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Affective Systems Induce Formal Thought Disorder in Early-Stage Psychosis

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Abstract

Although Formal Thought Disorder (FTD) has been described since early conceptualizations of psychosis, its underlying mechanisms are unclear. Evidence suggests FTD may be influenced by affective and cognitive systems; however, few have examined these relationships—with none focusing on Early-Stage Psychosis (EP). In this study, positive FTD and speech production were measured in sex- and race-matched EP ($n = 19$) and healthy control ($n = 19$) groups by assessing ‘reactivity’—a change in experimental compared to baseline conditions—across baseline, affective, and cognitive conditions. Relationships with functioning were also examined within each group. Three key findings emerged: 1) The EP group displayed large differences in positive FTD and speech production; 2) Those with EP exhibited affective reactivity for positive FTD; and 3) Positive FTD and affective reactivity were linked with poor real-world functioning in EP and these relationships did not considerably change when controlling for positive symptom (e.g., delusions, hallucinations) severity. Our findings provide preliminary evidence that affective, but not cognitive, systems play a critical role in positive FTD. Affective reactivity, in particular, may aid in predicting those with EP who go on to develop serious social impairments. Future work should focus on whether affective systems differentially influence those at separate points on the psychosis-spectrum in an effort to establish evidence-based treatments for FTD.

Key words: formal thought disorder; early psychosis; negative affect; cognitive load; functioning

General Scientific Summary

Although Formal Thought Disorder has been described since early conceptualizations of psychosis, its underlying mechanisms are unclear. The current study suggests that affective, but not cognitive, systems play a critical role in positive Formal Thought Disorder in people with early-stage psychosis. Affective systems were linked to lower social functioning in these individuals and may be useful for predicting which people with early-stage psychosis will go on to develop serious social impairments.

An essential component of communication is the ability to connect conscious thoughts. In people with psychosis, Formal Thought Disorder (FTD) represents disruptions in conscious thinking—disruptions that are typically exhibited behaviorally through disorganized speech (i.e., positive FTD; Docherty, 2012) and limited speech production (i.e., negative FTD; Roche, Creed, MacMahon, Brennan, & Clarke, 2014). Although FTD has been described since early conceptualizations of psychosis (Bleuler, 1911), its underlying mechanisms are poorly understood. To date, most FTD studies have focused on chronic psychosis (Cohen, McGovern, Dinzeo, & Covington, 2014; Docherty et al., 2013; Minor et al., 2015a); it is known, however, that FTD affects people across the schizophrenia-spectrum (Bearden, Wu, Caplan, & Cannon, 2011; Minor & Cohen, 2010). Despite this knowledge, a paucity of studies have investigated the mechanisms of FTD in Early-Stage Psychosis (EP).

A novel strategy for examining potential mechanisms involves tapping into constructs linked with FTD through experimental manipulation. This allows one to observe ‘reactivity’—a change in experimental compared to baseline conditions. Links have been postulated between reactivity and affective and cognitive systems, with greater FTD occurring whenever negative affect or cognitive demands are increased (Burbridge & Barch, 2002; Docherty, Hall, & Gordinier, 1998; Melinder & Barch, 2003). Yet few studies have directly examined the role of these systems in FTD—with none focusing on EP.

Evidence for the role of affective systems has surfaced from two bodies of research. First, a handful of studies have tested whether greater reactivity is observed when negative affect is induced in chronic psychosis and healthy controls (Burbridge & Barch, 2002; Docherty et al., 1998; Rubino et al., 2011), with large group differences emerging (Docherty et al., 1998). Second, stress vulnerability studies show that people’s reactions to emotional stressors vary; this

individual reactivity has been suggested to play a critical role in the progression from high-risk states to psychosis (Barrantes-Vidal, Chun, Myin-Germeys, & Kwapil, 2013) and in susceptibility to future psychotic episodes (Norman & Malla, 1993).

Less focus has been paid to cognitive systems in FTD, yet there is reason to believe reactivity may occur when cognitive demands are greater. Cognitive load theory proposes that increasing demands reduces cognitive resources due to working memory's limited capacity—making it difficult to attend to two tasks simultaneously (Plass, Moreno, & Brunken, 2010). This effect is pronounced in psychosis (Nuechterlein et al., 2011). To date, only two known studies have examined the cognitive load effect on FTD; both implemented dual-task paradigms (i.e., participants spoke while completing cognitive tasks) in chronic psychosis samples (Cohen et al., 2014; Melinder & Barch, 2003). In each, speech production decreased in the cognitive condition. Positive FTD was only measured in one study, however, and no comparison group was used (Melinder & Barch, 2003). The current study addresses these issues in an EP sample.

