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# Prospective memory predicts medication management ability and correlates with non-adherence to medications in individuals with clinically stable schizophrenia☆

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ABSTRACT

*Background:* Prospective memory (PM), the ability to remember to carry out an intended action in the future, is thought to relate closely to everyday functioning, such as medication adherence. PM impairment in schizophrenia may contribute to unintentional medication non-adherence. This study aimed to examine the relationship between PM, medication management and medication adherence.
*Methods:* Eighty-two stable patients with schizophrenia underwent assessment for PM and medication management ability by laboratory measures at baseline. Clinical symptoms, other neuropsychological functions and risk factors known to associate with non-adherence were also measured. Linear regression was used to identify predictors of medication management ability at baseline. Actual medication adherence was assessed three months later and logistic regression was used to identify predictors of non-adherence.
*Results:* In the linear regression model, time- and event-based PM together accounted for 72.3% of the variance in the performance of medication management at baseline. At three-month follow-up, the non-adherent group performed significantly more poorly in time- and event-based PM, and had poorer insight, more severe symptoms and poorer ability to manage medications, as compared to the adherent group. In the logistic regression model, insight and PANSS general score significantly predicted non-adherence in the community. Time- and event-based PM moderated the predictive power of insight and PANSS general score.
*Conclusions:* Our results support that PM performance robustly predicts medication management ability and may influence medication adherence in the community by moderating the effect of insight and symptom severity. Optimizing PM performance may improve medication adherence in the community, particularly for unintentional non-adherence.



## 1. Introduction

Prospective memory (PM) is the ability to remember to carry out an intended action in the future (Einstein and McDaniel, 1990). Contrary to traditional models of memory function such as retrospective memory, which is concerned with the ability to remember things in the past, PM is thought to be more closely related to clinical problems such as forgetting to attend an appointment or take medications (Shum et al., 2004; Altgassen et al., 2008; Twamley et al., 2008). According to Ellis (1996), PM involves (1) the formation of an intention that is paired with a specific retrieval cue; (2) the maintenance of the intention–cue pairing over a delayed interval while concurrently engaged in a foreground task; (3) self-initiated cue detection and recognition, with retrieval of the intention; and (4) execution of the intended task. PM is usually classified into time- (remembering to perform an intention at a specific time), event- (remembering to perform an intention when a cue appears), and activity-based (remembering to perform an intention upon the completion of an activity) PM, according to the nature of the cue associated with the future intention. Wang et al.'s (2009) meta-analysis concluded that patients with chronic schizophrenia (duration of illness (DOI) ranging from 4.7 to 26.1 years) have significant time-, event-, and activity-based PM impairments. PM impairments have also been reported recently in patients with early schizophrenia (Lui et al., 2011; Zhou et al., 2012).

Deficits in PM have been suggested to contribute to the highly disorganized lifestyle in people with schizophrenia (Altgassen et al., 2008), such as forgetting to turn up for medical appointments or take medications (Shum et al., 2004; Twamley et al., 2008). However, there is little empirical evidence to support that laboratory PM performance correlates with real-life functioning in patients with schizophrenia. The two studies conducted by Ritch et al. (2003) and Twamley et al. (2008) reported that poor PM performance predicts poor functional skills in schizophrenia; whereas Xiang et al. (2010)'s study did not support the correlation between PM and social functioning.

☆ Declare of interest: None.

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Psychosocial functioning is a multi-faceted construct and one important area of functioning that relates closely to the long-term outcome of schizophrenia is the ability to manage prescribed medication regimens. Such an ability, usually measured by role-play tasks, has been found to correlate with general cognitive ability (Patterson et al., 2002; Jeste et al., 2003) as well as with other cognitive functions including intelligence, problem solving, working memory, verbal learning and memory in patients with schizophrenia (Heinrichs et al., 2008). Woods et al. (2008) proposed that PM is a determinant for an individual's ability to manage medications. A number of studies conducted in individuals with HIV infections (Woods et al., 2009) and diabetes (Vedhara et al., 2004) have found that PM correlates with the degree of adherence to treatment, corroborating Woods et al.'s hypothesis. It is possible that the prospective forgetting in patients with schizophrenia results in unintentional non-adherence; yet empirical evidence in this clinical population is limited.

Non-adherence to oral and injectable antipsychotic medication is common in patients with schizophrenia, with a median rate of 55% (range: 24–88%; Fenton et al., 1997, for a review). Numerous factors such as poor insight, negative attitude towards medications, psychopathology, medication side-effects, substance abuse, and poor social support (Fenton et al., 1997; Kampman and Lehtinen, 1999; Lacro et al., 2002; Mohamed et al., 2009) have been associated with non-adherence. However, few studies have examined how PM impairment interplays with other factors in non-adherence.

Given that patients with schizophrenia usually have PM impairment (Wang et al., 2009), a cognitive component thought to determine medication management ability, we hypothesize that laboratory PM performance, as measured by a role-play task, predicts an individual's ability to manage medications. To extend the relationship between PM and drug-taking behaviour from the laboratory to clinical situations, we further examined the effect of baseline PM performance on medication adherence after a three-month interval. We hypothesize that impaired PM performance and impaired ability to manage medications could predict medication non-adherence three months later.

