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Comparing early signs and basic symptoms as methods for predicting psychotic relapse in clinical practice

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ABSTRACT

Background: Early signs interventions show promise but could be further developed. A recent review suggested that 'basic symptoms' should be added to conventional early signs to improve relapse prediction. This study builds on preliminary evidence that basic symptoms predict relapse and aimed to: 1. examine which phenomena participants report prior to relapse and how they describe them; 2. determine the best way of identifying pre-relapse basic symptoms; 3. assess current practice by comparing self- and casenote-reported pre-relapse experiences.

Methods: Participants with non-affective psychosis were recruited from UK mental health services. In-depth interviews (n = 23), verbal checklists of basic symptoms (n = 23) and casenote extracts (n = 208) were analysed using directed content analysis and non-parametric statistical tests.

Results: Three-quarters of interviewees reported basic symptoms and all reported conventional early signs and 'other' pre-relapse experiences. Interviewees provided rich descriptions of basic symptoms. Verbal checklist interviews asking specifically about basic symptoms identified these experiences more readily than open questions during in-depth interviews. Only 5% of casenotes recorded basic symptoms; interviewees were 16 times more likely to report basic symptoms than their casenotes did.

Conclusions: The majority of interviewees self-reported pre-relapse basic symptoms when asked specifically about these experiences but very few casenotes reported these symptoms. Basic symptoms may be potent predictors of relapse that clinicians miss. A self-report measure would aid monitoring of basic symptoms in routine clinical practice and would facilitate a prospective investigation comparing basic symptoms and conventional early signs as predictors of relapse.

1. Introduction

Relapse of psychosis is common (Robinson et al., 1999) and predicts distress (Maclean, 2008), impaired vocational and interpersonal functioning (Gumley and Schwannauer, 2006), long-term deterioration (Wiersma et al., 1998) and suicide (Appleby, 1992). It frequently results in hospital admission, the single biggest expense in schizophrenia's annual UK National Health Service cost of over £3.9 billion (Almond et al., 2004; Andrew et al., 2012), the USA equivalent being $22.7 billion (Wu et al., 2005). Interventions using early signs of deterioration to prompt timely preventative action can prevent relapse (Gumley et al., 2003; Herz et al., 2000; Lee et al., 2010), but could be further developed. Predictive validity of checklists such as the Early Signs Scale (ESS; Birchwood et al., 1989) could be improved by adding other hypothesised predictors such as basic symptoms (Eisner et al., 2013; Gumley et al., 2015).

'Basic symptoms' are subtle, sub-clinical disturbances in one's experience of oneself and the world that prospectively predict first episodes of psychosis (FEP) (Fusar-Poli et al., 2012; Schultze-Lutter et al., 2007). Typical basic symptoms include: perceptual changes such as colours' increased vividness; mild subjective cognitive problems; decreased tolerance of stressors. Overlap between lists of conventional early signs (e.g. ESS) and basic symptoms (e.g. Schizophrenia Proneness Index, Adult Version, SPI-A; Schultze-Lutter et al., 2007) is small (<5%). There is preliminary evidence that basic symptoms predict relapses of psychosis (Bechdolf et al., 2002; Gaebel and Riesbeck, 2014).

We aimed to investigate whether basic symptoms could be used to predict relapse in routine clinical practice and to compare them to

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conventional early signs in anticipation of developing and prospectively testing a basic symptoms measure. Using data from in-depth interviews, verbal checklists of basic symptoms and casenote extracts, we addressed the following research questions: 1. *Which pre-relapse experiences (early signs, basic symptoms, 'other') do participants report and how do they describe them?*; 2. *What is the best way of identifying basic symptoms: in-depth interview or verbal checklist?*; 3. *Which pre-relapse experiences (early signs, basic symptoms, 'other') are reported in casenotes?*

2. Methods

2.1. Ethics

Ethical approval was obtained from the Liverpool Central research ethics committee (ref: 12/NW/0091).

2.2. Which pre-relapse experiences do participants report? What is the best way of identifying basic symptoms?

2.2.1. Participants

Sample A: 23 patients were purposively sampled to include a range of characteristics from three NHS (National Health Service) Mental Health Trusts between May and November 2012. Inclusion criteria were: aged over 18 years; primary clinical diagnosis of non-affective psychosis (APA, 2000); admission to crisis team or inpatient unit in the past 6 months for acute psychosis; prescribed antipsychotic medication; no illicit drug use, or alcohol abuse or dependence, during the pre-relapse period; informed consent.

