

NIH Public Access

Author Manuscript

Psychiatry Res. Author manuscript; available in PMC 2012 May 15.

Published in final edited form as:

Psychiatry Res. 2011 May 15; 187(1-2): 301–303. doi:10.1016/j.psychres.2010.10.032.

Self-report and laboratory measures of impulsivity in patients with schizophrenia or schizoaffective disorder and healthy

controls

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Abstract

This study examined self-reported impulsivity and aggression and performance on the stop-signal task in patients with schizophrenia or schizoaffective disorder and healthy volunteers. Patients show increased stop-signal reaction time but no difference in post-error slowing, suggesting deficient inhibition but spared error monitoring. Response variability was increased in patients compared to controls.

1. Introduction

"Frontal" or "executive" abnormalities are prominent in patients with schizophrenia (Hoptman and Nolan, 2009); they perform poorly on tasks requiring cognitive control and contextual information processing (e.g., the Stroop (Schooler et al., 1997), the AX version of the Continuous Performance Test and go/no-go tasks (Cohen et al., 1999)). Risk for aggression is increased in patients with schizophrenia compared to individuals without serious mental illness (Swanson et al., 1990; Steadman et al., 1998; Brennan et al., 2000). Positive psychotic symptoms may be more severe in violent schizophrenic patients (Krakowski et al., 1999; Fresán et al., 2005), however, frontally mediated functions such as social cognition (Weiss et al., 2006) and impulse control (Hoptman et al., 2002; Kumari et al., 2009) are also impaired and there is evidence for relationships between frontotemporal disconnections and aggression (Hoptman et al., 2002; Hoptman et al., 2010). Aggression is also increased in non-psychotic conditions that affect impulse control. In Attention Deficit/ Hyperactivity disorder (ADHD) aggression is increased even in the absence of co-morbid conduct disorder or antisocial personality disorder (Retz and Rösler, 2007) and features of impulsivity and hyperactivity predict aggressive behaviors (Dowson and Blackwell, 2010). Thus, poor impulse control is seen as the basis of at least some aggression.

The stop-signal task (Logan et al., 1984) is widely used to study inhibitory deficits in ADHD (Schachar et al., 2000; Epstein et al., 2001), compulsive disorders (Morein-Zamir et al.,

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2010) and substance abuse/dependence (Fillmore and Rush, 2002). The SST consists of a primary "Go" task and a secondary "Stop" task which requires withholding responses when a stop-signal occurs. SST performance has been modeled as a race between the go process, initiated by presentation of an imperative go stimulus, and a stop process, triggered by presentation of the stop signal. If the stop process finishes first, the response is successfully inhibited. Successful inhibition depends on both the latency of the stop process and the length of the interval between onset of the go stimulus and presentation of the stop-signal: the stop-signal delay (SSD).

Systematically varying SSD enables estimation of the latency of the inhibition process, the stop signal reaction time (SSRT). In ADHD, deficient SST performance appears to be due to separable impairments in response inhibition and error monitoring. In addition to having significantly longer SSRTs than controls, ADHD participants show less slowing after errors on Stop trials, but post-error slowing is not correlated with SSRT (Schachar et al., 2004).

Patients with schizophrenia display abnormal SST performance, but the underlying impairments remain unclear. In one study, although SSRT was not increased in schizophrenia, the stop process was either more variable or less often triggered (Badcock et al., 2002). In another study, patients with schizophrenia had higher impulsivity ratings and increased SSRT, but there were no significant correlations between stop task inhibition measures and impulsivity ratings (Enticott et al., 2008). In that study, patients' performance suggested greater response variability rather than impaired inhibition triggering. In light of the partial disagreement between these results, and the implication of impulsivity in aggression, in the current study we examined self-reported impulsivity and aggression and SST performance in patients with schizophrenia and healthy volunteers.

