Published in final edited form as:
Psychiatry Res. 2014 December 15; 220(0): 31–36. doi:10.1016/j.psychres.2014.07.026.

Distress intolerance and clinical functioning in persons with schizophrenia

Katie L. Nugent[a,*], **Joshua Chiappelli**[a], **Laura M. Rowland**[a], **Stacey B. Daughters**[b], and **L. Elliot Hong**[a]

[a]Maryland Psychiatric Research Center, Department of Psychiatry, University of Maryland School of Medicine, Baltimore, Maryland USA 21228

[b]Department of Psychology, The University of North Carolina at Chapel Hill, Chapel Hill, NC USA 27599

Abstract

Impaired tolerance to distress may help explain part of the cognitive and functional impairments in schizophrenia. This project investigated distress intolerance in schizophrenia patients (SZ) as compared to controls, and whether distress intolerance represented an independent domain in relationship to symptoms, cognition, and functional capacity. Healthy controls (n=43) and SZ (n=65) completed a psychological distress challenge experiment and their levels of intolerance to distress were estimated. SZ showed increased distress intolerance such that they were significantly more likely to terminate the distress challenge session early compared to controls. Greater distress intolerance was associated with reduced functional capacity and worse cognitive performance in SZ. Mediation analyses suggested that distress intolerance had an independent effect on functional capacity, while some of this effect was mediated by cognitive performance. Our results suggest that distress intolerance is a promising domain for treatment research, and functional capacity may be improved by targeting treatments towards SZ patient's ability to tolerate distress.

Keywords

stress; affect reactivity; resilience; psychosis; cognition

*Correspondence concerning this article should be addressed to: Dr. Nugent, Maryland Psychiatric Research Center, P.O. Box 21247, Baltimore, MD 21228; Tel: (410) 402-6859; Fax: (410) 402-6023; knugent@mprc.umaryland.edu.

Author Disclosure
A portion of this work was presented at the International Congress on Schizophrenia Research on April 25, 2013.

Contributors
EH and SD designed the study. KN analyzed the data and wrote the first draft of the manuscript, and all authors (KN, JC, LR, SD, EH) wrote and read the subsequent drafts and approved the final submitted manuscript.

1. Introduction

Understanding the contributing factors to functional impairment in persons with schizophrenia remains a critical research area. Schizophrenia is marked by heightened sensitivity to stress (Norman and Malla, 1993; Corcoran et al., 2003; Walker et al., 2008). This sensitivity, combined with reduced cognitive reserve (Barnett et al., 2006), may predispose those with the illness to have difficulty successfully navigating stress-inducing situations and completing tasks that invoke stress. It is known that as a group, schizophrenia patients (SZ) have reduced drive to pursue goal directed behavior and display altered physiological responses to induced stress (Albus et al., 1982; Breier et al., 1988; Jansen et al., 1998; Jansen et al., 2000). For example, SZ exposed to a mental arithmetic stress test displayed an abnormal prolonged cardiac autonomic response which is hypothesized to arise from alterations in central brain structures which leave patients unable to “switch off” the stress response (Castro et al., 2008). This autonomic dysfunction was also found in unaffected first-degree relatives, suggesting that this abnormality has a genetic etiology rather than being due to arousal secondary to the disease or psychiatric medication effects (Bar et al., 2010). It is unknown if a maladaptive stress response contributes to their inability to complete tasks that evoke stress. We utilized a distress intolerance (defined as an inability to persist in goal directed behavior while experiencing affective distress) paradigm to test this question (Leyro et al., 2010). Distress tolerance is a meta-emotion construct encompassing an individual’s evaluations of experiencing aversive emotional states in respect to their tolerability, influence on emotion regulation and functioning, specifically including tendencies to either avoid or attenuate aversive experiences (Simons and Gaher, 2005). The definition of distress intolerance we employed bears resemblance to persistence, a trait-like dimension. Although the definition of persistence is not uniform, it is related to maintaining certain behavior for achieving reinforcement or a reward (Cloninger et al., 1991). Other authors have described completion of experimental tasks, some of which were designed to evoke frustration or distress, wherein the participants had the option to give up attempts at completing the task, as task persistence (Brandon et al., 2003). In the latter case, the construct is closely related to distress tolerance. The construct of task persistence is built upon Eisenberger’s learned industriousness theory, which holds that organisms with prior experience being rewarded for high effort are more likely to persist at effortful tasks than are organisms with histories of being rewarded for low effort (Eisenberger et al., 1992). Thus, distress intolerance and task persistence are similar in that both are operationalized by experimental tasks measuring the duration of a person’s attempt; however they differ in their theory upon which the construct is based.

