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Authors

Granholm, Eric
Ruiz, Ivan
Gallegos-Rodriguez, Yuliana
[et al.](#)

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Pupillary responses as a biomarker of diminished effort associated with defeatist attitudes and negative symptoms in schizophrenia

Dr. Eric Granholm^{1,2}, Mr. Ivan Ruiz¹, Dr. Yuliana Gallegos-Rodriguez¹, Dr. Jason Holden¹, and Mr. Peter C. Link¹

¹VA San Diego Healthcare System

²Department of Psychiatry, University of California, San Diego

Abstract

Background—The hypothesis that defeatist performance attitudes are associated with decreased goal-directed task effort and negative symptoms in consumers with schizophrenia was investigated by using pupillary responses as a biomarker of task effort. Pupillary dilation during cognitive tasks provides a biomarker of effort devoted to the task, with greater dilation indicating greater effort.

Methods—Defeatist attitudes were assessed in 149 consumers with schizophrenia or schizoaffective disorder and 50 healthy controls, and consumers were divided into three groups (tertile split) with respect to severity of defeatist attitudes. Pupillary dilation responses were recorded during a digit-span task with 3-, 6-, and 9-digit spans.

Results—Effort allocation (pupillary responses) to the task increased as the processing load increased from low (3-digits) to moderate (6-digits) demands in healthy controls and consumers with schizophrenia with mild and moderate severity of defeatist attitudes. In contrast, consumers with severe defeatist attitudes did not increase their effort when processing demands increased from low to moderate loads and these consumers showed significantly less effort in the 6-digit condition relative to consumers with mild defeatist attitudes. Moreover, consumers with severe defeatist attitudes showed significantly greater severity of negative symptoms relative to consumers with mild defeatist attitudes and negative symptoms were significantly correlated with defeatist attitudes.

Conclusions—These results suggest a relationship between defeatist performance attitudes, goal-directed task effort indexed by pupillary responses, and negative symptoms in schizophrenia.

Corresponding Author: Eric Granholm, Ph.D., VA San Diego Healthcare System (116B), 3350 La Jolla Village Drive, San Diego, CA 92161, egranholm@ucsd.edu.

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The findings have implications for using cognitive therapy to reduce defeatist attitudes that may contribute to diminished effort and negative symptoms in schizophrenia.

Keywords

Schizophrenia; Pupillometry; Effort; Negative Symptoms; Dysfunctional Attitudes; Motivation

Introduction

Negative symptoms account for much of the poor functional outcome in schizophrenia and are an unmet treatment need in a large proportion of patients (1). Negative symptoms consist of: 1) internal experiences, including apathy, amotivation, asociality and anhedonia; and 2) expressive behaviors, including blunted affect and alogia. In a promising recent theoretical model, Beck and colleagues (2–4) applied the generic cognitive model to schizophrenia and proposed that dysfunctional attitudes like defeatist performance beliefs (e.g., “Why bother trying, I always fail,” “It’s not worth the effort”) may contribute to negative symptoms in schizophrenia. In their model, negative appraisals about one’s self and one’s ability to perform goal-directed tasks contribute to negative symptoms, as well as a lack of engagement in goal-directed functioning tasks. Rector et al. (4) proposed that defeatist performance beliefs about the personal costs of applying energy can lead to passivity and avoidance of activities that require effort, as a defense against anticipated failure and negative evaluations by others.

Similarly, in social learning and self-efficacy theories of motivation in healthy individuals (5, 6), self-competency beliefs are central to motivation to engage in goal-directed activities and willingness to expend effort when tasks become more difficult. People who expect to succeed are more willing to try new tasks, choose harder tasks, and expend more effort (6, 7). Consistent with this model, several researchers (3, 4, 8–12) have found that consumers with schizophrenia have found that greater severity of defeatist beliefs is associated with greater severity of negative symptoms and (less consistently) poorer functioning.

The present study tested this model’s prediction that greater severity of defeatist performance beliefs are associated with diminished effort toward goal-directed tasks in consumers with schizophrenia. Defeatist performance beliefs were assessed and pupillary responses were used as a biomarker of the extent of effort allocated to a digit span recall task in consumers with schizophrenia and healthy controls. Pupillary responses have been shown to be a reliable and sensitive psychophysiological index of the amount of effort allocated during performance of a variety of cognitive tasks (13, 14). In numerous studies, pupil size recorded during cognitive tasks has been found to increase in response to increased task demands, regardless of the putative cognitive domain examined (e.g., memory, language, reasoning). For instance, Granholm and colleagues (15, 16) showed that pupillary responses recorded during a digit span recall task increased systematically with increased task demands (longer spans) in healthy controls and consumers with schizophrenia, until task demands (span length) exceeded abilities and expectations for success (e.g., >7 digits), when pupil size decreased. Further, consumers with schizophrenia showed decreased task effort

(decline in pupil dilation) at lower task demands (shorter span lengths) than healthy controls (16).

These findings reflect the often complex interactions between task and operator in terms of resource allocation response to changing task demands (17, 18). As demands exceed expectations for success, participants decide the additional effort required to perform a task is no longer “worth it” in terms of the expected probability of success and reward. Possibly due to defeatist performance beliefs, participants with schizophrenia decided it was no longer worth it to continue allocating effort to the digit span task at lower demands relative to healthy controls. In another study (19), consumers with schizophrenia again showed less effort allocation (smaller pupil dilation) at higher task demands during the span of apprehension task, and less effort allocation was associated with greater severity of negative symptoms.

