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# Affective modulation of target detection in deficit and non-deficit schizophrenia☆

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ABSTRACT

Emotional deficits are an integral feature of schizophrenia (SZ), but our understanding of these deficits is limited. In the present study, we examined whether the severity of emotional deficits reflects difficulty in the cognitive processing of affectively valenced stimuli. Healthy controls (HC; N = 170) and stable outpatients with SZ (N = 245), characterized as either deficit syndrome (DS; N = 62) or non-deficit syndrome (NDS; N = 183), completed an Affective Go/NoGo task requiring discrimination of positively, negatively or neutrally valenced words. Accuracy (***d′***) and response bias (***c***) were calculated for each of the three conditions, and a series of ANOVAs were carried out to examine group differences. Examination of accuracy revealed significant main effects of group and valence and a significant valence × group interaction, indicating that while affective valence impacted accuracy for the HC and NDS groups, the DS group maintained the same low level of accuracy across all levels of affective valence. Examination of response bias also revealed significant main effects of group and valence and a significant valence × group interaction. Specifically, within the HC and NDS groups, response bias did not differ between negatively and positively valenced words while response bias in the DS group was lowest for neutral, higher for negatively valenced and higher still for positively valenced words. These results suggest that emotional deficits in DS may be directly related to deficits in processing affective information. Moreover, although this deficit is observed across both positively and negatively valenced stimuli, it is most pronounced for positively valenced material.



## 1. Introduction

Deficit schizophrenia (DS) is a syndrome characterized by enduring negative symptoms such as restricted affect, diminished emotional range and poverty of speech (Kirkpatrick and Galderisi, 2008). Based on findings that patients characterized as DS differ from non-deficit (NDS) patients on a number of key clinical features - including symptoms, illness course, risk factors, and treatment response - DS has been conceptualized as a pathophysiologically distinct subset of patients with schizophrenia (Kirkpatrick et al., 2001; Kirkpatrick and Galderisi, 2008). Critically, DS is characterized by persistent negative symptoms that are believed to be idiopathic, rather than secondary, to the illness and are present during, as well as between, episodes of positive symptom exacerbation (Buchanan, 2007). Although studies seeking to identify unique neuropsychological characteristics of patients with DS have been somewhat mixed (Cohen and Docherty, 2004; Fervaha et al., 2016), a recent meta-analysis (Cohen et al., 2007) found significant differences between DS and NDS patients on olfaction, global cognition and social cognition. Moreover, in the empirical study reported in the same paper, the authors found that, compared to both controls and NDS patients, DS patients showed significantly poorer performance on facial emotion recognition, a cognitive domain consistently impaired in patients with broadly defined schizophrenia (SZ).

These findings are consistent with a wealth of studies that have demonstrated that patients with SZ exhibit profound deficits in the identification and recognition of emotion including both facial (Kohler et al., 2010) and auditory emotion recognition (Gold et al., 2012; Haskins et al., 1995; Kantrowitz et al., 2013; Leitman et al., 2005; Leitman et al., 2007). Moreover, additional work has demonstrated that these deficits are associated with the severity of negative symptoms (Kohler et al., 2010; Ventura et al., 2013) and more specifically, with DS (Strauss et al., 2008; Suslow et al., 2003a; Suslow et al.,

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2003b). Indeed, deficits in emotional expression are a central feature of DS and prior data suggests that relative to NDS, patients with DS have a diminished capacity to experience positive emotion, as measured by their responses to self-report measures (Herbener et al., 2005; Horan and Blanchard, 2003; Kirkpatrick and Buchanan, 1990a; Loas et al., 1996); they may also experience a reduced capacity for negative emotions (Fenton et al., 1997; Kirkpatrick and Buchanan, 1990a; Kirkpatrick et al., 1993; Loas et al., 1996; Subotnik et al., 2000; Tek et al., 2001). Collectively, these prior studies suggest that patients with SZ, particularly those with the most significant negative symptoms, evidence deficits in the perception, recognition and experience of emotion. However, few studies have examined the impact of emotional information on more basic cognitive responses in patients with SZ.

To date, only a handful of small studies have examined the automatic processing of emotional information in patients with SZ (Fear et al., 1996; Strauss et al., 2008; Suslow et al., 2005; Suslow et al., 2003a; Suslow et al., 2003b). These studies, however, have primarily relied on measures of reaction time that provide limited information about either the perceptual sensitivity to the emotional information presented or the biases in response patterns. Moreover, only one of these studies (Strauss et al., 2008) sought to examine whether these deficits were differentially related to DS. Specifically, Strauss et al. (2008) compared DS to NDS patients and found that DS patients evidenced greater attentional bias toward negative emotional information and less attentional bias toward positive information than either NDS patients or healthy controls. These findings are broadly consistent with other studies, which employed priming paradigms to assess automatic processing of emotional word pairs (Suslow et al., 2005; Suslow et al., 2003a; Suslow et al., 2003b) and found that negative symptoms were associated with a failure to automatically process positive but not negative information. Moreover, these findings are also consistent with the notion that emotional dysfunction is a central component of DS (Kring and Moran, 2008).

