., 2013). Finally, mentalization is a precondition for empathy (Hooker, Verosky, Germine, Knight & D'Esposito, 2008). Empathy, the capacity to understand and emulate other people's emotions, is an inhibitor of violent behaviour (Vachon, Lynam & Johnson, 2014). It has been argued that affective mentalization is more relevant than cognitive mentalization for affect regulation (Eizirik & Fonagy, 2009), self-other differentiation (Ebisch et al., 2014) and empathy (Hooker et al., 2008).

Other reasons why impairments in executive functions and mentalizing abilities may increase violence risk are confounding or mediation by substance use disorder (Keyes, Platt, Kaufman & McLaughlin, 2017; Sanvicente-Vieira et al., 2016) and low educational attainment (Au et al., 2015; Tompkins, 2015). Confounding by genetic (Zhang-James et al., 2018), neurobiological (e.g. hypofunction in the orbitofrontal cortex or anterior cingulate cortex [Raine, 2008]) and early environmental (e.g. poor nutrition [Paschall & Fishbein, 2002], maltreatment [Fonagy & Luyten, 2009]) risk factors is also possible. However, cognitive deficits are considered to be the primary mediator between biological risk factors and violent behaviour (Raine, 2008).

4.1.4. Cognition and violent behaviour in psychotic disorders

Impairments in executive functions and mentalizing abilities are associated with lack of insight (Aleman, Agrawal, Morgan & David, 2006; Konstantakopoulos et al., 2014) and, relatedly, treatment nonadherence (Boyer et al., 2012; Shad, Tamminga, Cullum, Haas & Keshavan, 2006). Insight refers to a person's acknowledgement of having an illness that requires treatment and evaluation of distorted beliefs (Beck, Baruch, Balter, Steer & Warman, 2004). A person who denies being ill or in need of treatment is unlikely to seek or comply with treatment (Higashi et al., 2013). This may lead to violent behaviour because delusions or hallucinations remain or worsen. A strong conviction that delusions or hallucinations are real may bring a person to act on them (Bjørkly, 2006).

Based on the foregoing, it may be hypothesized that deficits in executive functions and mentalizing abilities partly explain the excess risk of violent behaviour in psychotic disorders. The few studies investigating this hypothesis have produced conflicting results for executive functions (e.g. Barkataki et al., 2005; Fullam & Dolan, 2008; Lapierre et al., 1995; Krakowski et al., 2016; Serper, Beech, Harvey & Dill, 2008) and affective mentalizing ability (e.g. Abu-Akel & Abushua'leh, 2004; Frommann, Stroth, Brinkmeyer, Wölwer & Luckhaus, 2013; Silver, Goodman, Knoll, Isakov & Modai, 1997; Weiss et al., 2006). Moreover, these studies were limited by the use of small samples of male inpatients or prisoners, a single data source of violent behaviour and composite measures of executive functions. To my knowledge, only one study

has investigated cognitive mentalizing ability. In this study, better performance on the Unexpected Transfer Task (Perner & Wimmer, 1985) was significantly associated with lifetime violence, ascertained from medical records and interviews, in patients with schizophrenia (RR 1.2, $p < .05$). However, this finding may be attributed to selection bias: the sample was small ($N = 24$) and the violent patients were recruited from a high-security psychiatric hospital (Abu-Akel & Abushua'leh, 2004).

4.2. Methods

4.2.1. Neuropsychological tests

Neuropsychological tests were selected based on suitability for use in large, multisite projects and established validity and reliability. Unless otherwise specified, assessments took place at baseline.

Inhibition was measured with the Continuous Performance Test-HQ (CPT-HQ) (Neuechterlein & Dawson, 1984). A total of 300 letters appear in quasi-random order on a computer screen and the subject is instructed to press the space bar on a keyboard each time the letter "Q" is preceded by the letter "H" ($k = 28$). Letters are presented for 150 ms, with intervals of 850 ms. I used three performance indicators: (i) the number of hits (i.e. correct positive responses); (ii) the mean reaction time for hits; and (iii) the number of commission errors (i.e. false positive responses).

