Research paper

Cognitive complaints and predictors of perceived cognitive dysfunction in adults with major depressive disorder: Findings from the Cognitive Dysfunction in Asians with Depression (CogDAD) study

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ABSTRACT

Background: Several studies have described the presence of perceived cognitive dysfunction amongst Asian patients with major depressive disorder (MDD). To date, no study has been conducted investigating the predictors of perceived cognitive dysfunction amongst Asian MDD patients.

Methods: This was a post-hoc analysis of the Cognitive Dysfunction in Asian patients with Depression (CogDAD) study. Descriptive statistics were used to describe the most common cognitive complaints by patients. Univariate and multivariate analyses were performed to determine variables associated with perceived cognitive dysfunction (Perceived Deficit Questionnaire-Depression, PDQ-D).

Results: The CogDAD study population is comprised of MDD patients with mild-to-moderate depression (Patient Health Questionnaire 9-item [PHQ-9]: 11.3 ± 6.9) who reported perceived cognitive dysfunction (PDQ-D = 22.6 ± 16.2). The most common cognitive complaints were: mind drifting (42.3%), trouble making decision (39.6%) and trouble concentrating (38.0%). Predictors of perceived cognitive dysfunction were: being Southeast Asians (vs. Taiwanese) (p < 0.001), current episode longer than 8 weeks (vs. 1–8 weeks) (p < 0.05), the presence of disability (vs. no disability) (p < 0.05), younger age (p < 0.01), and higher PHQ-9 total scores (p < 0.001).

Limitations: The causal relationship between predictive variables and PDQ-D could not be tested due to the cross-sectional nature of the study. Furthermore, a neuropsychological test was not included in the CogDAD study and use of concomitant medications, including anti-depressants, could have impacted patient’s perceived cognitive ability.

Conclusions: The present study results suggest a potential role for subjective cognitive assessment in patients with MDD who are young, with long durations of depression or severe depression.

1. Introduction

Cognition is the mental process characterized by knowing, thinking, learning, understanding, and judging (Mosby, 2012). Depressed patients may have both ‘hot’ and ‘cold’ cognitive impairment (Roiser and Sahakian, 2013). While ‘hot’ cognitive impairment is a cognitive bias toward negative information and a misinterpretation of social cues, ‘cold’ cognitive impairment is the functional impairment of information processes in the absence of any emotional influence.

Regarding ‘cold’ cognitive impairment in major depressive disorder (MDD), cognitive dysfunction is consistent, replicable, nonspecific, and clinically significant (McIntyre et al., 2015). However, perceived
cognitive dysfunction (PCD) has been less studied and may not necessarily overlap with cognitive performance. A number of studies have shown that the cognitive performance is not consistently correlated with perceived cognitive abilities (Lahr et al., 2007; Mowla et al., 2008; Svendsen et al., 2012). The differences between cognitive performance and perceived cognitive function are important to note. While PCD is based on the patient’s experience of cognitive symptoms in everyday life, neurocognitive performance is measured in a controlled environment (Fehnel et al., 2016). Therefore, objective and subjective cognitive results are not interchangeable. In addition, it is not yet clear whether perceived functional impairment of information processes should be considered as ‘cold cognitive impairment’.

PCD in adults with MDD is common and associated with functional impairment. Depressed patients had more complaints than healthy controls in various cognitive domains, such as memory, concentration, thought expression/speed, word finding and problem solving (Iverson and Lam, 2013). In the Study of Aspects of Asian Depression (SAAD), 81% of 515 psychotropic drug-free patients with MDD had memory and/or concentration complaints in the week prior to assessment (Srisurapanont et al., 2015). This study also found an independent association between cognitive complaints and clinically significant disability. In the Epidemiological Research on Functioning Outcomes Related to Major depressive disorder in South Korea (PERFORM-K), irrespective of depression severity, patients with more severe PCD were likely to have higher impairment while working and greater overall disability/work productivity loss (Kim et al., 2016).

There were some limitations in SAAD and PERFORM-K studies. Firstly, the areas of attention and organization deficits in Asian patients with MDD have not been fully addressed. While SAAD assessed only memory and concentration complaints, PERFORM-K examined the overall PCD. Secondly, both studies did not examine factors correlated with overall PCD: SAAD examined factors correlated with memory and concentration complaints only; PERFORM-K study mainly examined the factors associated with disability.