Objectives and Hypotheses

This study had three aims. First, we examined whether people with EP exhibited greater positive FTD and decreased speech production compared to healthy controls in baseline, affective, and cognitive speech conditions. Second, we investigated whether affective or cognitive systems influenced FTD by testing if affective and cognitive reactivity were greater in EP. Third, we examined whether study variables were linked with real-world outcomes in EP by examining relationships with functioning. Based on previous studies of psychosis, we expected positive FTD (Docherty, 2012) and affective reactivity of positive FTD (St. Hilaire & Docherty, 2005) to be inversely associated with functioning in the EP group; speech production was

hypothesized to be positively related to functioning (Bowie & Harvey, 2008) in EP. In post-hoc analyses, we further investigated significant relationships with functioning by controlling for positive symptom severity (e.g., delusions, hallucinations). This provided an estimate of the specificity of functioning's relationship with FTD. This is the first known study to test whether positive FTD and speech production are linked to affective and cognitive reactivity in EP; examining these aims will provide preliminary evidence for the role of each system.

Method

Participants

Early-Stage Psychosis. Participants were recruited from the Eskenazi Midtown Prevention and Recovery Center for Early Psychosis (PARC), an outpatient EP treatment center. Inclusion criteria were: a) Diagnosis of Schizophrenia, Schizoaffective, Schizophreniform, or Psychotic Disorder NOS within five years as assessed by the Structured Clinical Interview for DSM-IV-TR Disorders-Patient Edition (SCID-I/P; First, Spitzer, Gibbon, & Williams, 2002); b) Age 18-40; c) English fluency; d) No current substance dependence; e) No history of neurological illness or injury resulting in loss of consciousness > 5 minutes; and f) Verbal I.Q. > 70. All EP participants were prescribed an oral antipsychotic and in non-acute phases of illness, with no change in medication or illness phase during the past month. In total, 20 EP participants were recruited and 19 were retained (one exclusion due to technical problems with speech files).

Controls. Healthy controls were 19 sex- and race-matched people recruited from the community (e.g., flyers, ads in local publications). Inclusion criteria were identical to EP with one exception: Previous diagnosis or reported history of psychosis symptoms was exclusionary.

All participants provided informed consent and received cash compensation. Procedures were approved by local Institutional Review Boards. Table 1 lists demographic and clinical data.

[INSERT TABLE ONE HERE]

Measures

Speech Paradigm. Participants were instructed to speak into a head-mounted microphone for approximately two minutes about negatively- (affective condition) and neutrally-valenced (baseline, cognitive conditions) memories. Negative topics focused on unpleasant memories from one's past and were chosen by the speaker, although prompts were also provided on the computer screen (e.g., "Tell us some stories about times when you were really disappointed about something"). Neutral topics focused on daily routine and place of residence; topics were counterbalanced across baseline and cognitive conditions.

In the cognitive condition, single- (i.e., baseline) and dual-task one-back visual working memory tests were consecutively employed. First, participants completed the baseline condition, focusing solely on the visual working memory test. Then, the dual-task condition was administered, where they completed the visual working memory test while simultaneously generating speech. Visual working memory tests consisted of symbols (e.g., '*', '#') presented up to 2000ms (at 1500ms intervals). Prior to viewing stimuli, participants were instructed to press 'v' with their left index finger when the symbol was identical to the preceding symbol and '7' with their right index finger when it was not identical. Percentage of correct responses was recorded for both conditions. Similar speech conditions have shown promise for increasing negative affect and cognitive demands (Melinder & Barch, 2003; Cohen, Hong, & Guevara,

2010) and two-minute samples have been used to differentiate psychometric schizotypy and non-schizotypy groups (Cohen, Morrison, Brown, & Minor, 2012; Minor & Cohen, 2010). Samples were later transcribed by trained Research Assistants.