The Response Shifting Task (RST), a modified version of the Competing Programs Task (Bilder, Turkel, Lipschutz-Broch & Lieberman, 1992), was used to assess cognitive flexibility. The RST requires set-shifting between imitation and reversal response rules. The stimulus words "left" and "right" appear quasi-randomly on a computer screen for 3 s and should be followed each time by a press on either the left (i.e. "z") or right (i.e. "/") side of the keyboard. In the imitation condition, the subject must press the key congruent with the meaning of the stimulus (e.g. "z" when the word "left" appears). In the reversal condition, the subject must press the key incongruent with the meaning of the stimulus (e.g. "/" when the word "left" appears). Each condition is presented twice in alternating blocks, which end after 20 responses or 8 consecutive correct responses. The subject can only rely on feedback, shown for 1 s after each response, to deduce the response rule of each block. Two performance indicators were used: (i) accuracy cost (i.e. the absolute difference between the percentage of correct responses in the imitation condition and the percentage of correct responses in the reversal condition); and (ii) reaction time cost (i.e. the absolute difference between the mean reaction time in the imitation condition and the mean reaction time in the reversal condition). The first response in each block, responses preceded by errors, responses with a reaction time shorter than 150 ms and reaction times for incorrect responses were excluded (Meiran, Levine, Meiran & Henik, 2000; Quee, 2012).

Fluid intelligence was measured with the Block Design test of the Dutch version of the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III) (Wechsler, 1997). The

subject is asked to arrange 4 to 16 red and white square blocks in colour patterns that match those made by the examiner or shown on cards. Each trial has a specified time limit (range: 90–240 s). Patterns that are laid incorrectly or outside the time limit are scored with 0 points. Scores for correct patterns depend on the number of tries and time to completion. If the subject lays 5 incorrect patterns in succession, the test is terminated and he or she receives a total score of 0 points. The maximum score is 68 points.

The Mazes Test of the Neuropsychological Assessment Battery (NAB) (Stern & White, 2003) was used to assess planning ability. The subject has to complete 7 progressively difficult mazes with time limits (range: 30–240 s) imposed on each. An uncompleted maze is scored with 0 points. Time to completion is divided in intervals that are scored with 1 to 3 or 5 points. If the subject fails to complete 3 mazes in a row, the test is terminated and he or she receives a total score of 0 points. The maximum score is 26 points. The NAB Mazes Test was administered at the third wave.

Cognitive mentalizing ability was measured with the Hinting Task (Corcoran, Mercer & Frith, 1995). The Hinting Task consists of 10 short stories, each involving an interaction between two characters, that are read aloud. Each story ends with one of the characters making an implicit statement. The subject is then asked to explain what the character really meant. An immediate correct answer is scored with 2 points. In case of an incorrect response, the subject is given a hint. Subsequent responses are scored with 1 point, if correct, or 0 points, if incorrect.

The Degraded Facial Affect Recognition Task (DFAR) (van 't Wout, Aleman, Kessels, Laroi & Kahn, 2004; van Dijke, van 't Wout, Ford & Aleman, 2016) was used to measure affective mentalizing ability. Photographs of four actors (two male and two female) with angry, happy, fearful and neutral faces appear in random order on a computer screen. The subject is instructed to identify the emotion expressed in each face by pressing the key with the corresponding number (i.e. "1"–"4"). There are 16 representations of each emotion, making the total number of trials 64. To increase the contribution of top-down processes, such as attention, mental imagery and feature binding, the photographs are passed through a filter that reduces visual contrast by 30%. For the same reason, half of the trials for angry, happy and fearful faces are displayed at 75% intensity (van Dijke et al., 2016). The percentage of correctly identified emotions was used as the performance indicator.