The present study aimed to expand on these findings by examining the relationship between DS and the automatic processing of emotional information using an Affective Go/NoGo paradigm. In our prior work utilizing this paradigm (Gopin et al., 2011), we found that patients with broadly defined SZ performed poorly on all aspects of the task relative to healthy subjects. Specifically, they were less accurate across all conditions regardless of affective valence and they were significantly less likely to respond to positively valenced emotional words, despite comparable response bias on neutral and negatively valenced emotional words. These results suggested that, in general, patients with SZ evidence a lack of normal responsiveness to affective material. Given prior findings suggesting that the processing of emotional information may be uniquely impaired in DS patients relative to NDS patients, we examined this relationship in a large sample of stable outpatients with DS, NDS and healthy controls. We hypothesized that relative to both the HC and NDS groups, the DS patients would be less accurate and evidence more bias during the processing of emotionally valenced information, with the greatest impairments observed for positively valenced stimuli.

## 2. Method

### 2.1. Participants

The sample was comprised of 245 chronic, stable outpatients with schizophrenia characterized as either deficit (N = 62) or non-deficit schizophrenia (N = 183) (see details below) and 170 healthy adult volunteers. Patients were recruited from the Zucker Hillside Hospital (ZHH), a division of Northwell Health, for an NIMH-funded study on functional outcome in schizophrenia (MH079800 to AKM). Exclusion criteria for patient participants included: a psychiatric hospitalization within the preceding 6 months, substance abuse diagnosis (within the past month), a history of CNS trauma, neurological disorder or mental retardation. Additionally, because prior data suggests that the presence of depressive symptoms significantly impact measures of affective bias, which was a key dependent measure in the present investigation, patients were excluded from the present study if they had a Hamilton Scale for Depression 17-item score > 7. Based on this latter criteria, we excluded 221 patients. Healthy participants were recruited from the general population via word of mouth, posted flyers and newspaper and internet advertisements for an NIMH-funded study of subclinical psychopathology (MH086756 to PD). Exclusion for healthy participants included: an Axis I affective or psychotic disorder diagnosis, active or recent substance abuse (as determined by urine toxicology) or any disorder known to affect the brain. Approximately 10% of the present sample overlaps with the participants used in our prior study (Gopin et al., 2011).

### 2.2. Clinical assessments

#### 2.2.1. Diagnostic interviews

Patients were administered the Structured Clinical Interview for the DSM-IV Axis I Disorders, Patient edition (SCID-I/P) (First et al., 1995b) by Ph.D. or Master's level raters. Information obtained from the SCID was supplemented by a review of medical records and interviews with family informants, whenever possible, and compiled into a narrative case summary. After a thorough review of the SCID and the corroborating information comprising the narrative case summary, diagnoses were determined by a consensus among a minimum of three senior ZHH faculty. Healthy participants were initially administered the Structured Clinical Interview for the DSM-IV, Non-Patient edition (SCID-I/NP) (First et al., 1995a) by Ph.D. or Master's level raters. Information obtained from the SCID was compiled into a narrative case summary and absence of pathology was determined by consensus among two senior members of the ZHH faculty.

#### 2.2.2. Symptom assessments

Patient participants were assessed using standard clinician-administered rating scales to assess symptom severity during the week preceding the interview. These scales included the Brief Psychiatric Rating Scale (BPRS-Hillside version) (Woerner et al., 1988), the Scale for the Assessment of Negative Symptoms (SANS-Hillside version) (Robinson et al., 2000) and the 17-item Hamilton Rating Scale for Depression (HRSD-17) (Hamilton, 1967). All clinician-administered scales were administered by Ph.D. or Master's level psychometricians. Inter-rater reliability on all measures, assessed annually using gold standard videotaped interviews, was high (all Kappa's > 0.80). All clinical assessments were completed on the same day as the Affective Go/No-go task.

#### 2.2.3. Deficit syndrome classification

In accordance with the proxy for the deficit syndrome (PDS) (Kirkpatrick et al., 1993), the BPRS was used to characterize the deficit (DS) and non-deficit (NDS) schizophrenia groups. The PDS is defined as the sum of the scores from the Brief Psychiatric Rating Scale of the anxiety, guilt feelings, depressive mood, and hostility items subtracted from the blunted affect item score. This calculation reflects the lack of negative affect and lack of dysphoria that are characteristic of patients with DS along with their high degree of negative symptoms. We operationally defined the DS group as those patients who scored in the top quartile on the PDS and those in the lower 2 quartiles as DS (Kirkpatrick et al., 1996). Cases identified using the PDS correlate strongly with a deficit syndrome diagnosis based on more comprehensive assessments such as the Schedule for the Deficit Syndrome (SDS) (Kirkpatrick et al., 1993). Moreover, studies examining the stability of the deficit syndrome classification using the PDS have shown the characterization to be stable over the short term (Kirkpatrick et al., 1996) and across a 20-year follow-up period (Strauss et al., 2010).