Distress intolerance has been found relevant to other psychiatric and pathological conditions, and adaptive response to stress is increasingly a target of psychological interventions (Daughters et al., 2005a; Daughters et al., 2005b; O’Cleirigh et al., 2007; Nock and Mendes, 2008). For example, high levels of affect reactivity and distress intolerance have been associated with poor outcome after substance abuse and pathological gambling treatment (Daughters et al., 2005a; Daughters et al., 2005b). Patients with distress intolerance experienced greater depression, substance use, and were less adherent to their medication (O’Cleirigh et al., 2007). Distress intolerance has also been found in adolescents

engaging in nonsuicidal self-injury (Nock and Mendes, 2008). To our knowledge, distress intolerance has not been examined in persons with schizophrenia in a laboratory setting.

We operationalized distress intolerance by measuring a behavioral response to laboratory tasks that induced psychological stress. We utilized paradigms in which participants had the option to terminate the distress challenge task early. To motivate participants not to terminate early, they were informed that their performance determined their monetary reward. Early termination of the stressful task could result from: increases in negative affect, decreased motivation to persist due to an inability to experience anticipatory pleasure, or from an impulsive decision, thus we assessed these attributes in relation to distress intolerance. Schizophrenia patients in particular have less anticipatory pleasure for goal directed activities (Gard 2007), thus we felt it was important to control for the constructs of anhedonia and avolition while exploring this stress paradigm. While cognitive functioning has previously been shown to represent a separate domain from stress induced emotional reactivity in SZ (Myin-Germeys et al., 2002), due to its association with functional outcome we investigated its relationship with distress intolerance. We investigated: 1) whether SZ had more or less intolerance to psychological distress as compared with healthy controls; 2) the extent to which negative and positive affect reactivity, clinical and cognitive impairments explained distress intolerance and functional capacity, and 3) the extent by which functional impairments in SZ are explained by distress intolerance.

2. Methods

2.1 Participants

Participants were 130 individuals, aged 18 to 62 years, including 43 healthy controls and 65 outpatients with schizophrenia or schizoaffective disorder. Participants gave written informed consent as approved by the University of Maryland Institutional Review Board. Major medical and neurological illnesses, history of head injury with cognitive sequelae, mental retardation, substance dependence within the past six months, or current substance abuse (except nicotine) were exclusionary. The Structured Clinical Interview for DSM-IV was administered to all participants to obtain diagnoses, which were based on consensus agreement from two psychiatrists (First et al., 1995). Controls had no current Axis I diagnoses and no family history of psychosis in the prior two generations. Six SZ patients were not taking any antipsychotic medication and the remaining 59 patients were on antipsychotic medications, including six on first generation antipsychotics and 53 on second generation antipsychotics. Of the patients on antipsychotics, 11 were also on an antidepressant, five were on a mood stabilizer, and five were on a benzodiazepine. The median chlorpromazine dose equivalent of antipsychotic medication among patients taking antipsychotics was 525 (standard deviation=615).

2.2 Measures

2.2.1 Clinical, cognitive and functional capacity assessment—Overall clinical symptoms were assessed by the 20 item Brief Psychiatric Rating Scale (BPRS), while impulsiveness was measured using the Barratt Impulsiveness Scale (Overall and Donald, 1962; Stanford et al., 2009). We measured negative symptoms using the Brief Negative

Symptom Scale (BNSS; Kirkpatrick et al., 2011), and examined the items comprising the anhedonia and avolition subscales in this analysis. Cognitive ability was assessed by a combined index of processing speed (Digit Symbol Coding subtest of the Wechsler Adult Intelligence Scale-3) and working memory (Digit Sequencing task from Brief Assessment of Cognition in Schizophrenia) which are considered the most robust cognitive domain deficits in SZ compared with controls (Dickinson et al., 2007; Knowles et al., 2010). Functional capacity was measured by the University of California, San Diego Performance-Based Skills Assessment-2 (UPSA-2; Mausbach et al., 2008).

2.2.2 Psychological stressor—Study participants completed an automated testing session which consisted of two psychological distress-inducing tasks, the order of which was varied randomly. One task was the computerized Paced Auditory Serial Addition Task (PASAT), during which participants used a computer mouse to select the correct sum of consecutive numbers presented briefly on a computer screen before the next number was presented [e.g. 2+4 (correct response=6) +5 (=9) +7 (=12)] (Lejuez et al., 2003). When an incorrect response was given, or a response was not given before the next number was presented, a loud (90 decibel) aversive explosion sound was played. The task consisted of two learning sessions followed by an experimental session. Speed of response and accuracy were measured and an algorithm automatically titrated the speed of the task presentation to provide similar challenges across participants.

The other task was the computerized Mirror-Tracing Persistence Task (MTPT; Strong et al., 2003). Participants were asked to trace a red dot along the outline of a star shaped image on the computer screen using the mouse. Tracing was challenging because the cursor movement was opposite to the movement of the mouse. Errors, such as tracing outside the line or keeping the mouse stationary, were met with a loud aversive explosion sound. The MTPT task consisted of three learning sessions followed by an experimental session. The width of the star outline was titrated automatically depending on performance to make the challenge more even across participants. For both tasks, participants could quit the experimental session at any time, but were informed that the better they performed the greater the monetary bonus they would receive. The experimental trial in each task could last up to seven minutes. Participants were not told the maximum amount of time allowed for either task. A monetary bonus of $20 was given for not quitting and $10 was given if the participant quit one or both of the tasks, although this was only revealed after completion of the testing session.