Face recognition ability was assessed with the short form of the Benton Facial Recognition Test (BFRT) (Benton, Sivan, Hamsher, Varney & Spreen, 1983). The BFRT uses photographs of male and female faces with hair and clothing cropped out. The subject is asked to match a target face with 1 or 3 out of 6 test faces in 13 trials. Correctly matched faces are scored with 1 point. The maximum score is 27 points.

4.2.2. Statistical analysis

Higher scores reflected better performance on all tests, except on certain subscales of the CPT-HQ (i.e. number of commission errors) and RST (i.e. accuracy cost, reaction time cost). Therefore, these scores were reversed. For the CPT-HQ and RST, I calculated composite scores by transforming the scores on the subscales to *z*-scores and then averaging the *z*-scores. This method for calculating composite scores is widely used in the literature (e.g. Harrison, Lophaven & Olsen, 2016; Mancuso, Horan, Kern & Green, 2011; Scarmeas, Albert, Manly & Stern, 2006). To reduce confounding by impairments in face recognition ability, patients with scores below 18 on the BFRT were excluded from the analysis of affective mentalization (Benton et al., 1983).

Analysis of covariance (ANCOVA) was used to compare the mean scores of violent and nonviolent patients for each neuropsychological test. Consistent with the ANCOVA literature, I will refer to the outcome of interest as the dependent variable, the exposure of interest as the independent variable and possible confounders as covariates. Violent behaviour at any time prior to test administration was the independent variable. Test scores served as the dependent variables. A confounder was defined as a variable that causes, but is not an intermediary between, the independent variable and dependent variable (Cole & Hernán, 2002). Based on theory, I selected age (Deary et al., 2009; Henry, Phillips, Ruffman & Bailey, 2013) and gender (Longenecker, Dickinson, Weinberger & Elvevåg, 2010; Zhang, Han et al., 2017) as covariates.

The independent variable and covariates were treated as fixed because they contained all values present in the population about which inferences were made (Huitema, 2011). I used type III sum of squares to adjust each main and, if appropriate, interaction effect in the models for all others (Hector, von Felten & Schmid, 2010). Type III sum of squares is also invariant to unequal group sizes, provided there are no empty cells (Hector et al., 2010). This was relevant here: the number of patients varied across the levels of violence and gender. The level of statistical significance was set at 5%. Given the modest number of hypotheses tested, I did not correct for multiplicity (Streiner, 2015). Analyses were performed using SPSS (version 21.0).

The assumptions of ANCOVA are as follows: (i) the errors are independent; (ii) the errors have a mean of 0; (iii) the errors are normally distributed; (iv) the variance of the errors is the same (i.e. homoscedastic) regardless of the level of the independent variable(s); and (v) the linear regression slopes of the dependent variable on the covariate(s) are homogeneous across the levels of the independent variable(s) (Huitema, 2011).

The errors can reasonably be assumed to be independent (see Chapter 3). As an auxiliary check, I inspected the scatterplots of the residuals versus fitted values and the scatterplots of the residuals versus the sites were the data were collected. None of the scatterplots showed clusters of residuals, which are indicative of dependent errors.

The errors will have a mean of 0 if the relationship between the dependent variable and each continuous covariate is linear. This assumption was assessed through

inspection of: (i) the scatterplots of the residuals versus fitted values; and (ii) LOWESS curves fitted to test scores versus age using a Gaussian kernel with a bandwidth of 0.8. None showed strong nonlinear trends. For the CPT-HQ, RST, DFAR and Hinting Task, the linear relationships appeared weak. However, it may still be important to remove variance explained by age. In addition, the loss in degrees of freedom by including age as a covariate is negligible with a sample size this large.