Based on these previous findings and the Beck model of negative symptoms, we hypothesized that consumers with schizophrenia would show greater severity of defeatist performance beliefs and smaller pupillary responses (less effort) relative to healthy controls on the digit span task, and that greater severity of defeatist attitudes would be associated with both smaller pupillary responses to increasing task demands and greater severity of negative symptoms. We also hypothesized that the relationship between defeatist attitudes and effort allocation would not be linear. Prior studies found only modest correlations between defeatist attitudes and motivational negative symptoms (r 's=.19–.28 (9–12)), suggesting only a weak linear relationship. It is possible that incremental increases in defeatist attitudes are not linked to incremental reductions in effort, especially at low levels of defeatist attitude severity. For example, individuals with minimal defeatist attitudes might allocate minimal effort at low task demands, because they are confident they can succeed without trying hard, whereas individuals with moderate defeatist attitudes might allocate greater effort, because they have doubts about their ability to succeed unless they try harder (e.g., compensatory effort). In contrast, individuals with severe defeatist attitudes, may be so hopeless about their ability to perform that they give up with only moderate increases in task demands. Thus, effort allocation may be unrelated to defeatist attitudes at lower levels of severity or may even increase from mild to moderate severity, and then decrease when attitudes become more severe (i.e., follow an inverted-U shaped function). A large sample (N=149) of consumers was included in the present study and divided into three groups based on a tertile split to examine subgroup effects and capture possible curvilinear relationships.

Methods and Materials

Participants

Participants included 149 consumers with schizophrenia (N=119) or schizoaffective disorder (N=30) and 50 healthy controls. Consumers were enrolled in randomized clinical trials of a nine-month group psychosocial intervention to improve functional outcome in schizophrenia (20, 21). Data reported in this study were collected at the baseline evaluation in these clinical trials, prior to any treatment. Consumers were recruited from outpatient clinics, residential and drop-in/clubhouse settings throughout San Diego County. Healthy controls were recruited through flyers and advertisements. Inclusion criteria were: 1) Age 18 or older; 2)

diagnosis of schizophrenia or schizoaffective disorder based on the Structured Clinical Interview for *DSM-IV* (22), or for healthy controls, no past or current anxiety, mood or psychotic disorders based on the Non-Patient SCID; and 3) capacity to consent. Participants in both groups were excluded for: 1) Alcohol or substance dependence diagnosis (*DSM-IV* criteria) other than nicotine or caffeine in the past 6 months; 2) ocular medications, injury, diseases or surgery that might affect pupil function; or 3) level of care required at baseline that would interfere with participation in outpatient therapy groups in the parent clinical trial. All but 10 consumers reported taking antipsychotic medications, and the mean chlorpromazine equivalent (23) dose for the sample was 791(SD=617). In addition, 53 (37%) reported taking anticholinergic medications, and 103 (71%) reported other psychotropic medications. Table 1 shows the sample demographics.

Measures

Defeatist Performance Attitudes—The Defeatist Performance Attitude Scale (DPAS) is a 15-item self-report subscale derived from factor analysis (24) of the commonly-used Dysfunctional Attitude Scale (25). The DPAS indexes endorsement of defeatist attitudes about one’s ability to perform goal-directed tasks (e.g., “If you cannot do something well, there is little point in doing it at all,” “People will probably think less of me if I make mistakes and fail”). Items are rated on a 1–7 Likert scale with higher scores indicating greater severity.

Clinical Symptom Measures—The Positive and Negative Syndrome Scale (PANSS) (26) and Scale for the Assessment of Negative Symptoms (SANS) (27) were administered. Based on factor analytic studies of the SANS (28–30), two negative symptom factors were derived: Diminished Expression (sum of items 1–5, 7, 9, 11, and 12) and Diminished Motivation (sum of items 14–16, and 18–21). Inter-rater reliability (interclass correlation) was .88 for PANSS total, .87 for PANSS positive, .83 for SANS total.

Digit Span Task—Pupillary responses were recorded while random digit spans of 3 (low load), 6 (moderate/near capacity load), and 9 (high/overload) digits were presented aurally at the rate of one digit per second. A laptop computer was used to present stimuli. Participants heard “ready” one second before the first digit and “repeat” one second after the last digit. The experimenter manually initiated pupillary response recording by pressing a button on the pupillometer when the word “ready” was presented. Participants completed 3, then 6, then 9 digit trials in blocks of two trials per condition (6 trials total), but additional trials were administered to replace trials judged to have excessive artifacts in a graphic display on the device, until two trials that appeared valid were recorded or four trials were attempted per digit span condition. The percentage of digits recalled in correct sequence was recorded.

Apparatus

A handheld NeurOptics PLR-100 pupillometer was used to record pupil diameter from the participant’s right eye at 10 Hz for up to 10 seconds, while participants viewed a gray dot on a white light background (~200 lux) inside in a viewing tube. The device was the size of a television remote with recording optics inside one end of a 1.5-inch viewing tube that surrounds the eye. Ambient light is blocked by the viewing tube and the participant closed

and held their hand over their other eye. Resolution of the device was excellent (mean error=.052mm; 99% CI=.048-.056; NeurOptics data, N=655). Given that most pupillary activity occurs with a frequency of less than 5 Hz, the sampling rate of 10 Hz was sufficient to provide appropriate pupillary response recordings and the study demonstrates the utility of this convenient handheld device for capturing cognitive effort allocation.

Data Reduction

A computer algorithm was used to remove blinks and artifacts (identified as large changes in diameter outside the possible rate of change) from digitized pupillary response waveforms (diameter samples in mm over time) and discarded data were replaced using linear interpolation. A trained technician also visually inspected raw and corrected graphic displays of pupil waveforms to verify artifact removal and dropped trials. Trials were discarded (<3%, see Supplementary Materials) if more than 50% of the trial waveform was comprised of artifacts. Cleaned trials were then averaged within each digit span condition and pupil diameter samples were averaged for each second of recording (10 per second), which corresponds to the presentation of digits at one-second intervals. Baseline pupil size (average of samples 4–7) at the start of each trial was then subtracted from pupil size at each second (each digit), to remove individual differences in pupil size. We did not use the first three samples as baseline, because participants often blinked in response to the onset of the light at the start of the trial. We selected samples at the time of the pupil light constriction reflex to control for possible individual differences in light constriction responses, although the groups did not differ significantly in light reflex constriction amplitude (the difference between the average of the first two samples and minimum diameter at the time of the light reaction) (group: $F(3,194)=0.36$, $p=.785$, $\eta^2_{\text{partial}}=.005$; group X digit-span condition: $F(6,388)=1.68$, $p=.126$, $\eta^2_{\text{partial}}=.025$). The primary dependent variable was pupillary response (change relative to baseline) at the last digit presented (at 4 s for 3-digit; 7 s for 6-digit; 10 s for 9-digit spans).