Formal Thought Disorder. Positive FTD was measured using the Communication Disturbances Index (CDI; Docherty, DeRosa, & Andreasen, 1996), a validated, behaviorally-based instrument that captures specific instances of disorganization from natural speech via a summary score (number of disorganized segments / total words X 100). Instances are counted if there is a lack of clarity of meaning or the intended meaning is unclear. In this study, the first author and a trained graduate student rated positive FTD, blind to group, and discrepancies were discussed in weekly consensus meetings (interrater reliability on 30 randomly selected narratives rated prior to consensus meeting: $r = 0.84$). Speech production was assessed by calculating the total number of words per second generated by each participant. Whereas higher CDI scores indicated greater positive FTD, fewer words per second represented less speech production.

Functioning. Global Functioning Scale: Social (GFS) and Role (GFR; Cornblatt et al., 2007) were used to assess functioning. Both have demonstrated high construct validity and interrater reliability in EP (Piskulic, Addington, Auther, & Cornblatt, 2011). The GFS measures age appropriate social contact/friendships and the GFR assesses performance and support required in one's primary role (defined as school or work for all study participants). Both use ten-point scales, with greater scores representing higher functioning.

Analyses

Analyses were conducted in four parts. First, a multivariate repeated-measures analysis of variance (MANOVA) was conducted to examine affect's role in FTD. Group (EP, control) was

the between-subjects independent variable (IV) and speech condition (baseline, affective) the within-subjects IV. Positive FTD and speech production were dependent variables (DV). Next, a MANOVA was run to assess cognition's role in FTD. Group was the between-subjects IV and condition (baseline, cognitive) and cognitive test (baseline, dual-task) were within-subjects IVs. Positive FTD, speech production, and cognitive performance (i.e., percentage correct) served as DVs. Significant main effects were probed using independent *t*-tests. Third, affective and cognitive reactivity scores were calculated for each participant by regressing positive FTD and speech production scores in experimental conditions from baseline conditions. Finally, correlations were used to investigate relationships with functioning in each group. To correct for multiple comparisons, significance was set at $p < 0.01$ for analyses without a priori hypotheses. Post-hoc analyses were run using partial correlations to determine whether significant relationships with functioning changed when controlling for positive symptoms—as measured by the positive factor subscale on the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987). All analyses were two-tailed. Outliers were reduced to within 3 SDs of the mean.

Results

FTD across Affective Conditions

The results of the repeated-measures MANOVA supported our hypothesis that the EP group would exhibit greater positive FTD and lower speech production than controls across baseline and affective conditions (Table 2). Regarding condition, significant main effects were observed for positive FTD, $F(1,36) = 4.78$, $p = 0.035$, but not speech production, $F(1,36) = 0.08$, $p < 0.775$. This indicates that positive FTD increased from the baseline to affective condition across both groups; speech production did not vary.

In line with hypothesis two, the EP group demonstrated a greater increase in positive FTD from the baseline to affective condition (see Figure 1A). Speech production did not yield a significant group by condition interaction, $F(1,36) = 0.02, p < 0.887$.

[INSERT FIGURE ONE HERE]

FTD across Cognitive Conditions

The repeated-measures MANOVA supported hypotheses that the EP group would demonstrate greater positive FTD, lower speech production, and worse cognitive performance than controls in baseline and cognitive conditions (Table 2). Individual condition main effects showed decreases in speech production, $F(1,36) = 21.73, p < 0.001$, and cognitive performance, $F(1,36) = 11.18, p = 0.002$, for all individuals in the cognitive compared to baseline condition. No significant change in positive FTD was detected across groups, $F(1,36) = 3.64, p = 0.064$.

[INSERT TABLE TWO HERE]

Contrary to our second hypothesis, no significant group by condition interactions were found for positive FTD (Figure 1B) or speech production, $F(1,36) = 0.71, p = 0.404$. In line with expectations, the EP group did exhibit a steeper cognitive performance decline than controls in the cognitive compared to the baseline condition, $F(1,36) = 4.70, p = 0.037$.