2. Methods

2.1 Participants

Patient participants were diagnosed with schizophrenia (n=40) or schizoaffective disorder (n=7) by DSM-IV criteria using the SCID-I/P (First et al., 2001) and were being treated with either second generation neuroleptics (n=28) or a combination of first- and second generation neuroleptics (n=11, data missing for 3 subjects). Healthy controls (n=49) did not meet criteria for any current Axis I disorders. Individuals meeting criteria for substance abuse within 6 months or substance dependence at any time were excluded. Current substance abstinence was verified by urine toxicology for outpatients (n=17) and healthy controls. All participants provided written informed consent as approved by the local Institutional Review Boards.

2.2 Questionnaires

The Barratt Impulsiveness Scale Version 11 (Patton et al., 1995), Buss-Perry Aggression Questionnaire (BPAQ; (Buss and Perry, 1992) and Life History of Aggression (LHA; Coccaro et al., 1997) were administered. Based on clinical experience and chart data, and blind to SST data, LHA data were rated for likelihood of validity. Only LHA scores deemed to be of at least medium confidence were retained. Severity of patients' current psychopathology was rated with the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987) and Clinical Global Impressions Scale (CGI; Guy, 1976). Substance use was measured using the Kreek-McHugh-Schluger-Kellogg scale (Kellog et al., 2003).

2.3 Stop signal task

The stop signal paradigm was adapted from Schachar et al. (2000). Visual stimuli were presented centrally on a computer display. Subjects responded manually by pressing mouse

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buttons. The participants' primary ("go") task was a choice reaction time (RT) task which required pressing one button in response to the letter "X" and the other button for "O". Each trial began with a central fixation (+), followed by the stimulus (1000 ms duration). Subjects were instructed to respond as rapidly and accurately as possible to letter stimuli. A visual stop signal, a bright red rectangle surrounding the letter stimulus, appeared on 25% of trials. The SSD was initially set to 250 ms and was decreased by 50 ms following successful (no response) stop trials and increased by 50 ms following unsuccessful stop trials, to approach an overall stop accuracy of 50%. There were 9 32-trial blocks, and the task lasted approximately 15 minutes.

2.4 Data analysis

Only blocks in which Go accuracy exceeded 85% and Stop accuracy fell between 85% and 15% were retained for analysis. Twelve subjects (5 patients and 7 controls) with fewer than 3 usable blocks were dropped from analysis. This resulted in 42 subjects in each group and no between-group difference in number of analyzable blocks (see Table 1). Excluded and retained subjects did not differ demographically. SSRT was calculated per block as average Go RT minus average SSD. Intra-individual coefficient of variation (ICV= standard deviation of Go RT / mean GoRT; (Stuss et al., 2003) indexed within-subject response variability. Group differences in continuous variables were analyzed by independent groups t-test or Mann-Whitney U-tests for nonnormal data; Fisher's exact test was used for categorical data.

3. Results

Demographic and clinical data and aggression and impulsivity scores and SST measures are listed in Table 1. Groups did not differ significantly in age, gender or race. Controls had more years of education, more alcohol use, and less tobacco use. Patients had higher impulsivity scores than controls. There were no group differences in Go RT. Go accuracy was higher in controls than patients. Controls were also more successful at inhibiting responses on Stop Trials. SSRT and ICV were higher in patients than controls. Across groups, there were significant correlations between SSRT and LHA (r=0.29, p=0.012), BPAQ (r=0.30, p=0.005) and BIS (r=0.33, p=0.002) and between ICV and LHA (r=0.26, p=0.025), BPAQ (r=0.42, p<0.001) and BIS (r=0.31, p=0.006). Controlling for group, the SSRT/BIS correlation remained significant (p=.054) as did the ICV/BPAQ correlation (p=. 008), with the SSRT/LHA correlation significant at a trend level (p=.07). In patients, PANSS Total scores were significantly and positively correlated with BPAQ total scores (r=0.50, p=0.001) and ICV (r=.48, p=.002) and with SSRT at the trend level (r=.30, p=.059), but not with BIS or LHA scores (ps>0.116).