## 2. Methods

### 2.1. Participants

Eighty-two patients (40 in-patients and 42 out-patients) with DSM-IV schizophrenia, ascertained by the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition) Axis I Disorders (First et al., 1995), were recruited from a regional hospital in Hong Kong. The in-patients were recruited not more than five days before their scheduled discharge. All participants were clinically stable enough for neuropsychological assessments, according to the FDA-NIMH-MATRICS criteria (Buchanan et al., 2011).

The exclusion criteria were (1) organic brain disorder; (2) neuromuscular disorder; (3) visual or auditory disability; (4) mental retardation; (5) active alcohol or substance abuse in the past one month, or history of alcohol or substance dependence in the past six months; (6) history of head injury; and (7) history of electroconvulsive therapy in the past six months.

Table 1 shows the characteristics of the participants (mean age = 37.29 years, SD = 11.11 years; mean DOI = 11.79 years, SD = 7.57 years). All the participants were receiving antipsychotic medications at the time of assessment. The total antipsychotic dosage was expressed as a percentage of the British National Formulary-maximum dose (*British National Formulary (BNF): March 2012 (63rd Revised edition)*), as more than 80% of the participants in this study were on atypical antipsychotics (Hung, 2007). We used the Abnormal Involuntary Movement Scale (AIMS; Smith et al., 1979), the Barnes Akathisia Rating Scale (BARS; Barnes, 1989), and the Extrapyramidal Symptom Rating Scale (ESRS; Chouinard and Margolese, 2005) to measure side-effects. Apart from antipsychotics, 21 participants were receiving anticholinergic medication at a dose of 2–6 mg of benzhexol daily, and three were receiving benzodiazepine (lorazepam 0.5 mg daily). All participants gave written informed consent. The study was approved by the Ethics Committee of the New Territories West Cluster of the Hospital Authority of Hong Kong.

**Table 1**
Characteristics of the participants.

| | Schizophrenia (N = 82) | |
|---|---|---|
| | n | Percent |
| Men | 40 | 48.8 |
| Right-handed | 79 | 96.3 |
| Inpatients | 40 | 48.8 |
| *Subtypes:* | | |
| Paranoid | 71 | 86.6 |
| Undifferentiated | 8 | 9.8 |
| Disorganized | 2 | 2.4 |
| Residual | 1 | 1.2 |
| On atypical antipsychotics | 62 | 82.9 |
| | Mean | SD |
| Age (year) | 37.29 | 11.11 |
| Education (year) | 10.95 | 3.17 |
| Duration of illness (year) | 11.79 | 7.57 |
| *PANSS* | | |
| Positive symptoms | 8.83 | 2.08 |
| Negative symptoms | 9.26 | 1.71 |
| General psychopathology (without G12) | 16.21 | 1.36 |
| *Medication* | | |
| Antipsychotic dose (% of BNF maximum) | 48.96 | 31.69 |
| Anticholinergic medication (mg/d) | 1.07 | 1.99 |
| No of prescribed medications | 1.84 | 0.98 |
| No of times medication is taken per day | 1.37 | 0.56 |
| *Medication side effects* | | |
| AIMS – Tardive dyskinesia | 0.05 | 0.35 |
| BARS – Akathisia | 0.17 | 0.41 |
| ESRS – Dystonia | 0.04 | 0.33 |
| ESRS – Parkinsonism | 0.46 | 0.80 |
| Insight – SUMD | 7.55 | 3.59 |
| Attitudes toward medication – DAI | 11.54 | 13.80 |

*Note.* PANSS = Positive and Negative Syndrome Scale; BNF = British National Formulary; AIMS = Abnormal Involuntary Movement Scale; BARS = Barnes Akathisia Rating Scale; ESRS = Extrapyramidal Symptom Rating Scale; SUMD = Scale to Assess Unawareness of Mental Disorder; DAI = Drug Attitude Inventory.

### 2.2. Medication management ability

The Medication Management Ability Assessment (MMAA) task (Patterson et al., 2002) is a structured and performance-based role-play task, simulating real-life drug-taking behaviour. The interviewer presented four mock medications to the participants, with clear instructions written on the pill bottles. There was a delay of an hour between the presentation and the actual test. The participants were then asked to describe how they would take the medications throughout the day and hand each dose to the interviewer. The interviewer recorded the following data: the pill type, the number of times per day that each prescription was taken, the number of capsules taken each time and whether they were taken with or without a meal. Points were deducted for deviations from the prescription instructions out of a maximum possible score of 33.

### 2.3. Laboratory PM assessment

A dual-task computerized paradigm was developed by Wang et al. (2008) to measure time-, event-, and activity-based PM. The details of the paradigm have been described elsewhere (Lui et al., 2011). There were four sessions, each lasting for six minutes. In each of the session, participants were engaged in an ongoing task, either semantic (judging whether a four-character phrase was an idiom or not) or perceptual (judging whether a perceptually degraded digit was the digit "0" or