Associations with Functioning

Relationships were functioning were examined in each group to test links with real-world variables (Table 3). In EP, positive FTD was associated with worse social functioning across all three speech conditions and worse role functioning in the baseline condition. Additionally, affective reactivity for positive FTD was associated with worse social functioning in EP. Post-hoc analyses showed that correlations between positive FTD and social functioning, Baseline: $r(17) = -0.40, p = 0.100$; Affective: $r(17) = -0.71, p < 0.001$; Cognitive: $r(17) = -0.47, p = 0.050$, and role functioning, Baseline: $r(17) = -0.63, p = 0.005$, did not considerably differ when controlling for PANSS positive symptoms. In controls, greater speech production was generally associated with better functioning. Overall, hypotheses that positive FTD and affective reactivity of positive FTD would be linked to worse social functioning in EP were supported. In most cases, these relationships were not affected when controlling for positive symptom severity. Hypotheses that positive FTD would be associated with role functioning were partially supported. Links between speech production and functioning were not observed in EP.

[INSERT TABLE THREE HERE]

Discussion

This study's primary goal was to examine how affective and cognitive systems influence positive FTD and speech production in EP. Three key findings emerged. First, when compared to controls, the EP group demonstrated large differences in both positive FTD and speech production. Second, people with EP exhibited a steeper increase in positive FTD from the baseline to the affective condition (i.e., affective reactivity). Third, positive FTD and affective

reactivity were associated with poor functioning in EP—but not controls—and these relationships did not generally change when accounting for positive symptom severity.

This is the first known study to show that both positive FTD and speech production are greater in EP. The large differences between EP and control groups were in line with those observed in chronic stages of illness (Docherty, 2012; Docherty et al., 2013). This suggests FTD is already nearing peak severity shortly after psychosis emerges. This is also the first study to examine affective and cognitive reactivity in EP. Of the two, cognitive systems appear to have a less clearly defined role, as cognitive reactivity was not observed in speech tasks. This suggests that, in EP, the cognitive load effect may not translate to positive FTD or speech production.

In contrast, affective systems played a prominent role in positive FTD. Results from this study support findings that affective reactivity is primarily restricted to positive FTD in people with psychotic disorder diagnoses. Comparison studies have shown affective reactivity is not present in those with depression (Rubino et al., 2011), non-acute phases of mania (Docherty et al., 1996), psychometric schizotypy (Minor & Cohen, 2010; Minor & Cohen, 2012), or first-degree relatives of people with schizophrenia (Docherty et al., 1998). The current finding signals the importance of affective systems in positive FTD in those recently diagnosed with a psychotic disorder. Future research should examine affective reactivity in clinical high-risk for psychosis cohorts to determine if it is present in a high-risk group who is already experiencing functional declines but have not developed full psychosis symptoms.

In EP, declines in social and role functioning are pronounced (Minor et al., 2015b; Woods et al., 2009). In this study, we found that positive FTD and affective reactivity were consistently linked with poor social functioning (accounting for up to 56% of social functioning's variance) and, in some cases, associated with poor role functioning (accounting for

up to 46% of the variance) in EP. Generally, positive symptom severity did not account for these relationships; thus, FTD and affective reactivity appear to have real-world implications in the early stages of psychosis. Findings here were in line with St. Hilaire and Docherty (2005), who observed that a schizophrenia cohort high in affective reactivity did not differ from a low reactivity group in work functioning, but demonstrated more social problems.

Findings from this study may hold important treatment implications. To date, few treatments have shown effectiveness for reducing FTD. However, there is evidence that many psychotic symptoms can be reduced with early intervention (Menezes, Arenovich, & Zipursky, 2006). From a treatment perspective, our finding of greater affective reactivity in EP could signal a need to teach emotion regulation strategies; these strategies could be implemented to reduce FTD when emotionally loaded topics are discussed. Based its strong link to social functioning, affective reactivity may also be a way of predicting which people with psychosis will exhibit the most severe disruptions in social relationships. By identifying individuals with social impairment early, it may provide a critical “window of opportunity” for clinicians to intervene and reduce long-term impairment (Birchwood, Todd, & Jackson, 1998).

A strength of this study is the use of a novel experimental paradigm to assess how affective and cognitive systems influence FTD. This strength is in line with recent calls from the National Institute of Mental Health to develop methods of identifying specific psychotic processes across the lifespan (National Advisory Mental Health Council, 2010; National Institute of Mental Health, 2008). Other strengths include the use of behavioral measures of FTD and speech production. A limitation is that comprehensive assessments of functioning were not used. Future studies should investigate performance-based functional assessments, which may allow a more sophisticated understanding of links between functioning, FTD, and reactivity. A second

limitation concerns the unstructured nature of the speech conditions. Our goal was to design tasks where subjects had flexibility to discuss a range of memories. We did test—and found no significant group difference in—frequency of negative emotion word use in the affective condition; however, one significant tradeoff of our approach is that narratives may have differed in some other important way (e.g., arousal). Future work should attempt to measure and account for any potential group differences in narratives. A third limitation is the small sample size. Although observed effects were large, future studies should replicate findings in EP samples adequately powered for medium effects.