### 2.3. Neurocognitive assessments

#### 2.3.1. The wide range achievement test (WRAT-3) reading subtest

The WRAT-3 (Wilkinson, 1993) requires that participants read 75 words of increasing difficulty and scores are based on the correct pronunciations of the words. The score obtained on the WRAT-3 is considered an estimate of general cognitive and reading ability in both healthy and patient samples (Nelson and O'Connell, 1978).

#### 2.3.2. Affective go /NoGo task

The Affective Go/NoGo task was comprised of three conditions: discrimination of positively valenced words, discrimination of negatively valenced words, and discrimination of animacy in words of neutral valence. Each condition was comprised of five blocks of 18 words each. Stimulus duration was 500 ms and inter-stimulus interval was 1000 ms for all conditions. The ratio of targets to non-targets was 50:50 in all conditions to prevent development of an overt response bias. Words in the emotional conditions had valences of >1.93 [based on Affective Norms of English Words [see (Garolera et al., 2007)], while words in the neutral condition had valences <1.90. For the emotional conditions, nouns, verbs, and adjectives were utilized; only nouns were used for the animacy condition. Across all conditions, words were matched on frequency of use, word length, and imageability (i.e., how concrete versus abstract) using the Medical Research Council (MRC) Psycholinguistic Database. In the positive affective condition, participants were instructed to press the spacebar on the keyboard whenever they viewed a word that they deemed to be positive ("happy"; e.g., sunshine) in the presence of negatively valenced distracters. Similarly, in the negative condition, participants were requested to respond every time they viewed a word that they deemed to be negative ("sad", "scary"; e.g., gun) in the context of positive non-targets. In the neutral animacy decision, condition participants were told to press each time that they viewed a word representing a living thing versus a nonliving object (e.g., cat vs. house).

The Affective Go/NoGo task is conceptualized as a target detection task in which shifts in response bias and discriminability would reflect over- or under-processing of the various classes of stimuli (positive, negative, neutral). For each Affective Go/NoGo condition (negative, positive, neutral), the percent of correct responses was calculated, as was the percent of false alarms. Using these computations, $\boldsymbol{d'}$ and $\boldsymbol{c}$ were calculated (Schulz et al., 2007; Stanislaw and Todorov, 1999). The variable $\boldsymbol{d'}$ represents a measure of the perceptual sensitivity both to accurate and inaccurate target responses and thereby, reflects the ability to distinguish targets from non-targets. A $\boldsymbol{d'}$ value of 0 would indicate a failure or an inability to distinguish targets from non-targets while larger values of $\boldsymbol{d'}$ would indicate a greater ability to make such distinctions. In contrast, $\boldsymbol{c}$, represents a measure of response bias or the minimum level of internal certainty needed to decide that a particular stimulus was present. Thus, $\boldsymbol{c}$ reflects the extent to which one response is more probable than another. While values of $\boldsymbol{c}$ close to 0 would reflect very little bias toward either the "go" or "no-go" response, negative values would indicate a bias toward the "go" response and positive values would indicate a bias toward the "no-go" response. Although historically $\boldsymbol{\beta}$ has been the most popular measure of response bias, $\boldsymbol{c}$, has been shown to be less affected by the accuracy of performance (Stanislaw and Todorov, 1999).

### 2.4. Statistical analysis

Two Mixed Factorial ANOVAs were conducted to compare DS, NDS and HC on performance during the negative, positive, and neutral conditions of the Affective Go/NoGo task. In these analyses, $\boldsymbol{d'}$ and $\boldsymbol{c}$ served as the dependent variables. A series of follow-up ANOVAs were then conducted to assess the nature of any significant interactions. Moreover, to ensure that any differences observed could not be attributed to differences in general cognitive or reading ability, we repeated all analyses using ANCOVA, including WRAT-3 standard score as a covariate. All analyses were carried out in SPSS v24.

## 3. Results

### 3.1. Demographics

Descriptive statistics for the 3 groups are provided in Table 1. Comparison of groups on racial composition revealed that Whites were significantly under-represented in the DS group ($\chi^2(4) = 11.98$;$p = .02$). Comparison of groups on sex and mean age revealed no significant differences. Comparison of groups on WRAT-3 standard scores (SS) revealed a significant main effect of group ($F(2,411) = 26.91$; $p < .001$). However, post-hoc analyses indicated that this effect was driven solely by the patient-control comparisons; there were no significant differences in WRAT-3 standard scores between the DS and NDS groups ($p = .65$). Mean PDS scores, as expected, significantly differed between the DS and NDS groups ($t(243) = 20.31$; $p < .001$) with the range of scores somewhat narrower for the DS group (−1.00–+3.00) than the NDS (−3.00 to −10.00). Comparison of DS and NDS groups on SANS Global scores revealed that the groups significantly differed on the Global ratings of Alogia ($F(1,244) = 18.25$; $p < .001$) and Flat Affect ($F(1,244) = 87.91$; $p < .001$) but not on Global Avolition or Anhedonia. No significant differences on HAMD-17 or BPRS Total were found. Finally, DS and NDS groups did not differ in type of antipsychotic medication used or in the frequency of use of anticholinergics, antidepressants, mood stabilizers or anxiolytics (all p's > .05).