The assumption of normally distributed errors was assessed by inspecting the scatterplots of the residuals versus fitted values and the histograms of the residuals. Ceiling effects were present for the CPT-HQ, RST and Hinting Task, as indicated by the asymmetrical distributions of the residuals across fitted values in the scatterplots, with the negative residuals being larger than the positive residuals, and negatively skewed distributions of the residuals in the histograms. The robustness of the ANCOVA *F*-test to non-normally distributed residuals depends on certain conditions. The most important of these relate to design (i.e. balanced or unbalanced), residual variance (i.e. homoscedastic or heteroscedastic), within-group regression slopes (i.e. homogenous or heterogeneous) and covariate distribution (i.e. normal or non-normal) (Harwell, 2003; Huitema, 2011). A meta-analysis of Monte Carlo simulations found that the Type I error rate of the *F*-test is maintained in an unbalanced ANCOVA with homoscedastic residual variance, homogeneous within-group regression slopes and a non-normally distributed covariate (Harwell, 2003). Since this was the case for all three models, I did not take remedial measures (e.g. transformation of the

dependent variable, bootstrapping, trimming means). The residual distributions of the models for the remaining neuropsychological tests were approximately normal.

Violations of the homoscedasticity assumption commonly take two forms: (i) the residual variance is constant across the levels of the independent variable(s) but increases or decreases across the levels of a covariate; and (ii) the residual variance increases or decreases across the levels of an independent variable but is constant across the levels of the covariate(s). ANCOVA, whether balanced or unbalanced, has been shown to be robust against the former (Huitema, 2011). The latter may be problematic in unbalanced ANCOVAs: the *F*-test is conservative if the residual variance is larger in the larger group(s) and liberal if the residual variance is smaller in the smaller group(s) (Huitema, 2011). From the scatterplots of the residuals versus fitted values, histograms of the residuals and the ratios between the residual variances, it was concluded that the errors were homoscedastic. The residuals did not systematically fan out with increasing or decreasing fitted values, and the distributions of the residuals were reasonably uniform across groups. The variance ratios, calculated by dividing the largest variance by the smallest (Blanca, Alarcón, Arnau, Bono & Bendayan, 2018), were all 1.1. The *F*-test maintains the nominal type I error rate under a wide variety of conditions (e.g. degree of inequality between group sizes, direction and degree of association between residual variance and group size) if the variance ratio is 1.5 or smaller (Blanca et al., 2018). The variance ratio was chosen over traditional tests of the homoscedasticity assumption (e.g. Bartlett's test

[Bartlett, 1937]; Levene's test [Levene, 1960]) because it does not rely on assumptions that may not be satisfied.

Homogeneity of within-group regression slopes was assessed by testing the interactions between violence, age and gender. This was done in one or two steps. In the first step, a model with the three-way interaction (i.e. violence*age*gender) was run. If the three-way interaction was nonsignificant, separate models were run with the two-way interactions of violence with age and gender (i.e. violence*age, violence*gender) in a second step. All lower order coefficients were included in the models. I set the level of statistical significance at 5%. It is sometimes recommended to use a more liberal threshold (e.g. 10%, 20%) because power to detect interactions is relatively low (Huitema, 2011). However, this unduly increases the probability of introducing a spurious association in the model (Durand, 2013). There were no significant interactions ($p \geq .156$).

Besides the abovementioned assumptions being met, other important conditions for valid inference are the absence of high multicolinearity and observations with excessive influence on the parameter estimate(s) of interest (Huitema, 2011). I used two indicators of high multicolinearity: (i) correlation coefficients between violence, age and gender with absolute values of .7 or higher (Dormann et al., 2013); and (ii) instability of the standard errors of the coefficients for violent behaviour in the corresponding linear regression models (Vatcheva et al., 2016). Violence and gender were dichotomous and age was continuous. Therefore, the correlations of violence and gender with age were calculated using the point-biserial correlation coefficient

(r_{pb}) and the correlation between violence and gender was calculated with the phi coefficient (Φ). The absolute values of r_{pb} and Φ were .1 or lower. There were no notable differences in the standard errors of the coefficients for violent behaviour between the linear regression models with and without the covariates age and gender. As a measure of influence, Cook's D_i (Cook, 1979) was used. Observations that warrant scrutiny are those exceeding the critical value of $F_{.5}(k + 1, N - k - 1)$, with k being the total number of independent variables and covariates in the model and N being the total number of observations (Huitema, 2011). For the models in the present study, $F_{.5}(4, \geq 509) = 0.8$. All values of Cook's D_i were considerably smaller ($D_i \leq 0.1$).

