



Research paper

Prospective memory deficits in patients with depression: A meta-analysis[☆]

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ABSTRACT

Background: Prospective memory (PM) can be impaired in patients with psychiatric disorders including depression. This meta-analysis systematically examined PM in patients with depression.

Methods: The meta-analysis was conducted according to the guidelines from Strengthening the Reporting of Observational Studies in Epidemiology (STROBE). Case-control studies on PM in patients with depression were included. Standardized mean differences (SMDs) and 95% confidence interval (CI) were calculated using random effect models.

Results: Ten case-control studies (n = 596) comparing patients with depression (n = 299) with healthy controls (n = 297) were included in the analyses. Compared with healthy controls, patients with depression had significant impairment in event-based PM (EBPM) [8 trials, n = 436; SMD: -0.87 (95%CI: -1.43, -0.31), P = 0.002; I² = 87%]. Significance was observed after removing two outlier trials [SMD: -0.44 (95%CI: -0.69, -0.20), P = 0.0004; I² = 23%] and also in 8 out of the 13 subgroup analyses. Similarly, time-based PM (TBPM) was significantly impaired in patients with depression [4 trials, n = 239; SMD: -0.89 (95%CI: -1.46, -0.31), P = 0.003; I² = 78%] when compared with healthy controls.

Conclusions: This meta-analysis showed that both TBPM and EBPM appeared to be impaired in patients with depression.

1. Introduction

Cognitive impairment occurs in up to two-thirds of patients with depression (Afridi et al., 2011; Butters et al., 2004) including first-episode patients (Lee et al., 2012) and those in remission (Bora et al., 2013). Among the cognitive domains affected in depression, prospective memory (PM), defined as the ability of formation, maintenance and execution of future intentions (Kvavilashvili and Ellis, 1996), has gained increasing attention (Albinski et al., 2012). In contrast, retrospective memory (RM) is a form of memory that involves remembering past information (Burgess and Shallice, 1997).

PM involves encoding an intention, retaining the information, executing the intention and evaluating the outcome (Elvevag et al., 2003).

PM includes the several subtypes according to the cues that trigger the execution of intention: time-based PM (TBPM) and event-based PM (EBPM). With a TBPM task, the individual remembers to perform an intention at a specific time in the future. In contrast, EBPM is triggered by an external event that serves as a reminder of a previously formed intention to be performed. In addition, a special PM subtype, activity-based PM (ABPM), has been described (Kvavilashvili and Ellis, 1996) which involves an external cue similar to EBPM, but the cue coincides with the end of an ongoing activity, thus does not interrupt of the activity, making it easy to perform. PM appears to be impaired in a number of neuropsychiatric disorders, such as schizophrenia (Liu et al., 2016; Zhou et al., 2012) and mood disorders (Lee et al., 2010).

Several brain areas are involved in PM process, particularly the

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prefrontal cortex (PFC) and the temporal cortex (Burgess et al., 2003; Okuda et al., 2007). Although both TBPM and EBPM require the activation of the prefrontal cortex (Okuda et al., 2007), the right polar prefrontal region is closely associated with TBPM tasks (Volle et al., 2011). Neurobiological dysfunction in these areas have also been implicated in depression. There is evidence that projections from the amygdala to anterior cingulate cortex (ACC) and also to PFC are impaired in depression (Davidson et al., 2002; Elliott et al., 1997). Altered PFC activation (Harvey et al., 2005; Wagner et al., 2006) as well as volumetric reduction in the gray matter of PFC (Botteron et al., 2002) have been associated with depression. Neural circuits involving these brain areas are likely to be involved in PM (Volle et al., 2011) and may act as an integrated circuit during PM tasks (Churchwell and Kesner, 2011; Goto and Grace, 2008). Therefore, PM deficit may arise from the functional dysconnectivity in these neural circuits (Greicius et al., 2007; Zeng et al., 2012). Although several previous reviews have described the neuropsychological changes in depression (Bosaipo et al., 2016; Vives et al., 2015), none have covered cognitive functions that reflect functional connectivity.

To date, 10 case-control studies on PM in depression have been published with inconsistent findings; six studies examined TBPM (Albiński et al., 2012; Li et al., 2013; Liu et al., 2013; Rude et al., 1999; Wang et al., 2009; Wang et al., 2012), eight studies examined EBPM (Altgassen et al., 2011, 2009; Chen et al., 2013; Li et al., 2013; Liu et al., 2013; Wang et al., 2009; Wang et al., 2012; Zhang and He, 2009) and four studies examined both PM types (Li et al., 2013; Liu et al., 2013; Wang et al., 2009; Wang et al., 2012).

A thorough search of the literature could not locate any systematic review or meta-analysis specifically examining PM in depression, which gave the impetus to conduct a comprehensive meta-analysis of PM in depression. Both English- and Chinese-language databases were included since the latter could not be readily accessed by the international readership.