### 3.2. Accuracy ($d'$)

The first Mixed Factorial ANOVA was carried out to examine the effect of affective valence (positive, negative, neutral), entered as a repeated measure, and group (HC, DS, NDS), entered as a fixed factor, on average accuracy ($\boldsymbol{d'}$). Because Mauchly's test indicated that the assumption of sphericity had been violated ($\chi^2(2) = 19.58$, $p < .001$), degrees of freedom for the effect of affective valence as well as the valence × group interaction were corrected using the Greenhouse-Geisser estimates of sphericity ($\varepsilon = 0.95$). Results indicated significant main effects of group ($F(2,406) = 72.57$; $p < .001$) and valence ($F(1.91,775.40) = 12.90$; $p < .001$) as well as a significant valence × group interaction ($F(3.82,775.40) = 2.50$; $p = .04$). The main effect of group is readily interpreted from Fig. 1 indicating that the HC group demonstrated the highest degree of accuracy on the task (Mean $\boldsymbol{d'} = 3.61$), the DS group demonstrated the lowest degree of accuracy (Mean $\boldsymbol{d'} = 2.49$) and the NDS group demonstrated a degree of accuracy intermediate to the HC and DS groups (Mean $\boldsymbol{d'} = 2.80$); all pairwise comparisons were significant at a $p < .01$. The main effect of emotional valence however, is better interpreted in the context of the significant valence × group interaction ($F(3.92,802.87) = 3.84$; $p = .004$), which suggests that the effect of affective valence varies across the HC, NDS and DS groups (see also Table 2).

To assist in interpreting this interaction, a series of post-hoc ANOVAs were carried out to examine the effect of valence (neutral, positive, negative) on accuracy ($\boldsymbol{d'}$) in each group (HC, NDS, DS) as well as the effect of group at each level of emotional valence. As seen in Fig. 1, when groups were compared across each level of affective valence, we found statistically significant differences in $\boldsymbol{d'}$ between all 3 groups on both positively and negatively valenced words such that the HC group had the highest accuracy, the DS group had the lowest and the NDS were intermediate (all p's < 0.01). Moreover, although the NDS and DS groups did not differ significantly from each other in accuracy on neutral words, they both significantly differed from the HC group (p's < 0.001). Also seen in Fig. 1, when we examined the effect of affective valence within each group, we found that the HC and NDS groups show a pattern in which accuracy on the positively and negatively valenced words did not differ from one another but accuracy for both valenced

**Table 1**
Sample characteristics and group comparisons.

| | HC (N = 170) | DS (N = 62) | NDS (N = 183) | Statistic | *p* value | Significant pairwise comparisons |
|---|---|---|---|---|---|---|
| Mean age (SD) | 38.98 (12.45) | 40.92 (10.92) | 41.80 (10.70) | F = 2.72 | 0.07 | |
| Race (N) | | | | $\chi^2 = 11.98$ | ***0.02*** | |
| White | 79 | 16 | 82 | | | |
| Black | 51 | 29 | 70 | | | |
| Other | 40 | 17 | 31 | | | |
| % Female | 30.60% | 21.00% | 26.20% | $\chi^2 = 2.29$ | 0.32 | |
| Mean WRAT-3 (SD) | 101.45 (8.24) | 91.52 (11.77) | 93.62 (14.01) | F = 26.91 | <***0.001*** | ***HC*** > ***DS,NDS*** |
| Mean PDS score (SD) | n/a | −0.39 (0.89) | −3.96 (1.81) | *t* = 20.31 | <***0.001*** | ***DS*** > ***NDS*** |
| Mean HRSD total (SD) | | 4.48 (1.89) | 4.64 (1.81) | *t* = 0.36 | 0.55 | |
| Mean BPRS total (SD) | | 27.98 (4.95) | 27.98 (5.66) | *t* = 0.94 | 0.33 | |
| Mean SANS avolition (SD) | | 2.53 (0.99) | 2.30 (1.34) | *t* = 1.55 | 0.21 | |
| Mean SANS anhedonia (SD) | | 2.05 (1.12) | 2.06 (1.09) | *t* = 0.005 | 0.94 | |
| Mean SANS alogia (SD) | | 1.81 (1.02) | 1.13 (1.10) | *t* = 18.25 | <***0.001*** | ***DS*** > ***NDS*** |
| Mean SANS affective Flattening (SD) | | 2.65 (0.85) | 1.23 (1.08) | *t* = 87.91 | <***0.001*** | ***DS*** > ***NDS*** |
| Antipsychotic medications | | | | $\chi^2 = 2.40$ | 0.30 | |
| First generation (N) | | 14 | 28 | | | |
| Second generation (N) | | 34 | 99 | | | |
| Clozapine (N) | | 14 | 56 | | | |
| Other medications | | | | | | |
| Antidepressants (N) | | 12 | 54 | $\chi^2 = 2.48$ | 0.12 | |
| Mood stabilizers (N) | | 42 | 102 | $\chi^2 = 1.30$ | 0.25 | |
| Anxiolytics (N) | | 7 | 34 | $\chi^2 = 1.96$ | 0.16 | |