4.3. Results

As shown in Table 4, patients with a lifetime history of violent behaviour performed worse than those without such a history on most neuropsychological tests. On average, they had fewer hits and longer reaction times for hits on the CPT-HQ, higher accuracy and reaction time cost scores on the RST and lower scores on the WAIS-III Block Design subtest, NAB Mazes Test and Hinting Task. The average number of commission errors on the CPT-HQ was lower and the average percentage of correctly identified emotions on the DFAR was higher in the violent group, indicating better performance.

However, the effect sizes were small. Lifetime violent behaviour explained no more than 1% of the variance in performance across neuropsychological tests. The only tests for which group differences reached statistical significance were the WAIS-III Block Design subtest (F [1, 847] = 5.1, p = .024) and Hinting Task (F [1, 839] = 9.4, p = .002).

4.4. Discussion

In a nationally representative sample of 891 patients with psychotic disorders, I have analysed the association between neuropsychological test performance and lifetime violent behaviour for an extensive range of executive functions and mentalizing abilities. Although the effect sizes were small, violent patients performed significantly worse than nonviolent patients on tests of fluid intelligence (i.e. WAIS-III Block Design test) and cognitive mentalization (i.e. Hinting Task).

As explained, violence in patients with relatively low fluid intelligence may be a maladaptive solution to or consequence of heightened stress reactivity in difficult situations. Impairments in cognitive mentalization may lead to violent behaviour through misinterpretation of social cues, affect dysregulation, blurring of self-other boundaries or lack of empathy. There was no significant difference between violent and nonviolent patients in affective mentalization, which is arguably more important than cognitive mentalization for regulating emotions, distinguishing between one's

own or others' mental states and empathising. This lends more credence to the misinterpretation of social cues – insofar they relate to other people's cognitive mental states – as a reason for violent behaviour in psychotic disorders. Alternative explanations for the findings are: (i) confounding or mediation by comorbid substance use disorder; (ii) confounding or mediation by low educational attainment; (iii) confounding by biological risk factors (e.g. genetics, neurobiological abnormalities); (iv) confounding by early environmental risk factors (e.g. poor nutrition, maltreatment); (v) mediation by poor insight; and (vi) mediation by treatment nonadherence.

Caution is advised when interpreting the findings. The small effect sizes indicate that impairments in fluid intelligence and cognitive mentalization are at best minor risk factors for violent behaviour in psychotic disorders with primarily theoretical relevance. Also, it cannot be ruled out that the significant associations are artefacts of unmeasured confounding.

4.4.1. Limitations

This study has several limitations that merit discussion. First, causality cannot be inferred because violence preceded test performance by an unknown amount of time. However, the relative stability of cognitive impairment makes the issue of temporality less material. I also did not control for potential confounders other than age and

gender. Either data were unavailable (e.g. neurobiological abnormalities, childhood maltreatment) or the potential confounder was allowed on the causal pathway between violent behaviour and executive function or mentalizing ability (e.g. comorbid substance use disorder, low educational attainment). Second, the LCS does not distinguish between subtypes of violence (e.g. reactive *vs* proactive [Weiss, 2012], life-course-persistent *vs* adolescence-limited [Naudts & Hodgins, 2006]) that may be differently related with executive functions and mentalizing abilities. Third, neuropsychological tests suffer from impurity and have limited ecological validity. Impurity occurs when performance on a test contains systematic variance attributable to other cognitive functions than the one targeted (Miyake & Friedman, 2012). An example is the WAIS-III Block Design test, which measures fluid intelligence and visual-spatial skills (Lera-Miguel et al., 2011). Ecological validity concerns the extent to which performance on a neuropsychological test can be generalized to real-world settings (Dawson & Marcotte, 2017). Neuropsychological tests are designed to detect clinically relevant impairments in cognitive functions. Furthermore, the demands placed on cognitive functions in real-world settings are more complex than in experimental settings. As a consequence, individuals who perform at or above the normative level on a neuropsychological test may still experience difficulties when cognitive functions are required in real-world settings. This is relevant, as cognitive impairments in violent individuals are often subclinical (Ogilvie et al., 2011). Fourth, the Hinting Task uses a verbal paradigm. Poverty of speech is a prominent symptom of psychotic disorders and may introduce bias in favour of mentalizing impairments