4. Discussion

Patients with schizophrenia often display behavioral problems that suggest impaired impulse control. In this sample, patients with schizophrenia scored higher than healthy controls on interview and questionnaire measures of impulsivity and aggression. Stop signal performance (SSRT) was correlated with impulsivity ratings and was impaired in patients. Although Go trial accuracy was high in both groups, controls were more accurate than patients. Patients responded as quickly as controls on Go trials. Slower SSRT in the absence of Go RT differences implies a selective deficit in inhibition in schizophrenia, as opposed to a general cognitive deficit. Patients also showed significantly greater response variability (ICV) which has previously been associated with dorsolateral and superior medial frontal lesions (Stuss et al., 2003).

There are several limitations to this study. First, the tracking algorithm used to adjust SSDs did not uniformly induce 50% Stop trial success and controls successfully inhibited more than patients. Nevertheless, control SSRTs were comparable to other published estimates (Badcock et al., 2002; Schachar et al., 2004; Enticott et al., 2006) and showed lawful relationships with other SST measures. Second, all patients were taking neuroleptic medications, which might affect performance. It is possible, for instance, that they might improve performance to the extent that they were efficacious. Third, extrapyamidal symptoms, which were not evaluated, might have affected performance. Fourth, groups differed in tobacco and alcohol use. Finally, questionnaire measures are susceptible to interpretational biases and may be less valid in patients. Nevertheless, predicted relationships were observed in both patients and controls.

In summary, SST performance differences between patients with schizophrenia and healthy controls are consistent with a specific impairment in response inhibition in schizophrenia. These abnormalities were associated with self-report measures of aggression and are consistent with deficits in inferior frontal, dorsolateral prefrontal and superior medial frontal function in schizophrenia.

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Table 1

Means (standard deviations) and ranges on aggression and impulsivity questionnaires and stop-signal measures in patients and controls.

	Patients (35 m, 7 f)	Controls (29m, 13 f)	$t(df)P^+$
Age	35.05 (9.94)	34.33 (10.77)	0.32 (82) 0.75
Education (years)	12.48 (2.00)	16.05 (2.31)	-7.58 (82) <0.001
Ethnicity	21 African American	14 African American	* p= 0.398
	19 Caucasian	26 Caucasian	
	2 Other	2 Other	
PANSS***	77.25 (16.18)		
CGI ^{***}	3.93 (1.35)		
BIS TOTAL	61.76 (7.08)	56.00 (9.95)	3.06 (74.07) 0.003
Go RT (ms)	577.26 (82.75)	577.59 (74.16)	-0.02 (82) 0.984
SSRT (ms)	300.32 (50.79)	249.77 (44.66)	4.84 (82) <0.001
Usable Stop Signal Blocks	6.83 (1.75)	6.81 (1.99)	0.06 (82) 0.954
Nonnormally distributed data ⁺			Mann-Whitney U statistic/p
LHA Total Score ^{**}	14.71 (10.15)	10.80 (6.37)	524/0.063
BPAQ TOTAL	62.88 (17.09)	51.95 (12.24)	548.5/0.001
Tobacco Use ⁺⁺	4.00 (4.11)	6.74 (4.76)	581/.006
Alcohol Use ⁺⁺	6.78 (3.32)	5.07 (3.71)	627.5/.002
Go Accuracy	0.95 (0.03)	0.98 (0.02)	306 /<0.001
Stop Accuracy	0.56 (0.11)	0.64 (.07)	481 /<0.001
ICV	0.30 (0.06)	0.22 (0.05)	293/<0.001

Note.

*Fisher's Exact Test,

 ** 35 patients and 40 controls provided valid data for the LHA,

*** missing for 2 subjects,

⁺as indicated by significant Shapiro-Wilks and/or Kolmogorov-Smirnoff statistics,

⁺⁺from Kreek-McHugh-Scluger-Kellogg (KMSK; Kellogg et al., 2003) scale