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Moment-to-moment associations between negative affect, aberrant salience, and paranoia

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Introduction: There is an ongoing debate about whether negative affect are consequences or triggers of paranoid thinking. It has also been suggested that aberrant salience is central to the development of delusions. This study modelled the moment-to-moment relationships between negative affect, aberrant salience, and paranoia in acute inpatients with psychosis.

Methods: Participants with active paranoid delusions were assessed using clinical rating scales and experience sampling method (ESM) over 14 days. ESM data were analysed using time-lagged multilevel regression modelling.

Results: Both negative affect and aberrant salience predicted an increase in paranoia at the next time point. Conversely, level of paranoia did not predict subsequent changes in negative affect or aberrant salience. Negative affect predicted an increase in aberrant salience at the next time point, and vice versa.

Conclusions: Negative affect and aberrant salience appear to drive and exacerbate paranoia, rather than being merely the sequelae of the symptom. Our results suggest both direct and indirect (via aberrant salience) pathways from negative affect to paranoia.

Keywords: experience sampling; ecological momentary assessment; paranoia; emotion; psychosis

Introduction

Individuals with paranoid delusions often experience negative affect, with depression and anxiety being the most frequently reported (Garety et al., 2005; Vorontsova, Garety, & Freeman, 2013; Startup et al., 2016). The link to depression and anxiety appears to be specific to paranoid delusions, with an inverse relationship being seen for grandiose delusions (Garety et al., 2013; Smith et al., 2006). Experimental studies and intervention trials attempting to delineate the direction of association between emotional processes and paranoia have indicated that changes in anxiety may lead to changes in paranoia (Freeman et al., 2015; Lincoln, Peter, Schäfer, & Moritz, 2009). Longitudinal studies

have revealed that initial levels of depression and anxiety predicted persistence of paranoid thinking over six to 24 months, whereas delusions did not predict negative affect (Fowler et al., 2012; Vorontsova et al., 2013). Therefore, it has been theorised that negative affect do not merely arise as consequences of delusions. Rather, they have been suggested to play a direct role in the formation and maintenance of paranoid thinking (Freeman & Garety, 2003; Hartley, Barrowclough, & Haddock, 2013).

Researchers have also begun to examine moment-to-moment associations between negative affect and paranoia using experience sampling methodology (ESM), yielding inconsistent results (Ben-Zeev, Morris, Swendsen, & Granholm, 2012; Thewissen et al., 2011). It is of note that these studies consisted of participants with a highly heterogeneous clinical profile, among whom only a proportion had any type of delusional experiences. Since psychological mechanisms may differ across psychotic symptoms and even subtypes of delusions (Garety et al., 2013), associations between psychological processes are more clearly elucidated by examining homogenous samples. To ensure that individuals were experiencing active delusions, the present study recruited patients from acute psychiatric wards.

It has been suggested that psychotic experiences originate from a sense of aberrant salience (attribution of novelty and personal significance to irrelevant stimuli; Kapur, 2003). Aberrant salience is postulated to be the experiential manifestation of dopamine dysregulation, whereas delusions arise from top-down cognitive activity that “makes sense of” the anomalous experiences (Howes & Kapur, 2009; Howes & Murray, 2014). Using ESM, Reininghaus et al. (2016) found that momentary aberrant salience differentiated groups that varied across the psychotic continuum, and Klippel et al. (2017) found that aberrant salience was positively associated with psychotic experiences. Although these studies validated the use of ESM as a measure of the

subjective momentary experience of aberrant salience, the moment-to-moment association between aberrant salience and paranoia remains untested. In addition, it has been suggested that negative affect may result in an increase in aberrant salience, further triggering the appraisal process (Garety et al., 2007; Kapur, 2003).

Using a time-lagged analysis of experience sampling data, the aim of the present study was to model the role of momentary levels of negative affect and aberrant salience in maintaining paranoia in individuals with active delusions. Hypotheses were:

- (1) Momentary level of negative affect will be associated with change in paranoia at the following timepoint
- (2) Momentary level of aberrant salience will be associated with change in paranoia at the following timepoint
- (3) Momentary level of negative affect will be associated with change in aberrant salience at the following timepoint

Method

Ethical approval for the study was granted by the South East London Research Ethics Committee 4 (10/H0807/44).