when assessed verbally (Sarfati, Hardy-Baylé, Brunet & Widlöcher, 1999). However, a meta-analysis of 29 studies found that individuals with schizophrenia (*N* = 1,518) performed similarly on neuropsychological tests of cognitive mentalization regardless of whether a verbal (*d* = –1.2, 95% CI [–1.5, –1.0]) or nonverbal (*d* = –1.3, 95% CI [–1.5, –1.0]) paradigm was used (Sprong et al., 2007). Finally, the CPT-HQ measures only one aspect of inhibition: selective attention. The others are cognitive inhibition and self-control. Selective attention allows one to focus on a particular stimulus, while ignoring others. Cognitive inhibition involves the suppression of irrelevant thoughts and typically supports working memory. Self-control refers to the regulation of thoughts and emotions in support of goal-directed behaviour (Diamond, 2013). As such, self-control may be expected to be most directly related to violence. However, selective attention and self-control are highly correlated (Friedman & Miyake, 2004) and modulated by largely the same neural systems (Cohen, Forbes, Mann & Blanchard, 2006).

4.4.2. Implications for clinical practice and recommendations for future studies

The findings provide little rationale for using fluid intelligence and cognitive mentalizing ability for risk assessment and prevention purposes. The risk assessment tools used most widely to predict violence in psychotic disorders (e.g. Level of Service Inventory [LSI] [Andrews & Bonta, 1995]; VRAG [Quinsey et al., 2006]; HCR-20

[Douglas et al., 2013]) do not contain items for cognitive functions, and the small effect sizes suggest that additional items for fluid intelligence and cognitive mentalization will confer marginal incremental improvements. Similarly, the small effect sizes indicate that interventions aimed at improving fluid intelligence or cognitive mentalization are likely insufficient to prevent violent behaviour in most patients.

To clarify causal mechanisms, I recommend that future studies use prospective designs, distinguish between subtypes of violence and test for additional potential confounders (e.g. genetics, childhood maltreatment) and mediators (e.g. low educational attainment, comorbid substance use disorder). Finally, the interplay between genetics, brain structure and function, cognition and environment in the development of violent behaviour deserves investigation (Raine, 2008).

5 | Conclusion

Two studies were conducted in a sample of 891 patients with psychotic disorders to investigate the associations between violent behaviour and: (i) problematic and nonproblematic use of pharmacologically different substance categories (i.e. alcohol, cannabis, stimulants, depressants and hallucinogens); and (ii) neuropsychological test performance for a wide range of executive functions (i.e. inhibition, cognitive flexibility, fluid intelligence and planning) and two aspects (i.e. cognitive and affective) of mentalization.

All substance categories increased the odds of violent behaviour. This was true for problematic and nonproblematic use. Violence in patients with substance use may result from acute or chronic intoxication or withdrawal, criminal activity to support an addiction or involvement in illegal drug markets. Violent patients had significantly but marginally lower scores than nonviolent patients on the neuropsychological tests of fluid intelligence and cognitive mentalization. When confronted with problems in daily life, patients with relatively low fluid intelligence may use violence as a

maladaptive solution or consequence of increased sensitivity to stress. Impairments in cognitive mentalization may lead to violent behaviour through misinterpretation of social cues. Alternatively, the findings may be explained by lack of effective treatment and biological (e.g. genetics, neurobiological abnormalities) and environmental (e.g. childhood maltreatment, unemployment) risk factors.