Statistical Analyses

A tertile split on DPAS scores was used to divide the schizophrenia sample into mild ($DPAS \leq 45$), moderate ($45 < DPAS \leq 59$) and severe ($DPAS > 59$) defeatist performance attitudes. The three DPAS subgroups did not differ significantly on any demographic or medication variable. A 4 group (3 DPAS subgroups and healthy controls) X 3 digit-span condition (3-, 6-, 9-digits) repeated measures analysis of variance (rmANOVA) was used to test differences between groups in pupillary responses and performance, one-way ANOVA was used to test for group differences within digit-span conditions, and Tukey's HSD test was used for pairwise group comparisons to control Type I error. One-way ANOVAs were used to test whether the three DPAS groups differed significantly in clinical symptoms, and Pearson's correlations examined the relationships between symptom variables, DPAS total, pupillary responses and recall accuracy. Alpha was $p < .05$, two-tailed.

Results

Defeatist Attitudes, Effort and Performance

Pupillary response waveforms are shown in Figure 1. The light onset at the start of the trial triggered a pupil constriction reflex, followed by systematic increase in pupil diameter with each digit presented. Figure 2 shows pupillary responses at the time the last digit was presented in each digit-span condition for healthy controls and consumers with schizophrenia in each DPAS group. Pupil dilation increased as the processing load increased from low (3-digits) to moderate/near-capacity (6-digits) demands, and then declined in the high/overload (9-digit) condition in healthy controls and consumers mild and moderate defeatist attitude severity. In contrast, consumers with severe defeatist attitudes did not increase effort allocation when processing demands increased from low to moderate loads.

These observations were confirmed in the rmANOVA, which showed significant effects for group ($F(3,195)=11.48$, $p<.001$, $\eta^2_{\text{partial}}=.15$), digit-span condition ($F(2,390)=28.78$, $p<.001$, $\eta^2_{\text{partial}}=.13$) and their interaction ($F(6,390)=2.25$, $p=.038$, $\eta^2_{\text{partial}}=.03$). One-way ANOVAs showed statistically significant group effects within the 3-digit, $F(3,195)=6.64$, $p<.001$, $\eta^2_{\text{partial}}=.09$, 6-digit, $F(3,195)=13.97$, $p<.001$, $\eta^2_{\text{partial}}=.18$, and 9-digit, $F(3,195)=5.65$, $p=.001$, $\eta^2_{\text{partial}}=.08$, conditions. Controls showed significantly greater pupillary responses relative to all three defeatist attitude groups in all three digit-span conditions (for 3-, 6- and 9-digits, Mild: d 's = .57, .73, .56; Moderate: d 's = .71, .89, .66; Severe: d 's = .82, 1.27, .74). Consumers with severe defeatist performance attitudes showed significantly smaller pupillary responses than consumers with mild defeatist attitudes in the 6-digit condition ($p=.040$, $d=.54$), but not in the 3-digit ($d=.26$) or 9-digit condition ($d=.19$). Consumers with moderate defeatist attitudes did not differ significantly from consumers with mild or severe defeatist attitudes in any digit-span condition (for 3-, 6- and 9-digits, Mild: d 's = -.14, -.15, -.10; Severe: d 's = .12, .38, .08). Defeatist attitudes were not significantly correlated with pupillary responses in the total schizophrenia sample ($N=149$; 3-digit: $r=-.09$; 6-digit: $r=-.16$; 9-digit: $r=-.05$), or in healthy controls ($N=50$; 3-digit: $r=-.04$; 6-digit: $r=-.07$; 9-digit: $r=-.10$). In the combined sample of consumers with schizophrenia and controls, the correlation between pupillary responses and recall performance was not significant in the 3-digit condition ($r=.09$), but was significant in the 6-digit ($r=.24$, $p=.001$), and 9-digit ($r=.27$, $p<.001$) conditions.

Figure 3 shows recall accuracy. The rmANOVA showed significant effects for group ($F(3,192)=11.58$, $p<.001$, $\eta^2_{\text{partial}}=.15$), digit-span condition ($F(2,384)=823.62$, $p<.001$, $\eta^2_{\text{partial}}=.81$) and their interaction ($F(6,384)=2.76$, $p=.012$, $\eta^2_{\text{partial}}=.04$). One-way ANOVAs showed that the groups differed significantly in the 6-digit, $F(3,194)=7.08$, $p<.001$, $\eta^2_{\text{partial}}=.10$, and 9-digit, $F(3,192)=14.04$, $p<.001$, $\eta^2_{\text{partial}}=.18$, conditions, but not the 3-digit condition, $F(3,194)=2.24$, $p=.085$, $\eta^2_{\text{partial}}=.03$. Controls showed significantly greater recall accuracy relative to all three DPAS groups in the 6- and 9-digit conditions (Mild: $d=.59$; .83; Moderate: $d=.66$, 1.06; Severe: $d=.89$, 1.19). Recall accuracy for consumers with mild defeatist attitudes did not differ significantly from the moderate or severe group in the 6- or 9-digit conditions (Moderate: $d=.06$; .24; Severe: $d=.30$, .36), and the moderate and severe groups also did not differ significantly ($d=.23$; .12). Defeatist attitudes were not

significantly correlated with recall accuracy in the total schizophrenia sample (N=149; 3-digit: $r=-.01$; 6-digit: $r=-.11$; 9-digit: $r=-.16$).