Both the PASAT and the MTPT have been widely used as measures of distress intolerance (Daughters et al., 2005b; McHugh et al., 2011). They both induce psychological stress, with the magnitude of reported distress not correlating with distress intolerance itself, suggesting that the task captures a person’s inability to tolerate distress rather than just their level of distress (McHugh et al., 2011). In our design, we combined both tasks to reduce potential biases which may arise due to differences in cognitive vs. manual skill.

2.2.3 Self-report of affect reactivity—Participants completed the Positive and Negative Affect Schedule (PANAS) at three time points (pre-test, after the first task, and after the second task) during the study session to measure subjective affect reactivity (Watson et al.,

1988). This scale consists of 10 negative affect symptoms and 10 positive affect symptoms rated on the scale 1=very slightly to 5=extremely. Negative affect represents a general dimension of subjective distress and includes the following mood states: afraid, scared, nervous, jittery, irritable, hostile, guilty, ashamed, upset, and distressed. Positive affect reflects a person's level of pleasurable engagement and includes these mood states: active, alert, attentive, determined, enthusiastic, excited, inspired, interested, proud, and strong.

2.3 Data analyses

The primary measure of *distress intolerance* was defined as quitting the experimental trial in at least one of the stressor tasks. We analyzed this data as an ordered, combined variable where 0=persists on both tasks (tolerant to the distress), 1=quit one task early (moderately intolerant/tolerant to distress), and 2=quit both tasks (implying intolerance to distress). Adaptive functioning was conceptualized as persisting until the end of the task, yet we also examined group differences in time spent on the experimental trial of both tasks. We calculated an average error rate as the number of aversive sounds divided by the total number of seconds spent on the experimental trial of each task. We also explored distress induced *affect reactivity*, as measured by the separate maximum changes in negative and positive affect immediately after completing the tasks compared with baseline.

Ordered logistic regressions were utilized to test group differences on distress intolerance, and to explore the relationship between clinical variables and distress intolerance (Anderson and Philips, 1981). Two t-tests examined the difference in average time spent on the experimental trials between groups. Group differences in demographics and clinical measures were examined with ANOVA, Chi square, and Fishers exact tests and *t*-tests were used to test differences between groups on maximum change in negative and positive affect. A repeated measures ANOVA explored group, reactivity (baseline vs. maximum change in affect), and the group x reactivity interaction in the positive and negative affect ratings. Finally, causal mediation analyses tested if distress intolerance mediated the association between clinical variables and functional capacity and if symptoms and cognition mediated the association between distress intolerance and functional capacity (Imai et al., 2010; Hicks and Tingley, 2011). All analyses were performed using Stata 12 (StataCorp, 2011).

3. Results

3.1 Clinical characteristics

Patients and controls were frequency-matched in age (P=0.489) and sex (P=0.085), however, patients had lower education (P=0.004) and a greater percentage of smokers (P=0.014) compared with controls (Table 1). SZ had significantly more psychiatric symptoms, greater impulsiveness, worse functional capacity, and worse cognitive performance (all P<0.001).

3.2 Distress intolerance in schizophrenia

SZ patients showed increased distress intolerance such that they were significantly more likely to terminate the tasks early as compared to controls (Table 2). SZ had 2.84 times greater odds of quitting one or both tasks versus persisting on both tasks as compared to

controls (P=0.005). SZ had higher distress intolerance in both PASAT and MPTC tasks as compared to controls. Sex, age and smoking status were not significantly associated with distress intolerance (all P≥0.15). Persons with above high school education had lower odds of quitting one or both tasks as compared to those with a high school education or less (OR=0.32, P=0.001). After controlling for education, the association between SZ and distress intolerance remained significant (OR=2.31, P=0.031 for SZ vs. controls). SZ spent significantly less time on the experimental trials as compared to controls (P<0.001).

3.3 Distress intolerance in relation to clinical symptoms, cognition, and functional capacity

In controls distress intolerance was not significantly associated with symptoms, impulsivity, cognition, errors on the tasks or functional capacity (Table 3). In SZ, less distress intolerance was significantly associated with greater functional capacity (OR=0.94, P=0.004) and greater cognitive performance (OR=0.45, P=0.016), but not with total symptoms, impulsiveness, anhedonia or avolition. SZ that performed the task with more errors had significantly greater distress intolerance (OR=3.57, P=0.001).

To further examine whether distress intolerance in SZ influences functional capacity independently, through clinical and cognitive impairments, or vice versa, we modeled the UPSA-2 total score as the outcome, with distress intolerance as the predictor and cognition and BPRS total symptom score as mediators (Figure 1A). Symptoms minimally mediated the effect, explaining 2% of the effect of distress intolerance, whereas cognitive performance moderately (43% of effect; 95% CI=26% – 94%) mediated the association between distress intolerance and functional capacity. Re-arranging the model where cognition and symptoms were the predictors and distress intolerance was the mediator (Figure 1B); we found that distress intolerance did not significantly mediate the relationship between symptoms and functional capacity (indirect and direct effects not significant), and minimally mediated the effect of cognitive performance, explaining 11% (95% CI=8% – 17%) of its effect on functional capacity.