Notes: Significant results are indicated in bold.
Abbreviations: SD: standard deviation; PDS: Proxy for Deficit Syndrome; HC: Healthy Controls; DS: Deficit Syndrome; NDS: Non-Deficit Syndrome; WRAT-3: Wide Range Achievement Test – 3rd Edition; HRSD: Hamilton Rating Scale for Depression; BPRS: Brief Psychiatric Rating Scale; SANS: Scale of the Assessment of Negative Symptoms.

word types was significantly higher than that of neutral words. DS patients, however, show a pattern in which accuracy on both types of affectively valenced words did not differ from accuracy on neutral words. This would suggest that patients in the DS group are less sensitive to the affective valence of words, regardless of whether the valence is positive or negative, than either healthy individuals or NDS patients.

### 3.3. Bias (c)

The second Mixed Factorial ANOVA examined the effect of affective valence (positive, negative, neutral), entered as a repeated measure, and group (HC, DS, NDS), entered as a fixed factor, on average affective bias (***c***). Because Mauchly's test indicated that the assumption of

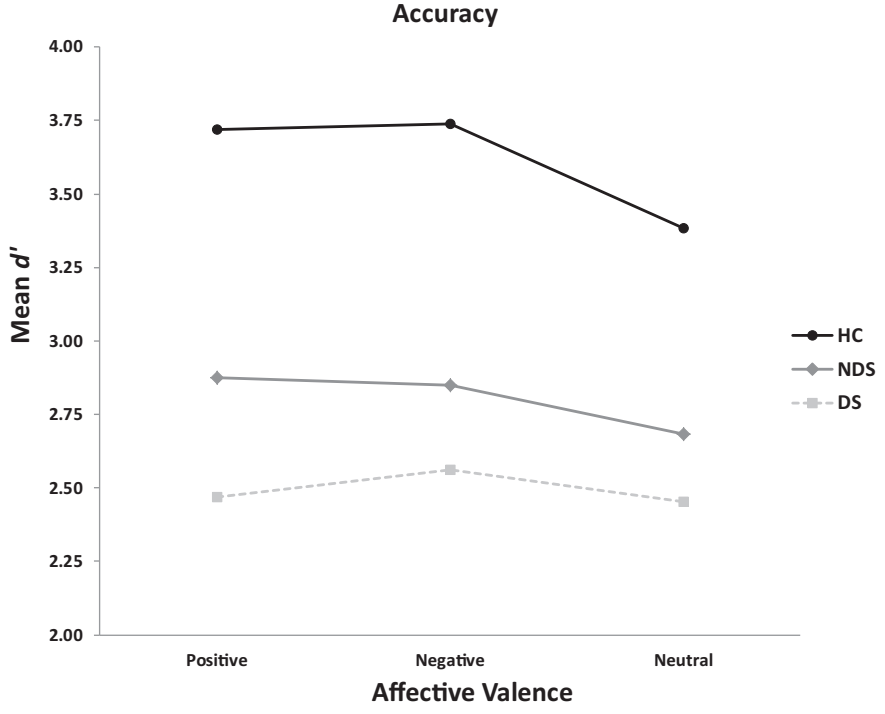


**Fig. 1.** Comparison of healthy controls (HC; N = 170), deficit syndrome (DS; N = 62) and non-deficit syndrome (NDS; N = 183) groups on average accuracy (***d'***) across positive, negative and neutral affective valence trials of a Go/NoGo task. Repeated measures ANOVA indicated significant main effects of group ($p < .001$) and valence ($p < .001$) as well as a significant valence × group interaction ($p = .04$).