Defeatist Attitudes and Clinical Symptoms

DPAS groups differed significantly in SANS Diminished Expression ($F(2,143)=5.21$, $p=.007$, $\eta^2_{\text{partial}}=.07$) and SANS Diminished Motivation ($F(2,143)=3.46$, $p=.034$, $\eta^2_{\text{partial}}=.05$). Mean SANS factor scores are shown in Figure 3 for each DPAS group. For SANS Diminished Expression, significant differences were found between the mild and severe ($p=.005$, $d=.64$) DPAS groups, but not between mild and moderate ($p=.079$, $d=.44$) nor between moderate and severe groups ($p=.568$, $d=.21$). For SANS Diminished Motivation, significant differences were again found between mild and severe DPAS groups ($p=.030$, $d=.52$), but not between mild and moderate ($p=.693$, $d=.16$) or moderate and severe ($p=.180$, $d=.36$) DPAS groups. Greater severity of defeatist attitudes (DPAS total) was significantly correlated with greater severity of SANS Diminished Expression ($r=.28$, $p=.001$) and SANS Diminished Motivation ($r=.23$, $p=.006$). Finally, pupillary responses were not significantly correlated with SANS Diminished Expression (3-digit: $r=-.06$; 6-digit: $r=-.12$; 9-digit: $r=-.04$), or Diminished Motivation (3-digit: $r=-.07$; 6-digit: $r=-.06$; 9-digit: $r=-.013$).

Discussion

This study examined associations between defeatist performance attitudes, goal-directed task effort and negative symptoms in consumers with schizophrenia. Effort allocation to a digit span recall task was objectively indexed by measuring pupillary dilation responses to the task, with greater dilation indicating greater task-devoted effort. Relative to healthy controls, consumers with schizophrenia showed significantly greater severity of defeatist performance attitudes and overall less effort (smaller pupillary responses) allocated to the task. Moreover, as in previous studies (15,16), healthy controls and consumers with mild to moderate severity of defeatist attitudes showed increased effort allocation as the processing load increased from low to moderate task demands, until task demands exceeded capacity limits, when they disengaged and stopped allocating effort in the high/overload condition. In contrast, consumers with severe defeatist attitudes did not increase effort allocation when processing demands increased from low to moderate loads and showed significantly less dilation in the moderate load condition relative to consumers with mild defeatist attitudes. This subgroup with severe defeatist attitudes also showed significantly greater severity of negative symptoms relative to consumers with mild defeatist attitudes, and negative symptoms were significantly correlated with severity of defeatist performance attitudes. These associations between defeatist attitudes, effort and negative symptoms were independent of depression severity and positive symptom severity (see Supplementary Materials). These results suggest a relationship between defeatist performance attitudes, goal-directed task effort and negative symptom severity in schizophrenia.

The results are consistent with a promising recent model of negative symptoms proposed by Beck and colleagues (2–4), as well as general motivation models, in which self-efficacy beliefs and expectations for success and reward play an important role in goal-directed task engagement (6,31,32). The present study established the crucial link between severe

defeatist attitudes and deficient goal-directed task effort. Consumers with the most severe defeatist performance attitudes showed the least goal-directed task effort and the most severe negative symptoms, suggesting defeatist performance beliefs and negative expectations for success and pleasure may contribute to the avoidance of effortful constructive and pleasurable activities in consumers with schizophrenia (3).

The correlation between DPAS scores and pupillary responses was weak and nonsignificant, but consumers with severe defeatist attitudes showed significantly smaller pupillary responses relative to consumers with mild defeatist attitudes in the 6-digit condition. These findings suggest a non-linear relationship, such that increments in severity of defeatist beliefs were not associated with proportional decrements in effort. Rather, only after a threshold level of severity of defeatist attitudes was reached, consumers were more likely to give up and disengage when challenged by increasing task difficulty. This finding has implications for future research; in that, studies may not detect linear associations between defeatist and motivation, effort, negative symptoms and functioning. Additional research is needed to replicate this subgroup finding and determine the best measures and cut-scores to identify which consumers are most likely to show negative symptoms linked to defeatist attitudes, as well as which consumers might benefit from interventions that target dysfunctional attitudes.

It is difficult to disentangle whether smaller pupillary responses reflected diminished effort or diminished capacity to perform the cognitive task (i.e., whether consumers “won’t” or “can’t” perform the task). In fact, Grant and Beck (3) suggested that capacity limitations could lead to failure experiences that contribute to the development and maintenance of defeatist performance beliefs, so associations between defeatist attitudes and both capacity limitations and diminished effort are predicted by the model. However, defeatist attitudes were not associated with capacity to perform the task (recall accuracy). In addition, since Grant and Beck’s (3) original report of an association between defeatist attitudes and neurocognitive impairment, other studies have not found strong associations (e.g., r ’s = $-.04$ to $-.19$; 12, 39, 40). Taken together, these findings suggest a stronger association between pupillary responses and effort rather than capacity. This is a cross-sectional correlational study, however, so it is not possible to confirm the direction of associations found between cognitive capacity, defeatist attitudes and effort allocation.

This avoidance and lack of effort associated with defeatist attitudes manifested as both diminished motivation and diminished expression. While less intuitive than the link between defeatist attitudes and diminished motivation, expressive negative symptoms may be behaviors linked to expected failure, rejection and negative social appraisal (4). That is, looking away, masking facial expressions, and avoiding speaking can serve to minimize social interactions due to either social disinterest, fear of rejection, low expectations for success, expected stigma, and/or anticipated negative consequences (e.g., “If I show my feelings, others will see my inadequacy,” “I can’t find the right words,” “I’m going to sound weird, strange, or stupid”). It is also possible that the association found between reduced pupillary responses and diminished expression is related to capacity limitations, given that smaller pupillary responses may reflect reduced capacity. Cohen and colleagues (41) found

diminished speech expressivity when consumers performed a cognitively-effortful task, which suggests diminished expression may be associated with reduced cognitive capacity.