Participants

Inclusion criteria were: in-patients with a clinical diagnosis of schizophrenia spectrum or other psychotic disorder; age 18 years or above; and current experience of persecutory delusions (scoring 2 or above on the Schedule for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984) item D1). Exclusion criteria were drug-induced psychosis, organic psychosis, and a primary diagnosis of substance misuse.

Measures

Experience sampling method (ESM) assessment

The ESM assessment included items on negative affect (NA), paranoia and aberrant salience (AS), which have been used in previous studies (Kimhy et al., 2006; Klippel et al., 2017; Myin-Germeys, Nicolson, & Delespaul, 2001; Reininghaus et al., 2016). ESM items used in this study are listed in Table 1.

As psychiatric inpatients tend to spend more time in bed, we opted for a less demanding sampling scheme than most ESM studies and asked participants to fill out seven (rather than 10) ESM questionnaires each day, but with an extended assessment period (i.e., 14 days; Kimhy, Myin-Germeys, Palmier-Claus, & Swendsen, 2012).

Details of the methodology and its validity are presented in greater detail in a separate paper (So, Peters, Swendsen, Garety, & Kapur, 2013).

[Table 1]

Clinical interview

Patients were interviewed at baseline by using the Positive and Negative Syndrome Scale for Schizophrenia (PANSS; Kay, Opler, & Fiszbein, 1987), the SAPS (Andreasen, 1984), and the Psychotic Symptom Rating Scales (PSYRATS; Haddock, McCarron, Tarrier, & Faragher, 1999).

Procedure

Consented participants completed the baseline interview and were provided with thorough instructions on how to complete the ESM assessment on an electronic device (Palm OS® version 5.2.1). Additional guidance and technical support was provided as required. Participants were debriefed about their ESM experience during the follow-up

interview.

Statistical analysis

Multilevel regression models were tested using XTMIXED command with maximum likelihood estimation in STATA 11. ESM variables were entered as level-1 variables and participant number was specified as a level-2 random effect variable. To test the hypothesised within-person associations between negative affect, aberrant salience, and paranoia, we conducted time-lagged analyses so that the IV at any given assessment (IV_t) predicted the outcome at the subsequent assessment on the same day (DV_{t+1}). Wherever a significant temporal relationship was found, we modelled the effect of the IV on *change* in DV by regressing DV_{t+1} on IV_t , controlling for DV at time point t (DV_t). In all models, NA, AS, and paranoia were within-person centred, controlling for gender and age. Following Delespaul (1995), participants who completed at least 33% of ESM entries were included in the analysis.

Results

Demographic and clinical characteristics

Among 26 patients who consented to participate in this study, 25 fulfilled the recruitment criteria. We excluded one patient who had a moderate level of grandiose delusions on the SAPS, as previous studies have shown that affect is significantly different in patients with both persecutory delusions and grandiose delusions (as opposed to those with persecutory delusions alone; Jolley et al., 2006). Of the remaining 24 patients, 14 completed at least 30 ESM entries and were included in the analysis. The total number of ESM observations for data analysis was 1,161 (mean 82.93, range 47-

93. The final sample did not differ from the excluded participants on any clinical measures.

The sample consisted of 8 (57.14%) males and 6 (42.86%) females. Average age was 34.07 years (range 20-63). Case-note psychiatric diagnoses were available for 13/14 patients as follows: 5 (38.46%) were diagnosed with schizophrenia, 5 (38.46%) with unspecified psychosis, 2 (15.38%) with a mood disorder with psychotic symptoms, and 1 (7.69%) with delusional disorder.

The baseline symptom severity scores were as follows: SAPS item D1 (persecutory delusions)=3.64 ($SD=0.93$), SAPS global delusions score=14.78 ($SD=4.84$), PSYRATS delusions score=16.86 ($SD=3.88$), PANSS positive symptom score=20.50 ($SD=4.33$), PANSS total score=64.07 ($SD=14.04$). Over 14 days, there was no significant change in momentary levels of paranoia ($B= -0.016$, $SE=0.012$, $p= .181$, NA ($B= 0.098$, $SE=0.013$, $p= .458$), and AS ($B= -0.006$, $SE=0.010$, $p= .569$).