**Table 2**
Mean accuracy (***d′***) and bias (**c**) by group.

| | Valence | Controls | NDS | DS | Significant pairwise comparisons |
|---|---|---|---|---|---|
| Accuracy (***d′***) | Positive (SD) | 3.72 (0.65) | 2.88 (1.04) | 2.47 (0.93) | Controls > NDS > DS |
| | Negative (SD) | 3.74 (0.65) | 2.85 (0.96) | 2.56 (1.06) | Controls > NDS > DS |
| | Neutral (SD) | 3.38 (0.69) | 2.68 (1.05) | 2.45 (1.04) | Controls > NDS, DS |
| Bias (***c***) | Positive (SD) | 0.14 (0.25) | 0.25 (0.42) | 0.34 (0.42) | Controls > NDS > DS |
| | Negative (SD) | 0.09 (0.30) | 0.25 (0.50) | 0.26 (0.40) | Controls > NDS, DS |
| | Neutral (SD) | 0.10 (0.28) | 0.12 (0.40) | 0.16 (0.30) | None |

Abbreviations: SD: standard deviation; HC: Healthy Controls; DS: Deficit Syndrome; NDS: Non-Deficit Syndrome.

sphericity had been violated ($\chi^2(2) = 21.34$, $p < .001$), degrees of freedom for the effect of affective valence as well as the valence × group interaction were corrected using the Greenhouse-Geisser estimates of sphericity ($\varepsilon = 0.95$). Results indicated significant main effects of group ($F(2,406) = 155.15$; $p < .001$) and valence ($F(1.90,772.36) = 11.49$; $p < .001$) as well as a significant valence × group interaction ($F(3.81,772.36) = 2.61$; $p = .04$). In this case, both main effects are better interpreted in the context of the significant interaction and to assist in interpreting the interaction, a series of post-hoc ANOVAs were carried out. These post-hoc analyses sought to examine the effect of affective valence (neutral, positive, negative) on bias in each group (HC, NDS, DS) as well as the effect of group at each level of affective bias.

As seen in Fig. 2 and Table 2, when groups were compared across each level of affective valence we found significant differences between all three groups on the positively valenced words such that HC's had the lowest degree of bias (Mean $\boldsymbol{c} = 0.14$), DS patients had the highest (Mean $\boldsymbol{c} = 0.35$) and NDS patients were intermediate (Mean $\boldsymbol{c} = 0.24$) ($F(2,410) = 7.91$; $p < .001$). Moreover, although DS and NDS groups did not significantly differ from each other on bias toward negatively valenced words (Mean $\boldsymbol{c} = 0.26$ and 0.25, respectively), both of these groups showed significantly more bias on these trials than the HC group (Mean $\boldsymbol{c} = 0.09$) ($F(2,410) = 7.52$; $p = .001$). There were no statistically significant differences in bias between the 3 groups on neutral words.

Also seen in Fig. 2, when we examined the effect of affective valence within each group, we found that the degree of bias associated with affectively valenced words varied by group. Specifically, we found that the HC group exhibited a statistically equivalent degree of bias regardless of whether the words were neutral, positively valenced or negatively valenced; in all cases this group evidenced very little bias, suggesting that they had a high degree of certainty about the valence of the word regardless of whether it was positively, negatively or neutrally valenced. The NDS group exhibited a statistically equivalent degree of bias across the positively and negatively valenced words, which were both significantly different from the neutral words ($p < .001$ and $p = .002$, respectively) indicating that although they had more difficulty with affective words, the affective valence of the words did not impact this bias. In contrast, the DS group exhibited a pattern in which the degree of bias differed significantly in all pairwise comparisons of affective valence such that response bias was lowest for neutral words, higher for negatively valenced words and higher still for positively valenced words (all p's < 0.02). Thus, although DS patients appear to have difficulty with both positively and negatively valenced words, they appear to have more difficulty with positively valenced words.

### *3.4. Effect of WRAT-3 scores*

To ensure that the aforementioned results, particularly those indicating significant differences between the DS and NDS groups, could