3.4 Affect reactivity

A repeated measures ANOVA showed a significant main effect of negative affect reactivity (F=34.93, df=2, P<0.001) and a group main effect (F=9.04, df=1, P=0.003), but no group x reactivity interaction (F=1.49, df=2, P=0.229). SZ (F=10.37, df=1, P=0.002) had higher negative affect ratings as compared to controls. The large main effect of negative affect reactivity but no significant interaction suggests that this paradigm reliably evoked negative affect reactivity across groups with SZ showing “normal” increases in negative. Importantly, baseline negative affect or reactivity were not significantly associated with distress intolerance in any group (all P>0.459), therefore distress intolerance was not primarily driven by negative affect. Negative affect reactivity was not significantly associated with symptoms, cognition, and functional capacity (all P>0.407).

For positive affect, a repeated measures ANOVA showed a significant main effect of reactivity (F=12.85, df=1, P<0.001) but no group main effect (F=0.34, df=1, P=0.562) or group x reactivity interaction (F=3.13, df=1, P=0.0.080). This suggests that the groups had similar positive affect at baseline, and the paradigm reliably decreased positive affect

equivalently across groups. Similar to negative affect, baseline positive affect or reactivity were not significantly associated with distress intolerance in any group (all $P>0.231$; Table 4). Positive affect reactivity was not significantly associated with the clinical measures (all $P>0.107$).

4. Discussion

In this study, we found relatively clear evidence of increased distress intolerance in SZ, which was significantly associated with their impaired functional capacity and cognition. Interestingly, distress intolerance was not associated with severity of psychiatric symptoms in SZ. Distress intolerance had an independent effect on functional capacity, and also an indirect effect on functional capacity through cognition.

Symptom severity and cognitive impairments are known to be related to functional capacity, which we replicated (Bowie and Harvey, 2005; Leifker et al., 2009). In line with prior work, SZ had greater negative affect at baseline, however in contrast to previous findings (Blanchard et al., 1998), SZ reported similar baseline positive affect as compared to controls. SZ and controls showed similar increases in negative affect and decreases in positive affect in response to the task, suggesting that: 1) SZ were not particularly more distressed, and 2) any potential lack of insight into SZ's affective state did not preclude a change in affective ratings. Thus, participation in this distress challenge did not result in greater emotional reactivity in SZ as has been seen in response to other stressors, such as daily hassles (Myin-Germeys et al., 2001). The novel finding here is that distress intolerance, measured by a laboratory based distress-inducing paradigm, independently predicted functional capacity within SZ but not in controls. Additionally, only in the SZ group did errors predict terminating the tasks early. While controls may have had idiosyncratic reasons for terminating the task early, such as low motivation for the monetary bonus or boredom, SZ seem particularly sensitive to making errors and/or the negative aversive stimulus in terms of task persistence. Perhaps past experiences of failures combined with lower cognitive reserve in certain persons with SZ predispose them to exhibit maladaptive responses to distress, manifested here as early task termination.

Neurobiological abnormalities found in patients with schizophrenia may explain why a larger proportion of patients were distress intolerant, and why this behavioral trait may be relevant to functional capacity. Persons with schizophrenia demonstrate blunted error-related responses in the anterior cingulate cortex which correspond to poorer performance. This decreased activation of the "reinforcement learning network" likely contributes to patients displaying behavior that is rigid and preservative rather than adaptive to circumstances and guided by outcome (Polli et al., 2008). Due to impairments in this network, SZ may have been less able to adapt their task strategy or performance, thus becoming more distressed or apathetic about pursing the reward. Additionally, unmedicated SZ patients have demonstrated reduced activation in the ventral striatum, a central component of the reward system, with reduced activation corresponding to greater negative symptoms (Juckel et al., 2006; Howes and Kapur, 2009). This abnormal activation likely interferes with processing of reward-predicting cues by dopamine release, further contributing to loss of motivation to pursue rewards.

Through the mediation analysis in SZ we found that distress intolerance only explained a small percentage of the total effect between cognition and functional capacity, but the cognitive measure mediated about half of the effect of distress intolerance on functional capacity. Our interpretation is that distress intolerance influences functional capacity in part independently and in part through cognition, such that SZ with reduced cognitive ability could not persist under distress and choose quitting to reduce their distress as negative reinforcement theory would predict. This result is consistent with evidence suggesting that patients with greater cognitive impairments in memory and executive functioning use more avoidant coping strategies when faced with stress (Lysaker et al., 2005). Since over half of the distress intolerance effect on functional capacity was independent of cognition, our results add support to the hypothesis that sensitivity to stress in SZ does not result from cognitive impairments alone (Myin-Germeys and van Os, 2007). As distress intolerance was not associated with impulsiveness, this finding cannot be explained by SZ patients making impulsive decisions.