Association of momentary level of negative affect with paranoia at the following time point

Time-lagged analysis revealed that NA_t significantly predicted $paranoia_{t+1}$ ($B=0.200$, $SE=0.038$, $p<.001$). Controlling for $paranoia_t$, the association remained significant ($B=0.177$, $SE=0.046$, $p<.001$). Therefore, NA predicted both the level of, and increase in, paranoia in the next time point, supporting the hypothesis. Conversely, while $paranoia_t$ significantly predicted NA_{t+1} ($B=0.244$, $SE=0.043$, $p<.001$), this prospective association was no longer significant when controlling for NA_t ($B=0.024$, $SE=0.051$, $p= .643$). Therefore, paranoia did not predict change in NA at the subsequent time point.

Association of momentary level of aberrant salience with paranoia at the following time point

Time-lagged analysis revealed that AS_t significantly predicted $paranoia_{t+1}$ ($B=0.299$, $SE=0.052$, $p<.001$). Controlling for $paranoia_t$, the association remained significant ($B=0.282$, $SE=0.057$, $p<.001$). Therefore, AS predicted both level of, and increase in, paranoia at the next time point, supporting the hypothesis. Conversely, $paranoia_t$ significantly predicted AS_{t+1} ($B=0.144$, $SE=0.032$, $p<.001$), but not after controlling for AS_t ($B=0.057$, $SE=0.034$, $p=.098$). Therefore, paranoia did not predict change in AS at the subsequent time point.

Association of momentary level of negative affect with aberrant salience at the following time point

Time-lagged analysis revealed that NA_t significantly predicted AS_{t+1} ($B=0.164$, $SE=0.031$, $p<.001$). Controlling for AS_t , the association remained significant ($B=0.088$, $SE=0.033$, $p=.009$). Similarly, AS_t significantly predicted NA_{t+1} ($B=0.429$, $SE=0.055$, $p<.001$), and this association also remained significant when controlling for NA_t ($B=0.270$, $SE=0.059$, $p<.001$). Therefore, NA predicted both level of, and increase in, AS at the next time point, and parallel findings were observed for AS in the prediction of NA at the next time point.

Results of the above multilevel time-lagged models are summarised schematically in Figure 1.

[Figure 1]

In view of the respective predictive effects from NA and AS to paranoia change (hypotheses 1-2), and the effect from NA to AS (hypothesis 3), we further examined the unique variance of the two IVs and explored the possibility that NA contributes to increase in paranoia via increasing AS. In the regression model of paranoia change with both NA_t and AS_t as IVs (Rabe-Hesketh and Skrondal (2008) $R^2=15.94\%$), both NA_t

($B=0.124$, $SE=0.048$, $p=.009$) and AS_t ($B=0.245$, $SE=0.059$, $p<.001$) remained significant predictors, but the magnitude of regression coefficient of NA_t decreased when compared to the model without AS_t . Therefore, although there was shared variance explained by both NA and AS, the two IVs had independent contributions to increase in paranoia at the next time point.

Discussion

This study examined the directional relationship between subjective levels of paranoia and negative affect. The major finding was that negative affect predicted the level of paranoia at the next time point. Importantly, we also adjusted analyses for initial levels of paranoia to test whether this prospective association involved actual change in the predicted variable. These conservative analyses confirmed the predictive role of negative affect. Although paranoia predicted level of negative affect at the next time-point, it did not predict change in negative affect. In other words, a unidirectional pattern was observed in which negative affect exacerbated paranoia momentarily, but not the reverse. Consistent with previous studies using an experimental or longitudinal design (Fowler et al., 2012; Lincoln et al., 2009; Vorontsova et al., 2013), our results lend support to the argument that negative affect contribute to maintenance of paranoia.

We also report, for the first time, the moment-to-moment relationship between aberrant salience and paranoia. A subjective experience of aberrant salience led to a subsequent increase in paranoia, but not the reverse. Therefore, rather than paying more attention to one's surroundings because of an existing paranoid belief, our data suggest that this aberrant sense of novelty and personal significance renders a person more susceptible to feeling paranoid over subsequent hours of the day.