It is difficult to accurately measure effort. Most available measures rely on questionable subjective self-reports, the assumption that poor performance under specific conditions (e.g., on easy tasks) reflects poor effort, or performance patterns on complex effortful decision-making tasks that may be impacted by executive function deficits. Pupillary responses provide an objective biomarker of effort that overcomes these potential problems with other measures. The present study and our prior research (16, 19) illustrate how pupillary responses might provide a useful biomarker of effort allocation in basic research, as well as pharmacologic and psychosocial clinical trials, on motivation, effort and negative symptoms in schizophrenia.

The results suggest that the attitudes and beliefs that people hold about effortful goal-directed tasks are a viable treatment target to improve negative symptoms in schizophrenia. There is mounting evidence that cognitive behavior therapy (CBT) interventions that target defeatist beliefs and social disinterest attitudes in schizophrenia can improve negative symptoms and functioning (20, 21, 33–38). For example, in a clinical trial of cognitive behavioral social skills training (CBSST) for consumers with schizophrenia (21), experiential negative symptoms and defeatist performance attitudes both improved to a significantly greater extent in CBSST relative to a goal-focused supportive contact condition. In another CBSST trial (20), greater improvement in defeatist attitudes during treatment was associated with better functional outcome nine months after treatment. These findings are consistent with two other open CBT trials that found significant improvement in both dysfunctional attitudes and negative symptoms; one found these improvements in consumers who had not been taking antipsychotic medication (37) and the other found that improvement in dysfunctional attitudes mediated improvement in negative symptoms (43). Defeatist performance attitudes and task effort, therefore, are potentially important change mechanisms to measure in CBT trials targeting negative symptoms and functioning. In addition, other interventions, like cognitive remediation, may also lead to improvements in self-efficacy and defeatist performance beliefs. As consumers practice cognitive tasks and compensate for cognitive impairments in the community, they may learn that they can improve their performance and succeed. Cognitive therapy techniques can be used to capitalize on these positive learning experiences and success experiences to challenge defeatist beliefs and increase self-esteem, which may contribute to improvements in negative symptoms and functioning in cognitive remediation programs. In particular, recent research (39, 42) has suggested that cognitive remediation programs might be strengthened by using cognitive therapy to target task-specific low success expectancies.

This study had several limitations. Participants were taking medications, which might impact pupillary responses and recall performance. However, key group differences in the 6-digit condition could not be explained by medication effects, because CPZE and other psychotropic medications were not associated with defeatist attitudes or pupillary responses in the 6-digit condition (see Supplementary Materials). Healthy controls and consumers with schizophrenia were not matched for gender, but no significant effects of gender were found within either group for pupillary responses, recall accuracy or DPAS scores. The sample in

the present study was a convenience sample of participants who volunteered for a clinical trial of a 9-month psychosocial intervention targeting functioning in schizophrenia, which might have created a sampling bias that could impact the generalizability of the findings (e.g., to individuals less motivated for an intensive psychosocial intervention). Despite this sampling bias, there was sufficient range of negative symptom severity, motivation, effort and defeatist attitudes to capture associations among these factors.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Kirkpatrick B, Fenton WS, Carpenter WT Jr, Marder SR. The NIMH-MATRICES consensus statement on negative symptoms. *Schizophr Bull.* 2006; 32:214–219. [PubMed: 16481659]
2. Beck, AT.; Rector, NA.; Stolar, NM.; Grant, PM. *Schizophrenia: Cognitive theory, Research, and Therapy.* New York: Guilford Press; 2009.
3. Grant PM, Beck AT. Defeatist beliefs as a mediator of cognitive impairment, negative symptoms, and functioning in schizophrenia. *Schizophr Bull.* 2009; 35:798–806. [PubMed: 18308717]
4. Rector NA, Beck AT, Stolar N. The negative symptoms of schizophrenia: A cognitive perspective. *Can J Psychiatry.* 2005; 50:247–257. [PubMed: 15968839]
5. Bandura, A. *Social Foundations of Thought and Action: A Social Cognitive Theory.* Englewood Cliffs, NJ: Prentice-Hall; 1986.
6. Bandura, A. *Self-efficacy: The Exercise of Control.* New York: W.H. Freeman; 1997.
7. Wigfield A, Eccles JS. Expectancy-value theory of achievement motivation. *Contemp Educ Psychol.* 2000; 25:68–81. [PubMed: 10620382]
8. Avery R, Startup M, Calabria K. The role of effort, cognitive expectancy appraisals and coping style in the maintenance of the negative symptoms of schizophrenia. *Psychiatry Res.* 2009; 167:36–46. [PubMed: 19339056]
9. Couture SM, Blanchard JJ, Bennett ME. Negative expectancy appraisals and defeatist performance beliefs and negative symptoms of schizophrenia. *Psychiatry Res.* 2011; 189:43–48. [PubMed: 21704387]
10. Green MF, Helleman G, Horan WP, Lee J, Wynn JK. From perception to functional outcome in schizophrenia: Modeling the role of ability and motivation. *Arch Gen Psychiatry.* 2012; 69:1216–1224. [PubMed: 23026889]
11. Horan WP, Rasseovsky Y, Kern RS, Lee J, Wynn JK, Green MF. Further support for the role of dysfunctional attitudes in models of real-world functioning in schizophrenia. *J Psychiatr Res.* 2010; 44:499–505. [PubMed: 20006849]
12. Quinlan T, Roesch S, Granholtm E. The role of dysfunctional attitudes in models of negative symptoms and functioning in schizophrenia. *Schizophr Bull.* 2014; 157:182–189.
13. Beatty J. Task-evoked pupillary responses, processing load, and the structure of processing resources. *Psychol Bull.* 1982; 91:276–292. [PubMed: 7071262]
14. Kahneman, D. *Attention and Effort.* Englewood Cliffs, N.J: Prentice-Hall; 1973.
15. Granholtm E, Asarnow RF, Sarkin AJ, Dykes KL. Pupillary responses index cognitive resource limitations. *Psychophysiology.* 1996; 33:457–461. [PubMed: 8753946]