Our main finding is important since the measure of functional capacity, the UPSA-2, is regarded as a direct and valid estimate of functional disability that is being used as an outcome measure in treatment studies and is a significant predictor of schizophrenia patient's ability to live independently (Harvey et al., 2007; Mausbach et al., 2008). Studies in other psychiatric conditions have also linked distress intolerance to less favorable clinical outcomes (Daughters et al., 2005a; Daughters et al., 2005b; O'Cleirigh et al., 2007; Nock and Mendes, 2008). The present finding leads to the question of whether remediation for functional capacity in schizophrenia could be achieved in part by targeting patients' ability to tolerate psychological distress.

Limitations of this work include that our distress intolerance paradigm always incorporated an aversive sound, thus we were unable to assess task persistence without the aversive feedback. The data is cross-sectional, so despite some evidence of directionality from the mediation analyses, it remains difficult to determine causality between distress intolerance and other measures. It may be useful for future studies to employ other stress paradigms, such as those involving response to cold, pain, or embarrassment, to investigate the range of distress intolerance exhibited by SZ. It is unknown how responses to laboratory induced stress reflect responses to real life stressors; this is another important topic for future investigation. However, assessing the response to a standardized laboratory stressor does provide valuable information about an individual's response to these types of psychologically stressful situations. Lastly, differences in task persistence may reflect individual differences in motivation to receive negative reinforcement (quitting the task and thus ending the aversive sound) relative to motivation to pursue positive reinforcement (greater payment for good performance). This is an important consideration since poor reward processing is a fundamental aspect of negative symptoms of schizophrenia (Gold et al., 2008). However, there was not a significant difference in BNSS scores between distress intolerant and distress tolerant patients in our sample, suggesting that distress intolerance in this population may not simply be a consequence of negative symptoms.

The current findings have implications for initiatives such as the NIMH Research Domain Criteria (RdoC) project that seek to identify and define dimensions of psychopathology that

cross nosological boundaries. Distress intolerance is prominent not only among individuals with psychotic disorders, but also those with substance abuse disorders, problematic gambling, and among self-injurious teens (Daughters et al., 2005a; Daughters et al., 2008; Nock and Mendes, 2008). “Frustrative non-reward” has been identified as an important construct in the negative valence domain of RdoC (NIMH, 2011), and distress intolerance paradigms such as that employed in this study may be a useful approach for examining this construct in human research.

In conclusion, we found SZ to be more likely than controls to experience distress intolerance, and distress intolerance has a large and independent influence on functional capacity, in addition to its indirect effect on functional capacity through cognition. Distress intolerance was not driven by greater affect reactivity. These results highlight the importance of distress intolerance as an important paradigm in the study of the etiology and treatment for schizophrenia.

Acknowledgments

We would like to thank our study participants and the staff of the Neuroimaging Research Program at the Maryland Psychiatric Research Center. This work was supported by National Institutes of Health grants T32MH067533, R01MH085646, R01DA027680, and R21DA033817.

References

Albus M, Ackenheil M, Engel RR, Müller F. Situational reactivity of autonomic functions in schizophrenic patients. Psychiatry Research. 1982; 6:361–370. [PubMed: 6955823]

Anderson J, Philips P. Regression, discrimination and measurement models for ordered categorical variables. Applied Statistics. 1981; 30:22–31.

Bar KJ, Berger S, Metzner M, Boettger MK, Schulz S, Ramachandraiah CT, Terhaar J, Voss A, Yeragani VK, Sauer H. Autonomic dysfunction in unaffected first-degree relatives of patients suffering from schizophrenia. Schizophrenia Bulletin. 2010; 36:1050–1058. [PubMed: 19366982]

Barnett J, Salmond C, Jones P, Sahakian B. Cognitive reserve in neuropsychiatry. Psychological Medicine. 2006; 36:1053–1064. [PubMed: 16854246]

Blanchard JJ, Mueser KT, Bellack AS. Anhedonia, positive and negative affect, and social functioning in schizophrenia. Schizophrenia Bulletin. 1998; 24:413–424. [PubMed: 9718633]

Bowie CR, Harvey PD. Cognition in Schizophrenia: Impairments, Determinants, and Functional Importance. The Psychiatric Clinics of North America. 2005; 28:613–633. [PubMed: 16122570]

Brandon TH, Herzog TA, Juliano LM, Irvin JE, Lazev AB, Simmons VN. Pretreatment task persistence predicts smoking cessation outcome. Journal of Abnormal Psychology. 2003; 112:448–456. [PubMed: 12943023]

Breier A, Wolkowitz OM, Doran AR, Bellar S, Pickar D. Neurobiological effects of lumbar puncture stress in psychiatric patients and healthy volunteers. Psychiatry Research. 1988; 25:187–194. [PubMed: 2845460]