Recently, investigators in Taiwan and Southeast Asia have carried out a study entitled ‘Cognitive Dysfunction in Asians with Depression’ (CogDAD). Its primary publication confirmed the finding of disability associated with PCD (Srisurapanont et al., 2017). In this secondary analysis, we described common cognitive complaints and determined the independent predictors of PCD in adult Asians with MDD.

2. Methods

This study was a post-hoc analysis of the results obtained from the CogDAD study, a non-interventional, multi-centre, multi-country, cross-sectional, observational study which assessed and described cognitive dysfunction in the Asian MDD population. Results of the CogDAD study have been reported elsewhere (Srisurapanont et al., 2017). The CogDAD study was conducted between 2014 and 2015 in Taiwan and five countries in Southeast Asia, including Indonesia, Philippines, Malaysia, Singapore, and Thailand. The study protocol was approved by the Institutional Review Board or the Ethics Committee of each study site. After the study details had been explained, all the participants provided written informed consent prior to participation in the study.

2.1. Participants

The CogDAD study enrolled patients with MDD aged between 21 and 65 years old. Exclusion criteria were: current diagnosis or past medical history of schizophrenia/other psychotic disorders, bipolar disorder, dementia/other neurodegenerative disease, alcohol/substance use dependence, or other psychiatric disorder; or previous enrollment in the present study or in a clinical trial.

2.2. Assessment

Apart from socio-demographic characteristics, we collected the data relevant to MDD history, MDD treatment, impact of MDD on work, and health resource use.

The Perceived Deficits Questionnaire for Depression (PDQ-D) (Fehnel et al., 2016; Lam et al., 2013), a modified version of the 20-item Perceived Deficits Questionnaire (Sullivan et al., 1990), was used to assessed the PCD. Its convergent validity was supported by its strong correlations with a measure of cognitive functioning and moderate correlations with some construct measures known to be associated with cognitive functioning, including health-related quality of life, productivity at work, and other functional impairment (Lam et al., 2013). Each item asked about the frequency of an experience of cognitive deficit in the past week, which can be rated as 0 (never), 1 (rarely), 2 (sometimes), 3 (often), and 4 (almost always). In this study, a “cognitive complaint” was defined as a score of 2 or more on any PDQ-D item. The questionnaire has four 5-item subscales: Attention/Concentration, Retrospective Memory, Prospective Memory, and Planning/Organization. PDQ-D total scores are computed by adding raw scores for all items.

Functional disability was assessed using the Sheehan Disability Scale (SDS) (Sheehan et al., 1996). This three-domain scale assesses perceived disability in the domains of work/school, social life/leisure activities, and family life/home duties. Each item is rated from 1 (no disability) to 10 (extreme disability). Those who had not worked or studied in the past week did not complete the ‘Work/School Work’ domain of the SDS (total SDS score was consequently not computed for patients who had not completed the ‘Work/School Work’ domain of the SDS). Participants with a score of 5 or more on at least one domain were defined as those having functional disability (American Psychiatric Association, 2000).

Depression severity was assessed using the 9-item Patient Health Questionnaire (PHQ-9) and the Clinical Global Impression – Severity (CGI-S) (Guy, 1976; Kroenke et al., 2001). The CGI-S is a standardised, generic tool completed by physicians, which rates the severity of an illness on a 7-point scale (a score of 1 indicates normal health and a score of 7 indicates extreme illness). (Guy, 1976) The 9-item Patient Health Questionnaire (PHQ-9) is completed by patients. A total score is calculated that ranges from 0 (absence of depression) to 27 (severe depression) (Kroenke et al., 2001).

2.3. Post-hoc statistical analyses

Data are presented as frequencies, percentages, means, and standard deviations. All patients included in the CogDAD study were included in the post-hoc analyses. Participants were divided into four groups based on the quartiles of PDQ-D total score. The Shapiro-Wilk normality test was used to determine the distribution of each continuous variable (Shapiro and Wilk, 1965). The Chi-square tests were applied to determine the proportion differences among groups. If the continuous data of all four quartile groups had normal distribution, the difference among groups on such variable was determined by using parametric tests, otherwise, nonparametric tests were applied.