16. Granholm E, Morris SK, Sarkin AJ, Asarnow RF, Jeste DV. Pupillary responses index overload of working memory resources in schizophrenia. *J Abnorm Psychol.* 1997; 106:458–467. [PubMed: 9241947]
17. Gophor, D.; Donchin, E. Workload - An examination of the concept. In: Boff, KR.; Kaufman, L.; Thomas, JP., editors. *Handbook of Perception and Human Performance.* New York: Wiley; 1986. p. 41-41-41-49.
18. Hockey GR. Compensatory control in the regulation of human performance under stress and high workload; a cognitive-energetical framework. *Biol Psychol.* 1997; 45:73–93. [PubMed: 9083645]
19. Granholm E, Verney SP, Perivoliotis D, Miura T. Effortful cognitive resource allocation and negative symptom severity in chronic schizophrenia. *Schizophr Bull.* 2007; 33:831–842. [PubMed: 16956985]
20. Granholm E, Holden J, Link PC, McQuaid JR, Jeste DV. Randomized controlled trial of cognitive behavioral social skills training for older consumers with schizophrenia: defeatist performance attitudes and functional outcome. *Am J Geriatric Psychiatry.* 2013; 21:251–262.
21. Granholm E, Holden J, Link PC, McQuaid JR. Randomized clinical trial of cognitive behavioral social skills training for schizophrenia: Improvement in functioning and experiential negative symptoms. *J Consult Clin Psychol.* 2014
22. First, MB.; Spitzer, R.; Robert, G.; Gibbon, M.; Gibbon, W.; Janet, BW. *Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition.* New York: Biometrics Research, New York State Psychiatric Institute; 2002.
23. Andreasen NC, Pressler M, Nopoulos P, Miller D, Ho BC. Antipsychotic dose equivalents and dose-years: a standardized method for comparing exposure to different drugs. *Biol Psychiatry.* 2010; 67:255–262. [PubMed: 19897178]
24. Cane DB, Olinger LJ, Gotlib IH, Kuiper NA. Factor Structure of the Dysfunctional Attitude Scale in a Student Population. *J Clin Psychol.* 1986; 42:307–309.
25. Weissman, AR.; Beck, AT. Development and validation of the Dysfunctional Attitudes Scale: A preliminary investigation. Paper presented at the 62nd Annual Meeting of the American Educational Research Association; Toronto, Ontario, Canada. 1978.
26. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull.* 1987; 13:261–276. [PubMed: 3616518]
27. Andreasen, NC. *Scale for the Assessment of Negative Symptoms (SANS).* Iowa City: The University of Iowa; 1982.
28. Blanchard JJ, Cohen AS. The structure of negative symptoms within schizophrenia: implications for assessment. *Schizophr Bull.* 2006; 32:238–245. [PubMed: 16254064]
29. Peralta V, Cuesta MJ. Dimensional structure of psychotic symptoms: an item-level analysis of SAPS and SANS symptoms in psychotic disorders. *Schizophr Res.* 1999; 38:13–26. [PubMed: 10427607]
30. Sayers SL, Curran PJ, Mueser KT. Factor structure and construct validity of the scale for the assessment of negative symptoms. *Psychol Assess.* 1996; 8:269–280.
31. Eccles JS, Wigfield A. Motivational beliefs, values, and goals. *Annu Rev Psychol.* 2002; 53:109–132. [PubMed: 11752481]
32. Llorens S, Schaufeli W, Bakker AB, Salanova M. Does a positive gain spiral of resources, efficacy beliefs and engagement exist? *Comput Hum Behav.* 2007; 23:825–841.
33. Granholm E, Ben-Zeev D, Link PC. Social disinterest attitudes and group cognitive-behavioral social skills training for functional disability in schizophrenia. *Schizophr Bull.* 2009; 35:874–883. [PubMed: 19628761]
34. Granholm E, McQuaid JR, McClure FS, Auslander LA, Perivoliotis D, Pedrelli P, et al. A randomized, controlled trial of cognitive behavioral social skills training for middle-aged and older outpatients with chronic schizophrenia. *Am J Psychiatry.* 2005; 162:520–529. [PubMed: 15741469]
35. Grant PM, Huh GA, Perivoliotis D, Stolar NM, Beck AT. Randomized trial to evaluate the efficacy of cognitive therapy for low-functioning patients with schizophrenia. *Arch Gen Psychiatry.* 2012; 69:121–127. [PubMed: 21969420]

36. Klingberg S, Wölwer W, Engel C, Wittorf A, Herrlich J, Meisner C, et al. Negative symptoms of schizophrenia as primary target of cognitive behavioral therapy: results of the randomized clinical TONES study. *Schizophr Bull.* 2011; 37(Suppl 2):S98–110. [PubMed: 21860053]
37. Morrison AP, Turkington D, Wardle M, Spencer H, Barratt S, Dudley R, et al. A preliminary exploration of predictors of outcome and cognitive mechanisms of change in cognitive behaviour therapy for psychosis in people not taking antipsychotic medication. *Behav Res Ther.* 2012; 50:163–167. [PubMed: 22209267]
38. Thase ME, Kingdon D, Turkington D. The promise of cognitive behavior therapy for treatment of severe mental disorders: a review of recent developments. *World Psychiatry.* 2014; 13:244–250. [PubMed: 25273290]
39. Strauss GP, Morra LF, Sullivan SK, Gold JM. The role of low cognitive effort and negative symptoms in neuropsychological impairment in schizophrenia. *Neuropsychology.* 2014; 29:282–91. [PubMed: 25000322]
40. Kiwanuka JN, Strauss GP, McMahon RP, Gold JM. Psychological predictors of functional outcome in people with schizophrenia. *Schizophr Res.* 2014; 157:299–304. [PubMed: 24878429]
41. Cohen AS, McGovern JE, Dinzeo TJ. Speech deficits in serious mental illness: A cognitive resource issue? *Schizophr Res.* 2014; 160:173–179. [PubMed: 25464920]
42. Choi J, Choi KH, Felice Reddy L, Fiszdon JM. Measuring motivation in schizophrenia: is a general state of motivation necessary for task-specific motivation? *Schizophr Res.* 2014; 153:209–13. [PubMed: 24529609]
43. Staring AB, Ter Huurne MA, van der Gaag M. Cognitive Behavioral Therapy for negative symptoms (CBT-n) in psychotic disorders: a pilot study. *J Behav Ther Exp Psychiatry.* 2013; 44:300–6. [PubMed: 23454550]