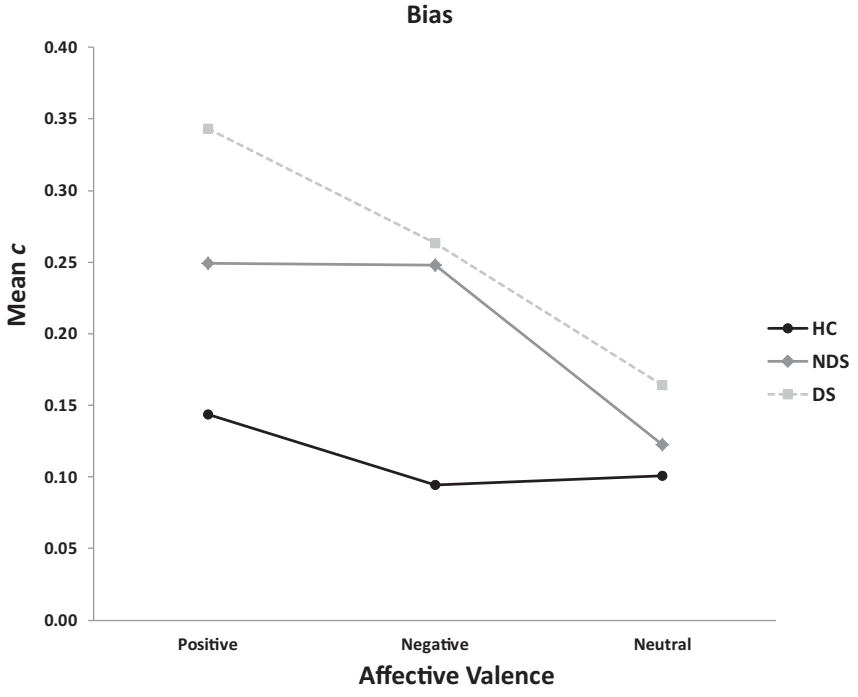


**Fig. 2.** Comparison of healthy controls (HC; N = 170), deficit syndrome (DS; N = 62) and non-deficit syndrome (NDS; N = 183) groups on average bias (c) across positive, negative and neutral affective valence trials of a Go/NoGo task. Repeated measures ANOVA indicated significant main effects of group ($p < .001$) and valence ($p < .001$) as well as a significant valence × group interaction ($p = .04$).

not be attributed to differences in general cognitive or reading ability, we repeated all analyses including WRAT-3 standard score as a covariate. In the analysis comparing groups on accuracy (***d'***), the inclusion of the WRAT-3 standard score as a covariate attenuated the main effect of valence ($F(1.91,768.30) = 1.63$; $p = .20$) but not the significant main effect of group ($F(2,402) = 43.05$; $p < .001$) or the valence × group interaction ($F(3.82,768.30) = 2.98$; $p = .02$). Similarly, in the analysis comparing groups on bias (***c***), the inclusion of the WRAT-3 standard score as a covariate attenuated the main effect of valence ($F(1.92,770.17) = 1.51$; $p = .22$) but not the significant main effect of group ($F(2,402) = 4.44$; $p = .01$) or the valence × group interaction ($F(3.83,770.17) = 2.37$; $p = .05$). Thus, although differences in general cognitive and reading ability, as measured by WRAT-3, does attenuate some of our findings, it does not fully account for the differences observed.

## 4. Discussion

The present results suggest that patients with Deficit syndrome (DS) are less sensitive to the affective valence of words, regardless of whether the valence is positive or negative, than either healthy individuals or non-deficit syndrome (NDS) patients. Moreover, although DS patients appear to have difficulty discriminating both positively and negatively valenced words, they appear to have more difficulty with positively valenced words. These findings are consistent with prior reports suggesting that difficulty with the automatic processing of emotional information is associated with the most severe deficits in emotional expressivity (Suslow et al., 2005; Suslow et al., 2003a; Suslow et al., 2003b). Moreover, these findings are also broadly consistent with one prior report that examined these effects in DS and NDS patients and found that positive information captured the attention of DS patients significantly less than either NDS patients or healthy controls (Strauss et al., 2008). In the present study we found that DS patients were much more likely to say that a positively valenced word was not present. Although these authors suggested that this effect might be attributable to a mood congruent automatic processing impairment in which positive emotional information fails to capture attention because of the mood state of these patients, given the present findings, this explanation seems unlikely. Specifically, in the present study, there were no differences between the DS and NDS groups in mood state as indicated by the HRSD scores. It should be noted, however, that in the present study we did observe several significant correlations between the severity of negative symptoms and both accuracy and bias on the Affective Go/NoGo task (see Table 3), the most consistent patterns of association were found for symptom domains that did not differ between the DS and NDS groups (i.e. avolition and anhedonia). This would suggest that the severity of symptoms alone cannot account for the performance differences we observed between the DS and NDS groups. Thus, it seems likely that deficits in the automatic processing of affective information are central to the deficit syndrome. This conclusion is consistent with the notion that emotional dysfunction is a central component of DS (Kring and Moran, 2008).

Given that the basic neuropsychological constructs of the original Go/NoGo task are preserved in the affective adaptation of the task (Schulz et al., 2007), it might be argued that the pattern of results we observed reflects more general deficits in executive function, a cognitive domain typically impaired in patients with SZ. However, recent work examining differences between DS and NDS patients on measures of executive function found no group differences on the non-affective version of the Go/NoGo task (Tyburski et al., 2017), suggesting that the differences we observed are directly related to the affective component of the task.

Prior neuroimaging studies utilizing the Affective Go/NoGo task have implicated the subgenual and rostral anterior regions of the cingulate gyrus in emotional response biases (Elliott et al., 2004; Elliott et al., 2000, 2002). Notably, previous studies, including both PET (Tamminga et al., 1992) and structural MRI (Cascella et al., 2010; Takayanagi et al., 2013), have implicated the anterior cingulate in DS. Collectively, these findings fit with prior suggestions (Cohen et al., 2007; Kirkpatrick and Buchanan, 1990b) that DS may reflect neuropathology beyond, and perhaps even different from, what is characteristic of NDS. Given the present findings, it seems likely that this neuropathology may be directly related to regions involved in the processing of emotional information. Further support for this notion comes from recent data using graph theoretical analysis which demonstrated that relative to NDS, DS patients evidence substantially altered intra-cortical relationships in regions typically activated during basic emotion understanding and emotion experience sharing (Wheeler et al., 2015).