The first regression model included all univariate variables statistically correlated with PCD (p < 0.05). Manual backward elimination was applied to construct the final model. All statistical analyses were carried out using Microsoft R Open 3.4.0 (Microsoft, Redmond, WA, USA; R Foundation for Statistical Computing, Vienna, Austria). We used the Rcmdr 2.3–2 for univariate analysis and the RcmdrPlugin.MPASstats 1.2.1 and RcmdrPlugin.NMBU 1.8.7 for ordinal logistic regression analysis. In addition, the pscl 1.5.2 was used to calculate the McFadden R2. Two-sided, p-values < 0.05 were considered statistically significant.
# The Study

### 3. Results

There were 664 participants with MDD who had a mean age of 46.5 (SD = 12.5) years, and a PHQ-9 mean score of 11.4 (SD = 7.0) (see Table 1). There were 226 Taiwanese (34.0%), 211 Malaysians (31.8%), 168 Thais (25.3%), 36 Singaporean (5.4%), 21 Indonesians (3.2%), and 2 Filipinos (0.3%). Of all participants, 440 (66.3%) were female, and 168 Thais (25.3%), 36 Singaporean (5.4%), 21 Indonesians (3.2%), and 2 Filipinos (0.3%). Of all participants, 440 (66.3%) were female, and 168 (25.3%) in quartile 3 (PDQ-D total scores = 20–239). The most common cognitive complaint was mind drifting (n = 281, 42.3%), followed by trouble concentrating (n = 263, 39.6%), and trouble making decision (n = 252, 38.0%). The univariate analysis revealed that Southeast Asians had significantly higher PDQ-D total scores than Taiwanese (χ² = 70.39, df = 3, p < 0.01) (see Table 3). Other factors associated with higher PDQ-D total scores were current depressive episode longer than 8 weeks (χ² = 19.45, df = 3, p < 0.01), and disability (χ² = 83.41, df = 3, p < 0.01). Characteristics associated with worse PDQ-D total scores were younger age (H = 61.29, p < 0.01), longer years of education (H = 14.03, p < 0.01), greater number of previous episodes (H = 10.82, p = 0.01), and worse depression severity as assessed by higher PHQ-9 total scores (H = 295.32, p < 0.01) and higher CGI-S scores (H = 116.75, p < 0.01) (Table 3).  

### 4. Discussion

This study was carried out in Asian adults with MDD. Their PHQ-9 mean score of 11.4 suggested that they had mild to moderately severe depression. About three-fourths of this sample had cognitive complaints. The most common cognitive symptom was mind drifting, the mind (or concentration) moving about from place to place aimlessly. An attention deficit was the most prominent area of PCD. The severity of PCD might vary among ethnic groups. Predictors of PCD included long duration of depressive episode, younger age, and severe depression.  

To our knowledge, this is the first study that identified a difference in PCD severity between ethnic groups. Differences in depressive symptoms among Asian ethnic groups are less studied and still controversial. Only few studies of PCD have been carried out in multi-ethnic groups of depressed patients. While the study of Iverson and Lam was carried out in Canadian patients (Iverson and Lam, 2013), PERFORM-K included only Korean patients (Kim et al., 2016). Although SAAD included multi-ethnic groups, ethnic differences were not examined in the secondary analysis of subjective memory and concentration complaints. While a multi-ethnic study of depressive symptoms found that Korean patients reported more severe symptoms of depressed mood, guilt, agitation, psychic anxiety, and genital symptoms than Japanese and Chinese counterparts (Nakane et al., 1991), the other analysis of SAAD data found only unremarkable differences of depressive symptom severity among six Asian ethnic groups (Sulaiman et al., 2014). The present finding that depressed patients in Southeast Asian have more severe PCD than Taiwanese counterparts should be confirmed in future studies.  