Both studies benefited from the use of a nationally representative sample of patients from different care settings (e.g. psychiatric hospitals, residential facilities, outpatient clinics) and multiple data sources for the measurement of violent behaviour (i.e. patients, collateral informants and case notes). A general limitation was that unknown temporality and unmeasured confounding prohibited causal inference. Important study-specific limitations were the inclusion of patients using more than one substance category, not differentiating between subtypes of violence (e.g. reactive *vs* proactive, life-course-persistent *vs* adolescence-limited) and the impurity and questionable ecological validity of neuropsychological tests.

The findings have several implications for clinical practice. To begin, risk assessment and prevention should consider problematic and nonproblematic use of all substance categories. However, it is unknown whether multiple items for problematic and nonproblematic use of different substance categories improve the predictive validity of risk assessment tools with a single item for problematic use of any substance. The small effect sizes suggest that impairments in fluid intelligence and cognitive mentalization have mainly theoretical relevance: risk assessment tools with items for fluid intelligence and cognitive mentalizing ability likely have little or

no incremental validity relative to those without, and interventions aimed at enhancing fluid intelligence or cognitive mentalizing ability are probably inadequate to prevent violent behaviour in most patients. Future studies may improve our understanding of causal mechanisms by using even larger samples to isolate the effects of substance categories, differentiating between subtypes of violence, using prospective designs and testing additional possible confounders and mediators.

Tables

Table 1. Demographic and clinical characteristics of patients with psychotic disorders (*N* = 891) by lifetime violent behaviour.

	Lifetime violent behaviour	
	Yes (*n* = 183)	No (*n* = 708)
Demographic characteristics		
Age, mean (SD) in years	25.9 (6.3)	27.6 (7.2)
Male	145 (79)	543 (77)
Caucasian	137 (76)	559 (80)
Finished secondary school	146 (78)	620 (88)
Clinical characteristics		
Primary diagnosis		
Schizophrenia	136 (74)	479 (68)
Schizoaffective disorder	18 (10)	90 (13)
Psychotic Disorder NOS	18 (10)	57 (8)
Other	11 (6)	82 (12)
Age of onset, mean (SD) in years	21.7 (5.6)	23.4 (6.6)
Lifetime psychiatric hospitalization	164 (92)	519 (75)

Note. Data are *n* (%), unless otherwise specified.
Abbreviation: NOS = not otherwise specified.

Table 2. Prevalence and adjusted odds ratios of lifetime violent behaviour by severity of lifetime use of different substance categories in patients with psychotic disorders (*N* = 891).

	n (%)			aOR (95% CI)[a]		
Substance category	PU	NPU	NU	PU *vs* NPU or NU	PU *vs* NU	NPU *vs* NU
Alcohol	83 (24.4)	75 (19.1)	22 (16.1)	1.5 (1.1-2.1)	1.7 (1.0-3.0)	1.2 (0.7-2.1)
Cannabis	90 (24.0)	45 (21.4)	44 (15.3)	1.3 (0.9-1.9)	1.5 (1.0-2.4)	1.4 (0.8-2.2)
Stimulants	43 (30.5)	31 (23.1)	98 (17.3)	1.8 (1.2-2.7)	2.0 (1.3-3.0)	1.4 (0.9-2.3)
Depressants	15 (33.3)	18 (24.3)	134 (18.8)	1.9 (1.0-3.7)	2.0 (1.0-3.9)	1.3 (0.8-2.4)
Hallucinogens	12 (26.7)	41 (29.9)	113 (17.5)	1.3 (0.7-2.7)	1.6 (0.8-3.2)	2.0 (1.3-3.1)
Other	28 (28.6)	42 (28.4)	100 (16.8)	1.5 (0.9-2.4)	1.9 (1.1-3.1)	1.9 (1.2-2.9)

Note. Due to missing data, the total number of patients varies per substance category.
Abbreviations: aOR = adjusted odds ratio; CI = confidence interval; NPU = nonproblematic use; NU = no use; PU = problematic use.
[a] Adjusted for age, gender and educational level.