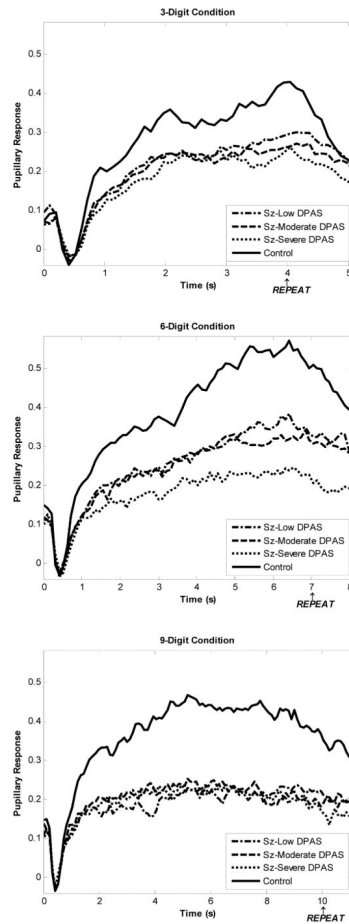


Figure 1. Pupillary responses (change in diameter in mm relative to baseline) are shown for consumers with schizophrenia (SZ) with low, moderate and severe defeatist performance attitudes (DPAS) and healthy controls in the 3-, 6-, and 9-digit span conditions. At trial onset, participants heard the word “ready” when the background luminance changed from dark to light, which triggered an initial light constriction reflex, and digits were presented at the rate of one per second (first digit was presented at 1 second, second digit at 2 seconds, etc.), until the word “repeat” prompted digit recall.

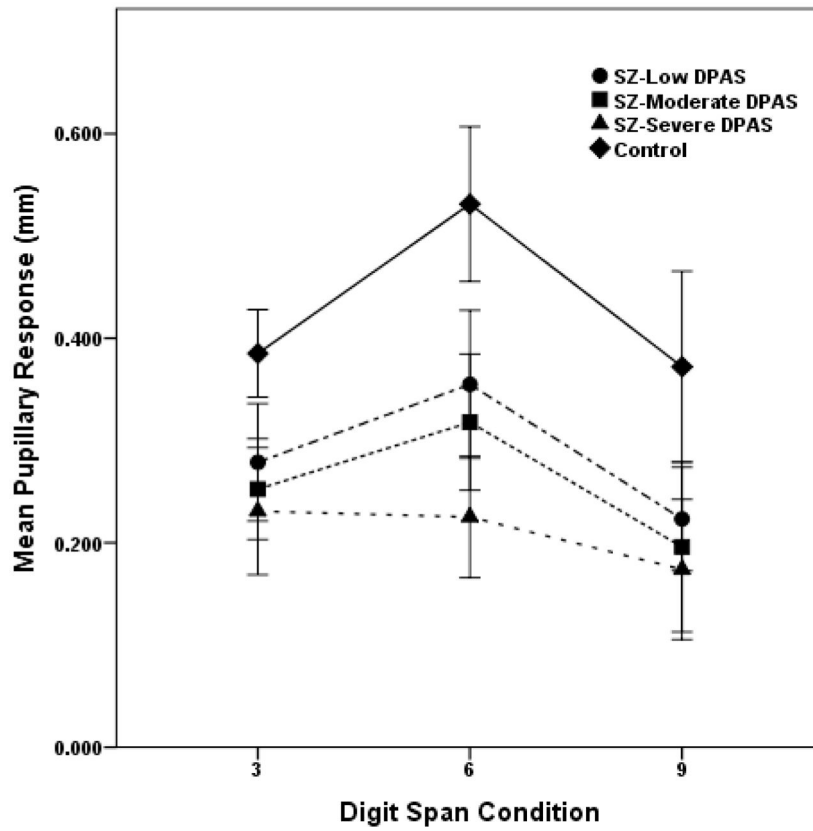


Figure 2. Pupillary responses (change in diameter in mm relative to baseline) are shown for consumers with schizophrenia (SZ) with low, moderate and severe defeatist performance attitudes (DPAS) and healthy controls at the time the last digit was presented in the 3- (4 sec), 6- (7 sec), and 9-digit (10 sec) span conditions. Error bars are 95% CI of mean.