Although negative affect interacted with aberrant salience dynamically across moments, negative affect and aberrant salience both contributed uniquely to subsequent

change in paranoia. Our results suggest, albeit tentatively, that there may be both direct and indirect (via increasing aberrant salience) effects of negative affect on paranoia, which warrants further examination with larger samples. The model with NA_t , AS_t and $paranoia_t$ only explained 15.94% of the total variance of $paranoia_{t+1}$. Therefore, other factors are likely to be involved in maintaining paranoia as well.

This study had several limitations. The sample consisted of a small number of patients who were hospitalised at the time of assessment. Some of them were discharged in the middle of the study, and it is unclear how the change in clinical care might have had an impact on the generalizability of the results. Besides, the single-item measure of paranoia only captures one aspect of paranoia and its reliability information is lacking. In addition, as the ESM scheduling was randomly generated by the computer, the duration of the assessment time lag varied across days and participants. Therefore, we cannot conclude with precision the length of time necessary for the time-lagged associations to occur.

(2000 words)

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Table 1. ESM items of negative affect, aberrant salience and paranoia

Variable	ESM item	Mean (SD)	Proportion of ESM observations with rating 4 and above ^a	Internal consistency ^b
Negative affect	“How irritated do you feel right now?”	2.77 (2.19)	25.58%	0.89
	“How low do you feel right now?”	2.93 (2.15)	28.60%	
	“How tense do you feel right now?”	2.77 (2.12)	25.84%	
Aberrant salience	“At this moment, how much do things around you grab your attention?”	3.15 (2.14)	27.30%	0.79
	“At this moment, how much do you feel that everything seems to have some meaning?”	3.09 (2.45)	28.85%	
	“At this moment, how much do you notice things that you have not noticed before?”	2.41 (2.01)	20.24%	
Paranoia	“How suspicious do you feel right now?”	2.37 (2.02)	19.29%	/

^aAll items were assessed on a 7-point Likert scale (from 1, “not at all”, to 7, “very much”)

^bInternal consistency was calculated under a generalizability theory framework (Cranford et al., 2006)

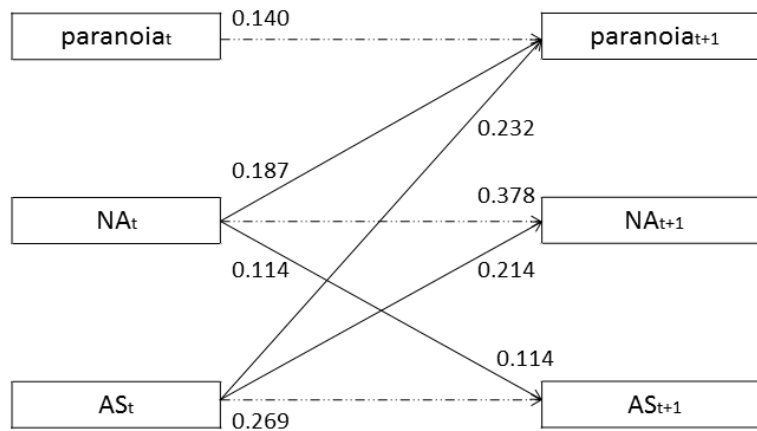


Figure 1. Schematic representation of between-moment relationships between paranoia, negative affect and aberrant salience (data are from 14 participants over 14 days, i.e. a total of 1161 included assessment points)

Note: Each line represents one multi-level regression model. Dotted lines represent between-moment relationships within the same variables. Solid lines represent between-moment relationships across variables, controlling for the DV at the initial time point (i.e., the effect of IV on change in DV). Effect size (i.e., standardized beta) is shown on each path. Only statistically significant paths are shown.

NA_t : negative affect at a given time point

NA_{t+1} : negative affect at the subsequent time point

AS_t : aberrant salience at a given time point

AS_{t+1} : aberrant salience at the subsequent time point

$paranoia_t$: paranoia at a given time point

$paranoia_{t+1}$: paranoia at the subsequent time point