Several limitations of the present work should be noted. First, although we demonstrated that the DS and NDS groups did not differ in terms of their prescribed medications, dosing information was often based on patient self-report rather than medical records and was not deemed reliable and thus, we did not compare groups on antipsychotic dose. However, in prior work examining differences between DS and NDS on automatic emotional processing that did account for antipsychotic dosing (Strauss et al., 2008), no relationship between dose and affective processing was found. Second, although differences between males and females on measures of emotion processing have consistently been reported [see (Horan et al., 2013; Kring and Moran, 2008)], due to the small number of females in the DS group (21%) we were unable to examine sex differences in the present study. Third, due to concerns about the impact of depressive symptoms on affective processing, we chose to exclude patients with a Hamilton Scale for Depression (HRSD) rating > 7. While we believe this is a strength of our analytic strategy, it should be noted that the PDS relies, in part, on symptoms that are rated on both the BPRS and HRSD. Thus, excluding patients based on the HRSD rating likely restricted the range of PDS scores we obtained. However, to ensure that this exclusion criteria did not impact the assignment of patients to either the NDS and DS groups, we went back to the full sample, unselected for HRSD scores, determined PDS status and then compared these assignments to the NDS

**Table 3**
Correlations between global scores on the Scale for the Assessment of Negative Symptoms (SANS) and accuracy (***d'***) and bias (c) on positive, negative and neutral trials of the Affective Go/NoGo Task. Significant correlations are shown in bold.

| SANS domain | | *Accuracy* (***d'***) | | | *Bias* (***c***) | | |
|---|---|---|---|---|---|---|---|
| | | Positive | Negative | Neutral | Positive | Negative | Neutral |
| Avolition | *r* | −0.19 | −0.24 | −0.20 | 0.14 | 0.01 | 0.1 |
| | *p* | ***0.02*** | ***0.001*** | ***0.01*** | NS | NS | NS |
| Asociality/anhedonia | *r* | −0.20 | −0.21 | −0.18 | 0.19 | 0.12 | 0.16 |
| | *p* | ***0.01*** | ***0.004*** | ***0.04*** | ***0.02*** | NS | 0.07 |
| Alogia | *r* | −0.24 | −0.23 | −0.15 | 0.21 | 0.004 | 0.16 |
| | *p* | ***0.001*** | ***0.002*** | NS | ***0.008*** | NS | 0.08 |
| Affective flattening | *r* | −0.20 | −0.16 | −0.09 | 0.14 | 0.09 | 0.11 |
| | *p* | ***0.01*** | 0.07 | NS | NS | NS | NS |

Note: NS = p value > .10.

and DS assignments in our restricted sample. This comparison indicated that all 62 patients in our DS group were also classified as DS in the full sample. Notably, however, of the 183 patients in our NDS group, 13 were classified as DS in the full sample. This would suggest that if excluding patients based on their HRSD scores did have an effect, it was likely to increase the stringency with which patients were categorized as DS. Fourth, cognitive deficits in language-based tasks have been shown to discriminate among DS from NDS patients (Ahmed et al., 2018) and the present findings, that differences between the DS and NDS groups were attenuated when WRAT-3 scores were included in the ANCOVA models, suggests that suing a non-language based measures of automatic affective processing may be more informative. Thus, future studies using alternative tasks may further validate the results of the present study. Finally, although the PDS measure of the deficit syndrome has been shown to be both reliable and stable over the short-term (Kirkpatrick et al., 1996) and long-term (Strauss et al., 2010), more precise measures of this construct (Kirkpatrick et al., 1989) would have been preferred.

Nevertheless, the present results provide strong support for the existence of automatic affective processing deficits in patients with SZ and more specific deficits in the processing of positively valenced stimuli in those patients with deficit syndrome. Moreover, given that deficits in emotional expression are a central feature of DS, our findings suggest that difficulty with the automatic processing of affective stimuli may underlie more general deficits in emotional expressivity. Additional work seeking to examine these relationships may provide unique opportunities for the identification of novel treatment targets aimed at ameliorating these debilitating symptoms.

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**Contributors**

Authors PD and CBG designed the study and conducted all analyses. Authors ADB and AKM assisted in the preparation of the manuscript. All authors contributed to and have approved the final manuscript.

## Conflicts of interest

Drs. DeRosse, Gopin and Barber report no competing interests. Dr. Malhotra has served as consultant or speaker for Bristol-Myers Squibb, Astra Zeneca, Vanda Pharmaceuticals and Clinical Data, Inc., and has received research support from Pfizer, Janssen Pharmaceuticals, Bristol-Myers Squibb, and Eli Lilly.

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