Castro MN, Vigo DE, Weidema H, Fahrer RD, Chu EM, De Achaval D, Nogués M, Leiguarda RC, Cardinali DP, Guinjoan SM. Heart rate variability response to mental arithmetic stress in patients with schizophrenia:: Autonomic response to stress in schizophrenia. Schizophrenia Research. 2008; 99:294–303. [PubMed: 17913466]

Cloninger CR, Przybeck TR, Svrakic DM. The tridimensional personality questionnaire: US normative data. Psychological Reports. 1991; 69:1047–1057. [PubMed: 1784653]

Corcoran C, Walker E, Huot R, Mittal V, Tessner K, Kestler L, Malaspina D. The stress cascade and schizophrenia: etiology and onset. Schizophrenia Bulletin. 2003; 29:671–692. [PubMed: 14989406]

Daughters SB, Lejuez CW, Strong DR, Brown RA, Breen RB, Lesieur HR. The relationship among negative affect, distress tolerance, and length of gambling abstinence attempt. Journal of Gambling Studies. 2005a; 21:363–378. [PubMed: 16311873]

Daughters SB, Lejuez C, Kahler CW, Strong DR, Brown RA. Psychological distress tolerance and duration of most recent abstinence attempt among residential treatment-seeking substance abusers. Psychology of Addictive Behaviors. 2005b; 19:208–211. [PubMed: 16011392]

Daughters SB, Sargeant MN, Bornovalova MA, Gratz KL, Lejuez C. The relationship between distress tolerance and antisocial personality disorder among male inner-city treatment seeking substance users. Journal of Personality Disorders. 2008; 22:509–524. [PubMed: 18834298]

Dickinson D, Ramsey ME, Gold JM. Overlooking the obvious: a meta-analytic comparison of digit symbol coding tasks and other cognitive measures in schizophrenia. Archives of General Psychiatry. 2007; 64:532–542. [PubMed: 17485605]

Eisenberger R, Kuhlman DM, Cotterell N. Effects of social values, effort training, and goal structure on task persistence. Journal of Research in Personality. 1992; 26:258–272.

First, M.; Spitzer, R.; Williams, J.; Gibbon, M. Structured clinical interview for DSM-IV-patient edition (SCID-P). Biometric Research; New York: 1995.

Gold JM, Waltz JA, Prentice KJ, Morris SE, Heerey EA. Reward processing in schizophrenia: a deficit in the representation of value. Schizophrenia Bulletin. 2008; 34:835–847. [PubMed: 18591195]

Harvey PD, Velligan DI, Bellack AS. Performance-based measures of functional skills: usefulness in clinical treatment studies. Schizophrenia Bulletin. 2007; 33:1138–1148. [PubMed: 17493956]

Hicks R, Tingley D. Causal mediation analysis. Stata Journal. 2011; 11:605–619.

Howes OD, Kapur S. The dopamine hypothesis of schizophrenia: version III--the final common pathway. Schizophrenia Bulletin. 2009; 35:549–562. [PubMed: 19325164]

Imai K, Keele L, Tingley D. A general approach to causal mediation analysis. Psychological Methods. 2010; 15:309–314. [PubMed: 20954780]

Jansen LM, Gispen-de Wied CC, Kahn RS. Selective impairments in the stress response in schizophrenic patients. Psychopharmacology. 2000; 149:319–325. [PubMed: 10823414]

Jansen L, Gispen-de Wied CC, Gademan PJ, De Jonge RC, van der Linden Jeroen A, Kahn RS. Blunted cortisol response to a psychosocial stressor in schizophrenia. Schizophrenia Research. 1998; 33:87–94. [PubMed: 9783348]

Juckel G, Schlagenhauf F, Koslowski M, Wüstenberg T, Villringer A, Knutson B, Wrase J, Heinz A. Dysfunction of ventral striatal reward prediction in schizophrenia. Neuroimage. 2006; 29:409–416. [PubMed: 16139525]

Kirkpatrick B, Strauss GP, Nguyen L, Fischer BA, Daniel DG, Cienfuegos A, Marder SR. The brief negative symptom scale: psychometric properties. Schizophrenia Bulletin. 2011; 37:300–305. [PubMed: 20558531]

Knowles EE, David AS, Reichenberg A. Processing speed deficits in schizophrenia: reexamining the evidence. American Journal of Psychiatry. 2010; 167:828–835. [PubMed: 20439390]

Leifker FR, Bowie CR, Harvey PD. Determinants of everyday outcomes in schizophrenia: the influences of cognitive impairment, functional capacity, and symptoms. Schizophrenia Research. 2009; 115:82–87. [PubMed: 19775869]

Lejuez C, Kahler CW, Brown RA. A modified computer version of the Paced Auditory Serial Addition Task (PASAT) as a laboratory-based stressor. The Behavior Therapist. 2003; 26:290–293.