2.2.2. Data collection

In-depth interview: open questions explored events, feelings and experiences in the three months prior to the most recent relapse (topic guide available on request). Verbal checklist of basic symptoms: assessed experiences of basic symptoms in the three months prior to the recent relapse, based on the SPI-A, (Schultze-Lutter et al., 2007). The SPI-A (56 items) includes two overlapping lists of basic symptoms that predict FEP, 'COGDIS' (Cognitive Disturbances, 9 items) and 'COPER' (Cognitive-Perceptive basic symptoms, 14 items), in addition to 38 other basic symptoms (Schultze-Lutter et al., 2007). All interviews were audio-recorded and transcribed verbatim.

2.3. Which pre-relapse experiences are reported in casenotes?

2.3.1. Participants

Sample A: 21/23 in-depth interview and verbal checklist participants consented to their casenotes being examined. Sample B: 187 patients (approximately 10% of those eligible) were randomly selected (stratified by clinical team) from those aged over 18 with a clinical diagnosis of non-affective psychosis (WHO, 1992) and attending Community Mental Health Teams in one NHS Mental Health Trust in November 2010. Since data was obtained from a pseudo-anonymised dataset gathered for an audit, separate ethical approval and patient consent were not required (BMA, 2014).

2.3.2. Data collection

Five research assistants examined participants' electronic casenotes ($n = 208$) and extracted demographic information and verbatim quotations from the section of the most recent CPA review entitled "early warning signs", "relapse indicators" or "crisis plan".

2.4. Analysis

2.4.1. Directed content analysis

Directed content analysis (Hsieh and Shannon, 2005) was used to quantify pre-relapse experiences. Supplementary material Section B gives details of this process. All transcripts were coded according to the stage of the relapse process being described (pre-relapse, during relapse, unrelated to relapse). Pre-relapse experiences were then coded, with codes grouped into early signs, basic symptoms and 'other' pre-relapse experiences. Inter-rater reliability was assessed (supplementary material Section B).

2.4.2. Statistical analysis

Non-parametric statistics were used due to the relatively small size of the interview sample (see supplementary material Section B). For all analyses, findings were considered significant at $p = 0.05$.

3. Results

3.1. Sample characteristics

Table 1 shows demographic and clinical characteristics of the two samples.

3.2. Inter-rater reliability

Casenote data extraction: mean percentage agreement with consensus extraction was 95.7% after training and 91.4% during data collection. Stage-of-relapse coding: weighted kappa was 0.74. Pre-relapse experience coding: ICCs and kappas were calculated for three types of item (early signs, basic symptoms, other) and three types of data (in-depth interviews, verbal checklist, casenotes). ICCs all exceeded 0.72 and kappa values all exceeded 0.60.

3.3. Which pre-relapse experiences do participants report and how do they describe them?

3.3.1. Estimated sensitivity (early signs, basic symptoms, 'other')

Three-quarters (74%) of participants reported ≥ 1 basic symptom, with all participants reporting both conventional early signs and 'other' pre-relapse experiences. Sensitivity here refers to the proportion of relapses correctly identified by a putative predictor. Since all participants in the interview sample had relapsed, it equates to the proportion reporting a particular pre-relapse experience (i.e. 74% for basic symptoms, 100% for early signs, 100% for 'other'). No demographic or clinical characteristics listed in Table 1 significantly predicted reporting ≥ 1 basic symptom.

3.3.2. Number of pre-relapse experiences reported (early signs, basic symptoms, 'other')

Fig. 1 shows the number of basic symptoms, early signs and 'other' experiences reported to begin or increase pre-relapse. Participants reported significantly more ($z = 3.12$, $p = 0.002$) early signs (Median = 5; IQR = 3,6) than they did basic symptoms (Median = 2, IQR = 0,5). However, 35% (6/17) of those reporting basic symptoms, reported at least as many basic symptoms as they did conventional early signs. Furthermore, reported pre-relapse experiences were idiosyncratic, with a wide range of experiences reported (79 experiences) and most (57%) reported by ≤2 participants.

3.3.3. Estimated specificity (basic symptoms only)

Fourteen participants reported that they experienced basic symptoms at times unrelated to relapse (with no increase prior to relapse). Specificity, generally the proportion of non-cases correctly identified by negative test values was estimated by the proportion of the sample who did not report having experienced basic symptoms at times unrelated to relapse (39% for any basic symptoms; 70% for COGDIS; 61% for COPER).

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