In sum, this study offer preliminary evidence that affective, but not cognitive, systems play a critical role in positive FTD within EP. Greater positive FTD and affective reactivity held important ramifications, as both were linked to poor functioning. Affective reactivity, in particular, may predict which people with EP will develop social impairments. Our findings highlight the need to implement evidence-based treatment early—when long-term impairment can be reduced. Future studies should replicate results at different points on the psychosis-spectrum to determine how affective systems influence FTD at other stages of psychosis.

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Table 1

Demographic and Clinical Variables in Early-Stage Psychosis and Healthy Control Groups

| Variable | Early-Stage Psychosis (<i>n</i> = 19) | | Healthy Control (<i>n</i> = 19) | |
|-----------------------------------|--|-----------|----------------------------------|-----------|
| | <i>M</i> | <i>SD</i> | <i>M</i> | <i>SD</i> |
| Age | 24.89 | 4.65 | 23.89 | 5.62 |
| Sex | | | | |
| Male (%) | 16 (84.2) | | 16 (84.3) | |
| Female (%) | 3 (15.8) | | 3 (15.8) | |
| Race | | | | |
| African-American (%) | 12 (63.2) | | 12 (63.2) | |
| Caucasian (%) | 6 (31.6) | | 6 (31.6) | |
| Multiracial (%) | 1 (5.3) | | 1 (5.3) | |
| Education | | | | |
| Bachelor's degree (%) | 2 (10.5) | | 4 (21.1) | |
| Some college (%) | 6 (31.6) | | 12 (63.2) | |
| HS Diploma/ GED (%) | 5 (26.3) | | 3 (15.8) | |
| No HS diploma/GED (%) | 6 (31.6) | | 0 (0.0) | |
| Socioeconomic Status ^a | | | | |
| Parental SES | 2.94 | 1.11 | 3.37 | 1.38 |
| Current Symptoms ^b | | | | |
| Total Symptoms | 53.05 | 14.33 | | |
| Positive Symptoms | 15.00 | 5.35 | | |
| Negative Symptoms | 13.84 | 6.54 | | |

| Current Functioning | <i>M</i> | <i>SD</i> | <i>M</i> | <i>SD</i> |
|-----------------------|----------|-----------|----------|-----------|
| Social Functioning*** | 4.89 | 1.94 | 7.79 | 1.36 |
| Role Functioning*** | 4.16 | 2.32 | 7.89 | 1.82 |

Note. HS = high school; SES = socioeconomic status.

^aScored using the Hollingshead Index (Hollingshead, 1975) and rated using an increasing 5-point scale. ^bScored using the Positive and Negative Syndrome Scale.

*** $p < 0.001$.

Table 2

Group Comparisons of Formal Thought Disorder and Cognitive Performance

| | EP (<i>n</i> = 19) | | HC (<i>n</i> = 19) | | <i>d</i> |
|----------------------------|---------------------|-----------|---------------------|-----------|----------|
| | <i>M</i> | <i>SD</i> | <i>M</i> | <i>SD</i> | |
| Baseline Condition | | | | | |
| Positive FTD* | 1.26 | 0.96 | 0.60 | 0.38 | 0.90 |
| Speech Production*** | 1.68 | 0.63 | 2.50 | 0.42 | -1.53 |
| Affective Condition | | | | | |
| Positive FTD** | 1.91 | 1.49 | 0.51 | 0.29 | 1.30 |
| Speech Production*** | 1.71 | 0.63 | 2.52 | 0.50 | -1.42 |
| Cognitive Condition | | | | | |
| Positive FTD** | 1.66 | 1.39 | 0.67 | 0.57 | 0.93 |
| Speech Production*** | 1.36 | 0.63 | 2.28 | 0.40 | -1.74 |
| Single Task (% Correct) ** | 78.54 | 13.71 | 89.47 | 8.59 | -0.96 |
| Dual Task (% Correct) *** | 63.45 | 18.91 | 86.26 | 9.51 | -1.52 |

Note. FTD = formal thought disorder; EP = early-stage psychosis; HC = healthy controls.