Lysaker PH, Davis LW, Lightfoot J, Hunter N, Stasburger A. Association of neurocognition, anxiety, positive and negative symptoms with coping preference in schizophrenia spectrum disorders. Schizophrenia Research. 2005; 80:163–171. [PubMed: 16125370]

Mausbach BT, Bowie CR, Harvey PD, Twamley EW, Goldman SR, Jeste DV, Patterson TL. Usefulness of the UCSD Performance-Based Skills Assessment (UPSA) for predicting residential independence in patients with chronic schizophrenia. Journal of Psychiatric Research. 2008; 42:320–327. [PubMed: 17303168]

McHugh RK, Daughters SB, Lejuez CW, Murray HW, Hearon BA, Gorka SM, Otto MW. Shared variance among self-report and behavioral measures of distress intolerance. Cognitive Therapy and Research. 2011; 35:266–275. [PubMed: 23894216]

Myin-Germeys I, Krabbendam L, Jolles J, Delespaul PA, van Os J. Are cognitive impairments associated with sensitivity to stress in schizophrenia? An experience sampling study. American Journal of Psychiatry. 2002; 159:443–449. [PubMed: 11870009]

Myin-Germeys I, van Os J. Stress-reactivity in psychosis: evidence for an affective pathway to psychosis. Clinical Psychology Review. 2007; 27:409–424. [PubMed: 17222489]

Myin-Germeys I, van Os J, Schwartz JE, Stone AA, Delespaul PA. Emotional reactivity to daily life stress in psychosis. Archives of General Psychiatry. 2001; 58:1137. [PubMed: 11735842]

NIMH. Negative Valence Systems: Workshop Proceedings; 2011.

Nock MK, Mendes WB. Physiological arousal, distress tolerance, and social problem-solving deficits among adolescent self-injurers. Journal of Consulting and Clinical Psychology. 2008; 76:28–38. [PubMed: 18229980]

Norman RM, Malla AK. Stressful life events and schizophrenia. I: A review of the research. The British Journal of Psychiatry. 1993; 162:161–166. [PubMed: 8435685]

O'Cleirigh C, Ironson G, Smits JAJ. Does distress tolerance moderate the impact of major life events on psychosocial variables and behaviors important in the management of HIV? Behavior Therapy. 2007; 38:314–323. [PubMed: 17697855]

Overall JE, Donald RG. The brief psychiatric rating scale. Psychological Reports. 1962; 10:799–812.

Polli FE, Barton JJ, Thakkar KN, Greve DN, Goff DC, Rauch SL, Manoach DS. Reduced error-related activation in two anterior cingulate circuits is related to impaired performance in schizophrenia. Brain. 2008; 131:971–986. [PubMed: 18158315]

Simons JS, Gaher RM. The Distress Tolerance Scale: Development and validation of a self-report measure. Motivation and Emotion. 2005; 29:83–102.

Stanford MS, Mathias CW, Dougherty DM, Lake SL, Anderson NE, Patton JH. Fifty years of the Barratt Impulsiveness Scale: An update and review. Personality and Individual Differences. 2009; 47:385–395.

StataCorp. Stata Statistical Software: Release 12. 2011

Strong D, Lejuez C, Daughters S, Marinello M, Kahler C, Brown R. The computerized mirror tracing task version 1. 2003 Unpublished manual.

Walker E, Mittal V, Tessner K. Stress and the hypothalamic pituitary adrenal axis in the developmental course of schizophrenia. Annual Review of Clinical Psychology. 2008; 4:189–216.

Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. Journal of Personality and Social Psychology. 1988; 54:1063–1070. [PubMed: 3397865]

Highlights

- Schizophrenia patients and healthy controls completed a psychological distress task.
- SZ displayed distress intolerance, more often quitting the distress challenge early.
- Distress intolerance corresponded to worse functional capacity and cognition in SZ.
- Treatment targeting SZ patient's ability to tolerate distress may improve functioning.

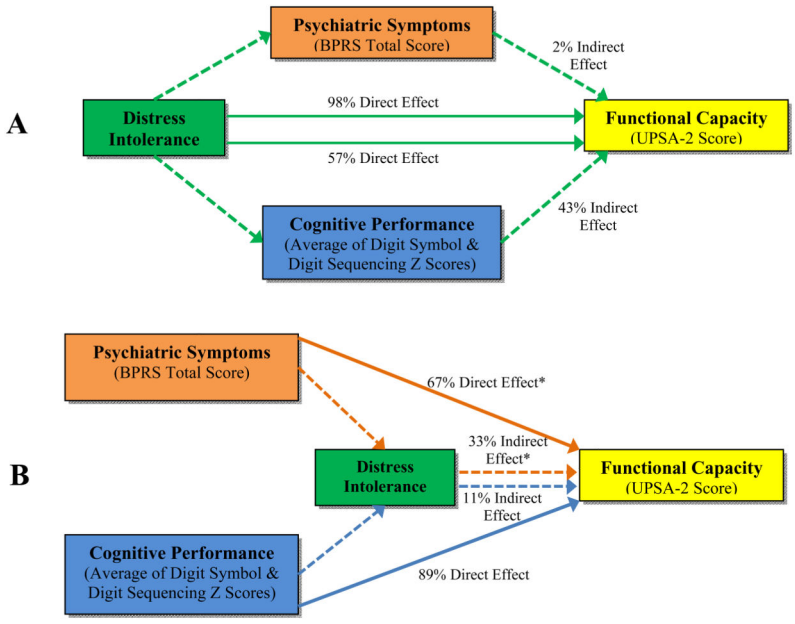

Figure 1.