Several results of the present study are in line with previous studies,
<table>
<thead>
<tr>
<th>Significant difference among groups&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Patients with PDQ-20-D score of 0–9 (n = 161)</th>
<th>Patients with PDQ-20-D score of 10–19 (n = 160)</th>
<th>Patients with PDQ-20-D score of 20–31 (n = 168)</th>
<th>Patients with PDQ-20-D score ≥ 32 (n = 175)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>113 (25.7%)</td>
<td>107 (24.3%)</td>
<td>103 (23.4%)</td>
<td>117 (26.6%)</td>
</tr>
<tr>
<td>Male</td>
<td>48 (21.4%)</td>
<td>53 (23.7%)</td>
<td>65 (29.0%)</td>
<td>58 (25.9%)</td>
</tr>
<tr>
<td>Nationality, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taiwanese</td>
<td>90 (39.8%)</td>
<td>68 (30.3%)</td>
<td>35 (15.5%)</td>
<td>33 (14.6%)</td>
</tr>
<tr>
<td>Southeast Asian</td>
<td>71 (16.2%)</td>
<td>92 (21.0%)</td>
<td>133 (30.4%)</td>
<td>142 (32.4%)</td>
</tr>
<tr>
<td>Work status, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not working</td>
<td>18 (18.9%)</td>
<td>23 (24.2%)</td>
<td>30 (31.6%)</td>
<td>24 (25.3%)</td>
</tr>
<tr>
<td>Working</td>
<td>143 (25.1%)</td>
<td>137 (24.1%)</td>
<td>138 (24.3%)</td>
<td>151 (26.5%)</td>
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<td>Current episode &gt; 8 weeks, n (%)</td>
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<td>No</td>
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<td>21 (17.8%)</td>
<td>32 (27.1%)</td>
<td>48 (40.7%)</td>
</tr>
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<td>Yes</td>
<td>144 (26.4%)</td>
<td>139 (25.5%)</td>
<td>136 (24.9%)</td>
<td>127 (23.3%)</td>
</tr>
<tr>
<td>Patients being treated with antidepressants, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>18 (19.6%)</td>
<td>21 (22.8%)</td>
<td>21 (22.8%)</td>
<td>32 (34.8%)</td>
</tr>
<tr>
<td>Yes</td>
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<td>139 (24.3%)</td>
<td>147 (25.7%)</td>
<td>143 (25.0%)</td>
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<tr>
<td>Patients being treated with anxiolytics/hypnotics, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>No</td>
<td>46 (24.9%)</td>
<td>47 (25.4%)</td>
<td>48 (25.9%)</td>
<td>44 (23.8%)</td>
</tr>
<tr>
<td>Yes</td>
<td>115 (24.9%)</td>
<td>113 (24.3%)</td>
<td>120 (25.1%)</td>
<td>131 (27.3%)</td>
</tr>
<tr>
<td>Disability (SDS score ≥ 5 on ≥ 1 domain), n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>No</td>
<td>108 (35.6%)</td>
<td>89 (29.4%)</td>
<td>71 (23.4%)</td>
<td>35 (11.6%)</td>
</tr>
<tr>
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<td>53 (14.7%)</td>
<td>71 (19.7%)</td>
<td>97 (26.9%)</td>
<td>140 (38.8%)</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>52.0 (10.1)</td>
<td>48.5 (11.5)</td>
<td>43.9 (12.5)</td>
<td>42.2 (13.0)</td>
</tr>
<tr>
<td>Years of education, mean (SD)</td>
<td>11.9 (4.8)</td>
<td>12.8 (5.0)</td>
<td>13.4 (4.4)</td>
<td>12.9 (4.4)</td>
</tr>
<tr>
<td>Number of previous episodes, mean (SD)</td>
<td>1.1 (2.0)</td>
<td>1.1 (2.1)</td>
<td>1.6 (3.2)</td>
<td>2.3 (5.0)</td>
</tr>
<tr>
<td>PHQ-9 total score, mean (SD)</td>
<td>5.5 (4.8)</td>
<td>9.2 (5.1)</td>
<td>11.8 (5.1)</td>
<td>18.3 (5.5)</td>
</tr>
<tr>
<td>CGI-S score, mean (SD)</td>
<td>2.7 (1.0)</td>
<td>3.0 (0.8)</td>
<td>3.5 (0.9)</td>
<td>3.8 (0.9)</td>
</tr>
</tbody>
</table>

<sup>a</sup> χ² tests for categorical data, Kruskal-Wallis H test for continuous data, df = 3 for all comparisons.