***p* < 0.01; *** *p* < 0.001

Table 3

Correlations Between Functioning, Formal Thought Disorder, Speech Production, and Reactivity

| Baseline Condition | Early-Stage Psychosis ($n = 19$) | | Healthy Control ($n = 19$) | |
|-----------------------|------------------------------------|-------------|------------------------------|-------------|
| | Social Fx r | Role Fx r | Social Fx r | Role Fx r |
| Positive FTD | -0.52* | -0.68** | -0.10 | -0.03 |
| Speech Production | 0.08 | 0.05 | 0.10 | 0.56*+ |
| Affective Condition | | | | |
| Positive FTD | -0.75*** | -0.41+ | 0.07 | -0.47*+ |
| Pos FTD Aff React | -0.51* | 0.15 | 0.14 | -0.25 |
| Speech Production | -0.13 | -0.13 | 0.47*+ | 0.44+ |
| Speech Prod Aff React | -0.35 | -0.30 | 0.68** | 0.01 |
| Cognitive Condition | | | | |
| Positive FTD | -0.54* | -0.45+ | 0.14 | -0.19 |
| Pos FTD Cog React | -0.25 | 0.09 | 0.19 | -0.14 |
| Speech Production | -0.10 | 0.11 | 0.11 | 0.51*+ |
| Speech Prod Cog React | -0.25 | 0.10 | 0.02 | -0.04 |

Note. Fx = functioning; FTD = formal thought disorder; Pos = positive; Neg = negative; Aff = affective; Prod = production; React = reactivity; Cog = cognitive.

+ $p < 0.10$; *+ $p < 0.05$ (significance set at $p < 0.01$ for analysis); * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

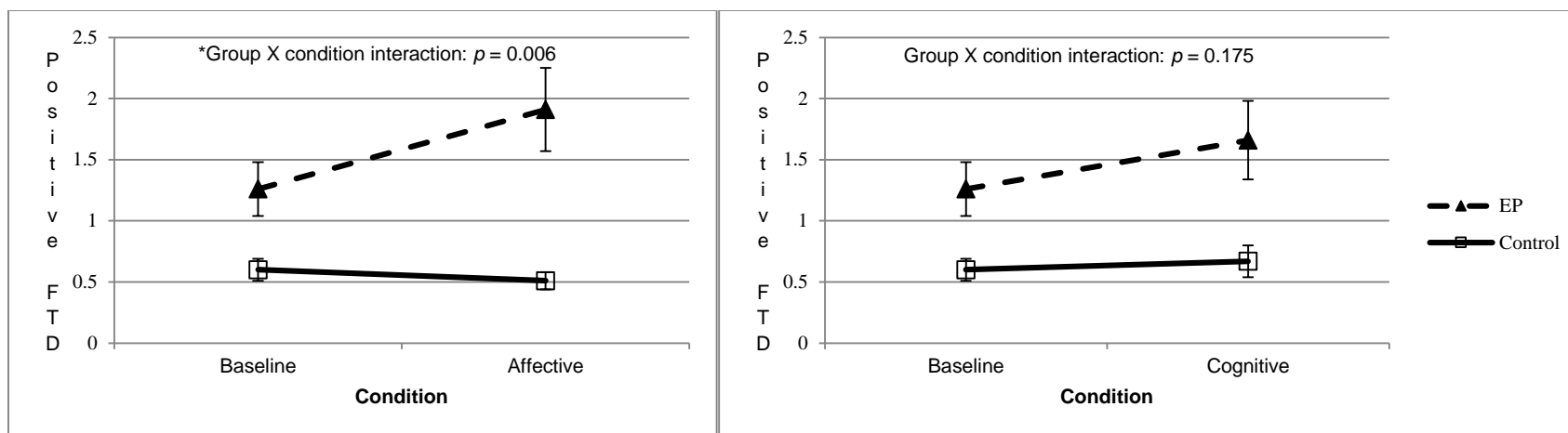


Figure 1. Change in positive formal thought disorder from baseline to experimental conditions in Early-Stage Psychosis (EP) and control groups.