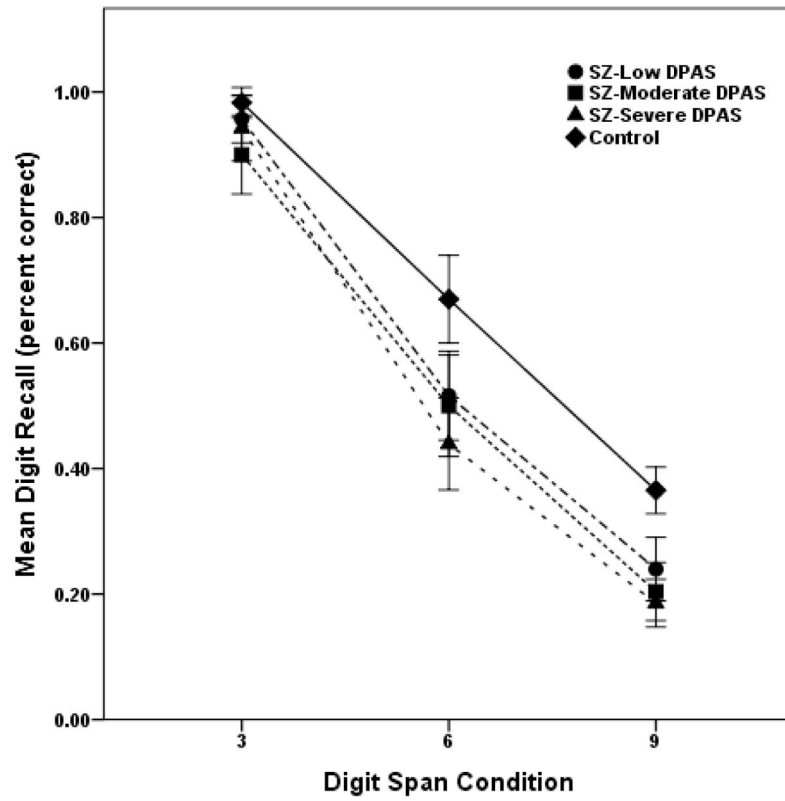


Figure 3. Percent of digits recalled in correct order is shown for consumers with schizophrenia (SZ) with low, moderate and severe defeatist performance attitudes (DPAS) and healthy controls in the 3-, 6-, and 9-digit span conditions. Error bars are 95% CI of mean.

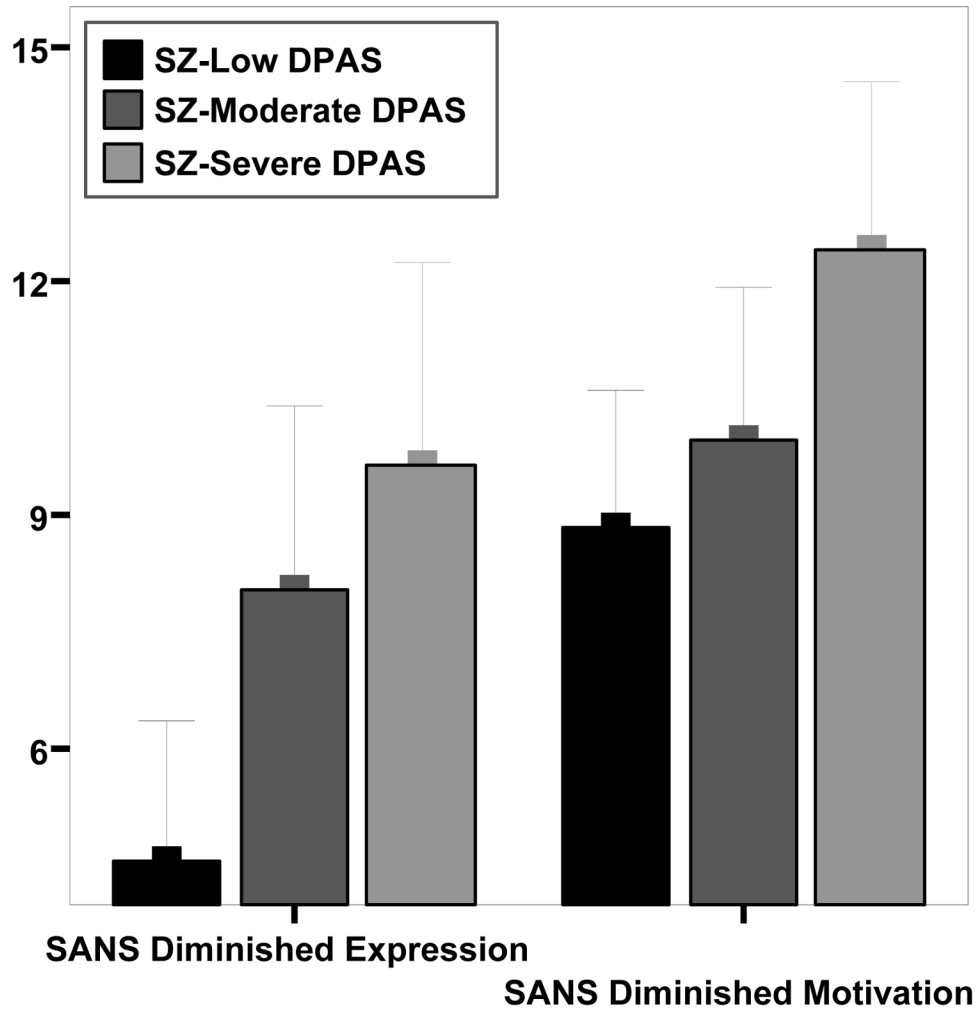


Figure 4. Negative symptom factor scores for Diminished Motivation and Diminished Expression are shown for consumers with schizophrenia (SZ) with low, moderate and severe defeatist performance attitudes (DPAS). Error bars are 95% CI of mean.

Table 1

Participant characteristics

Characteristic	Healthy Control (N=50)		Schizophrenia (N=149)		Statistical Analysis		
	N or Mean	% or SD	N or Mean	% or SD	χ^2 or <i>t</i>	<i>df</i>	<i>p</i>
Male [†]	17	34	98	66	$\chi^2 = 15.49$	1	.000
Caucasian	34	68	85	57	$\chi^2 = 1.87$	1	.172
Age (years)	41.5	14.9	44.4	10.5	<i>t</i> = 1.54	197	.126
Education (years)	14.8	2.3	12.3	2.0	<i>t</i> = 7.24	196	.000
DPAS Total	27.4	9.5	51.8	17.2	<i>t</i> = 9.39	195	.000

Notes:

[†]No significant gender effects were found within healthy controls or consumers with schizophrenia for Defeatist Performance Attitude Scale (DPAS) total or pupillary responses in any digit-span condition.