2. Methods

2.1. Search strategy and selection criteria

This meta-analysis was conducted according to the guidelines of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) (Elm et al., 2007). A systematic review was performed covering English (PubMed, PsycINFO, Embase, Cochrane Library databases) and Chinese databases (WanFang, Chinese Biomedical and China Journal Net databases) from their inception until Nov 4, 2016 with search items listed as follows: ("prospective memory"[All Fields] OR "prospective memories"[All Fields]) AND ("depressive disorder"[MeSH Terms] OR "depression"[MeSH Terms] OR "unipolar depression"[All Fields] OR "neurotic depression"[All Fields] OR "endogenous depression"[All Fields] OR "depressive syndrome"[All Fields] OR "melancholia"[All Fields]). Reference lists were searched manually for additional studies from identified and relevant review article.

The following selection criteria were used based on the *PICOS* acronym: **Participants:** depression according to any diagnostic criteria. **Intervention:** not applicable. **Comparison:** healthy controls. **Outcomes:** EBPM, TBPM, ABPM, and overall PM performance. **Study design:** case-control studies examining PM in depression with meta-analyzable data. Case reports/series and reviews were excluded.

2.2. Data extraction

Data extraction was independently performed by two reviewers (WZ and YYW). Any disagreement was resolved by consensus or the involvement of a third reviewer (FCZ). If the same data was reported in more than one article, only the paper with more complete data was included. If the PM performance was evaluated using different parameters in a study, only the data on the principal parameter were

included in order to avoid inter-dependence. First/correspondence authors were contacted for additional information if necessary.

2.3. Statistical methods

For PM and its subtypes, standard mean differences (SMDs) and their 95% CI were calculated as different PM measures were used in the included studies. In order to address heterogeneity, the random effect model in all analyses was conducted according to the recommendation of DerSimonian and Laird (DerSimonian and Laird, 1986). When the I^2 value was greater than 50%, one sensitivity analysis was performed by removing two outlying studies (SMD = -1.0) (Chen et al., 2013; Wang et al., 2009). Furthermore, 6 subgroup analyses were conducted to determine the reasons for heterogeneity including: 1) Chinese vs. non-Chinese studies; 2) age (years): ≥ 29.6 vs. < 29.6 (using the median split of patients' age); 3) education (years): ≥ 12 vs. < 12 years (using the median split of patients receiving school education); 4) depression severity: moderate vs. severe, defined by the Hamilton Depression Scale (HAMD) or Beck Depression Inventory (BDI) total score; 5) gender predominance: male predominance ($\geq 60\%$) vs. no gender predominance vs. female predominance ($\geq 60\%$); 6) antidepressants: patients on no antidepressants at entry vs. patients receiving antidepressants at entry. Four meta-regression analyses were conducted based on 1) mean age; 2) education level (years); 3) percentage of males; and 4) BDI total score at baseline. Publication bias was assessed using funnel plots, Egger's intercept (Egger et al., 1997), Duval and Tweedie's trim-and-fill procedure (Duval and Tweedie, 2000) and the fail-safe method (Rosenthal, 1979) that estimates the number of studies needed to change the findings. All statistical analyses were conducted using the Review Manager Version 5.3 software (<http://www.cochrane.org>) and the Comprehensive Meta-Analysis software, Version 2 (<http://www.meta-analysis.com>). The significance level was set at 0.05 (two-sided).

2.4. Assessment of study quality

The quality of the included studies was evaluated using the Newcastle-Ottawa Scale (NOS) (O'Connell, 2002). Furthermore, the grading of recommendations assessment, development, and evaluation (GRADE) system (Atkins et al., 2004; Balshem et al., 2011) was used to assess the quality of evidence and the strength of the result of meta-analyzable outcomes.

3. Results

3.1. Results of the search

The original search from the above databases yielded 139 electronic records (Fig. 1). Finally, 10 eligible case-control studies, including 5 published in English (Albinski et al., 2012; Altgassen et al., 2011, 2009; Li et al., 2013; Rude et al., 1999) and 5 in Chinese (Chen et al., 2013; Liu et al., 2013; Wang et al., 2009, 2012; Zhang and He, 2009) were included in the analysis.

3.2. Study characteristics

Ten case-control studies ($n = 596$) compared patients with depression ($n = 299$) and healthy controls ($n = 297$). Of the ten studies (Table 1), five were conducted in China ($n = 253$), two in the Switzerland ($n = 119$), one each in Poland ($n = 120$), Australia ($n = 64$), and the USA ($n = 40$). One study (Albinski et al., 2012) did not provide meta-analyzable data and another one (Rude et al., 1999) only provided mean values, which were not analyzable. Eventually, there were 4 case-control studies with meta-analyzable TBPM data and 8 with meta-analyzable EBPM data.

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