<sup>*</sup> p ≤ 0.01.
in particular the SAAD findings (Srisurapanont et al., 2015). Firstly, the present study confirmed the high prevalence of cognitive complaints in patients with MDD: 81.6% of the SAAD sample reported memory and/or concentration complaints, 75.88% of the present study had cognitive complaints, and 91.9% of Canadian patients with depression in another study reported cognitive complaints (Iverson and Lam, 2013). The differences in these figures might reflect slight differences in the clinical profile of the study populations and different measures used for assessing PCD. Secondly, although the present sample was less depressed than the SAAD study population, these findings confirmed that depression severity is an independent correlate of PCD. Using a Montgomery–Åsberg Depression Rating Scale (MADRS) mean score of 31 as the cutoff between moderate and severe depression (Müller et al., 2003), the MADRS mean score of 29.4 (SD = 8.0) in the SAAD sample indicated moderate to severe depression. The mean PHQ-9 score of 11.4 (SD = 7.0) found in this study suggested that most of the present sample had mild to moderately severe depression (Kroenke et al., 2003). Taken together, the findings of both studies suggest that depression is an independent predictor of PCD, no matter the severity.

Similar to the SAAD, which identified a correlation between younger age and subjective cognitive symptoms (Srisurapanont et al., 2013), the present study identified younger age as an independent correlate of PCD. This finding supports earlier studies reporting that cognitive complaints are common amongst children and adolescents with MDD (Bortolato and Carvalho, 2014). It has been posited that clinically significant dysfunction of subjective cognition may be an early symptom of MDD. Clinicians should therefore assess subjective cognition early in their MDD patients’ course of illness.

5. Limitations

This study had a number of limitations. Firstly, the causal relationship between variables and PDQ-D cannot be tested due to the cross-sectional nature of the study. Secondly, although we know that neurocognitive dysfunction may not be correlated with PCD, we did not apply a neuropsychological test in this study. Therefore, the study focused on cognitive dysfunction as perceived by patients. Thirdly, the present participants were on several kinds of medications, including antidepressants, which can cause sedation or have anti-cholinergic effects affecting patients’ perceived cognitive ability (Campbell et al., 2009). Fourthly, given that cognitive function is associated with age and education, another limitation was the lack of methodology plan to balance these variables among countries. This weak point might affect some results of the present study, e.g., the difference in PCD severity between Taiwanese and Southeast Asian patients with MDD. Finally, similar to other international studies, patient-reported outcomes (PROs) were administered in English with a potential for nuances to be lost in translation.

The present study describes the clinical profile of MDD patients who also have PCD. Together with previous findings, the present results suggest a need for PCD assessment in adult patients with MDD, especially young patients with a long duration of severe depressive episode. Although statistical correlations between PCD and cognitive performance have yet to be confirmed, PCD assessments provide complementary evidence of cognitive impairment to objective assessments of cognitive performance. Firstly, perceived cognitive ability is more related to real-world situation than neurocognitive tasks (Feinberg et al., 2016). Secondly, neurocognitive impairment is based on the deviation of the healthy persons’ norm, this approach may be inconclusive for those with high cognitive reserve (Jones et al., 2011). Thirdly, a comprehensive assessment of neurocognitive performance needs time, highly trained skills, normative data obtained from various age/ethnic groups, and complex scoring methods (Bakkour et al., 2014). PCD assessments that are quick to administer may therefore be particularly useful in everyday clinical practice. Lastly, more and more studies have shown that PCD is an independent predictor of disability (Kim et al., 2016; Potvin et al., 2016); the impact of PCD on patient’s quality of life is worth exploring.

In conclusion, cognitive complaints are common in patients with MDD. This study reported that attention deficit was the most prominent problem, and mind drifting was the most common symptom. PCD might be more severe in some ethnic groups, for example those living in Southeast Asia. Other predictors of PCD are long duration of depressive episode, disability, younger age, and severe depression.

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Declaration of interest

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References