Mediation analysis of cognition index, symptoms, and distress intolerance on functional capacity in schizophrenia patients. 1A: Mediation analysis showing the percent of distress intolerance's total effect on functional capacity mediated by psychiatric symptoms and cognitive performance. 1B: Mediation analysis showing the percent of psychiatric symptom's total effect on functional capacity mediated by distress intolerance, as well as the percent of cognitive performance's total effect on functional capacity mediated by distress intolerance. *=95% confidence interval contains zero, effect is not significant. UPSA-2: University of California Performance Skills Assessment 2. BPRS: Brief Psychiatric Rating Scale.

Table 1

Sample demographics and clinical measures

Variable	Healthy Controls n=43	SZ Patients n=65	Healthy Controls vs. SZ	
			Test Statistic	*P* value
Age in years*	38.5 (12.8)	36.8 (12.1)	t=0.69	0.489
Male sex, %	51.2%	67.7%	X^2=2.98	0.085
Race (% Caucasian: Black: Other)**	60:35:5	40:57:3	X^2=4.87	0.027
Education (% high school or less vs. % some college or college graduate)	23:77	51:49	X^2=8.18	0.004
Smoking Status, % current smokers	25.6%	49.2%	X^2=6.04	0.014
Brief Psychiatric Rating Scale Total Score*	23.3 (3.0)	40.6 (10.7)	t=−10.25	<0.001
Barratt Impulsiveness Scale Total Score*	56.4 (9.5)	66.1(9.9)	t=−5.02	<0.001
Brief Negative Symptom Scale Anhedonia*	0.6 (1.2)	5.1 (5.1)	t=−5.65	<0.001
Brief Negative Symptom Scale Avolition*	1.0 (2.1)	3.9 (3.1)	t=−5.32	<0.001
Cognitive Ability*	0.43 (0.7)	−0.35 (0.8)	t=5.34	<0.001
University of California San Diego Performance-Based Skills Assessment-2 Total Score*	82.9 (9.1)	72.9 (13.3)	t=4.32	<0.001

*Mean (SD);

**Statistics based on Caucasian vs. African American race.

Table 2

Distress intolerance by participant group

Variable	Healthy Controls n=43	SZ Patients n=65	Healthy Controls vs. SZ	
			Odds Ratio	*P* value
Distress intolerance (% quitting no tasks: % quitting 1 task: % quitting both tasks)	44:44:11	26:37:37	2.84	0.005
Quit PASAT (Addition Task), %	14	36	3.39	0.017
Quit MTPT (Star Tracing Task), %	53	71	2.13	0.069

Table 3

Relationship between distress intolerance and clinical symptoms, cognition, task errors and functional capacity

Model	Healthy Controls n=43				SZ Patients n=65			
	OR	95% CI		*P* value	OR	95% CI		*P* value
BPRS Total Score	0.92	0.76	1.11	0.373	1.02	0.98	1.07	0.226
BIS Total Score	1.00	0.94	1.06	0.875	0.98	0.94	1.03	0.443
BNSS Anhedonia	1.44	0.86	2.42	0.161	1.06	0.96	1.16	0.252
BNSS Avolition	0.98	0.74	1.29	0.866	1.16	0.99	1.36	0.066
Average % Error	1.30	0.61	2.80	0.500	3.57	1.70	7.47	0.001
Cognitive Ability	1.09	0.42	2.80	0.859	0.45	0.24	0.86	0.016
UPSA-2 Total Score	1.05	0.98	1.12	0.139	0.94	0.91	0.98	0.004

* Results represent the output from seven separate ordered logistic regression models. BPRS=Brief Psychiatric Rating Scale, BIS=Barratt Impulsiveness Scale-11, BNSS=Brief Negative Symptom Scale, UPSA-2=University of California San Diego Performance-Based Skills Assessment.

Table 4

Relationship between distress intolerance and measures of affect reactivity

Variable	Healthy Controls n=43	SZ Patients n=65	Combined Sample		SZ Patients Only	
			OR	*P* value	OR	*P* value
Negative Affect at Baseline[#]	1.11 (0.19)	1.40[*] (0.57)	1.41	0.405	1.17	0.723
Maximum Change in Negative Affect[#]	0.49 (0.63)	0.69 (0.78)	1.19	0.482	1.19	0.545
Positive Affect at Baseline[#]	3.06 (0.91)	3.07 (1.06)	1.18	0.353	1.20	0.403
Maximum Change in Positive Affect[#]	−0.14 (0.74)	−0.40 (0.78)	0.68	0.108	1.15	0.642

[#]mean (SD);

[*]Significant difference between SZ patients and controls, p=0.003; OR: Odds ratio for association with distress intolerance.

Psychiatry Res. Author manuscript; available in PMC 2015 December 15.