Table 3. Prevalence and adjusted odds ratios of lifetime violent behaviour by frequency of lifetime use of different substance categories in patients with psychotic disorders (*N* = 891).

	n (%)			aOR (95% CI)[a]		
Substance category	DU	NDU	NU	DU *vs* NDU or NU	DU *vs* NU	NDU *vs* NU
Cannabis	99 (24.1)	36 (21.1)	44 (15.4)	1.4 (1.0-1.9)	1.5 (1.0-2.3)	1.3 (0.8-2.2)
Stimulants	25 (36.8)	48 (24.1)	98 (17.3)	2.2 (1.3-3.8)	2.6 (1.5-4.5)	1.5 (1.0-2.2)
Depressants	15 (29.4)	18 (29.0)	134 (18.8)	1.7 (0.9-3.1)	1.7 (1.0-3.3)	1.7 (1.0-3.0)
Hallucinogens	43 (29.9)	6 (22.2)	113 (17.5)	1.9 (1.3-2.9)	1.9 (1.3-3.0)	-
Other	8 (34.8)	57 (26.8)	100 (16.8)	-	-	1.7 (1.2-2.6)

Note. Due to missing data, the total number of patients varies per substance category.
Abbreviations: aOR = adjusted odds ratio; CI = Confidence Interval; DU = daily use; NDU = nondaily use; NU = no use.
[a] Adjusted for age, gender and educational level.

Table 4. Performance on neuropsychological tests by lifetime violent behaviour in patients with psychotic disorders (*N* = 891).

		Unadjusted M (SD)		Adjusted M (SE)[a]				
Targeted cognitive function	Neuropsychological test	V (*n* = 183)	NV (*n* = 708)	V (*n* = 183)	NV (*n* = 708)	*F* (*df1*, *df2*)	*p*	η_p^2
Executive functions								
Attentional inhibition	CPT-HQ	0.0 (0.5)	0.0 (0.6)	0.0 (0.0)	0.0 (0.0)	0.3 (1, 782)	.568	.000
	Number of hits	26.1 (3.0)	26.4 (2.8)					
	Mean reaction time hits	439.7 (83.0)	427.9 (86.6)					
	Number of commission errors	2.6 (10.8)	3.0 (15.3)					
Cognitive flexibility	RST	0.0 (0.8)	0.0 (0.8)	-0.1 (0.1)	0.0 (0.0)	1.3 (1, 758)	.260	.002
	Accuracy cost	24.4 (25.5)	22.2 (23.6)					
	Reaction time cost	262.4 (188.8)	252.9 (189.2)					
Fluid intelligence	WAIS-III Block Design test	38.15 (17.5)	41.0 (16.9)	37.8 (1.3)	41.1 (0.7)	5.1 (1, 847)	.024	.006
Planning	NAB Mazes Test	16.7 (6.3)	16.9 (6.3)	16.2 (0.5)	17.1 (0.3)	2.5 (1, 505)	.117	.005
Mentalization								
Affective	DFAR	69.1 (10.2)	68.9 (10.7)	69.0 (0.8)	68.9 (0.4)	0.0 (1, 761)	.926	.000
Cognitive	Hinting Task	16.7 (2.9)	17.7 (2.7)	17.0 (0.2)	17.7 (0.1)	9.4 (1, 839)	.002	.011

Note. The total number of patients varies per test due to missing data.
Abbreviations: CPT-HQ = Continuous Performance Test-HQ; DFAR = Degraded Facial Affect Recognition Task; NAB = Neuropsychological Assessment Battery; NV = no lifetime history of violent behaviour; RST = Response Shifting Task; SD = standard deviation; SE = standard error; M =mean; V = lifetime history of violent behaviour; WAIS-III = Wechsler Adult Intelligence Scale-Third Edition.
[a] Adjusted for age and gender.

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