Behavioural dysexecutive syndrome after stroke: abridged secondary publication

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KEY MESSAGES

1. Behavioural dysexecutive syndrome (BDES) was common among stroke survivors. Its prevalence at 3 months post-stroke was 18.7%.
2. More severe anxiety symptoms, presence of current depression, and poor cognitive functioning predicted BDES at 3 months post-stroke.
3. No radiological variable was found to be associated with BDES.
4. BDES was related to poor executive function that involves conceptualisation, category fluency, motor programming, sensitivity to interference, inhibitory control, environmental autonomy, and semantic memory.
5. All patients with BDES at the 3-month follow-up were found to be remitted at the 40-month follow-up assessment. No patients from the non-BDES group developed BDES at the 38-month follow-up.
6. All stroke patients showed significant improvement in BDES symptoms at 38 months post-stroke.
7. BDES imposes a psychological burden on stroke patients and should not be neglected. Early identification and multidisciplinary intervention for BDES is essential.

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Introduction

Dysexecutive syndrome (DES) is an impairment of executive functions.[1] Executive functions involve goal setting, planning, action initiation and inhibition, social cognition, theory of mind, insight, and metacognition.[2,3] DES comprises behavioural and cognitive domains,[4] and behavioural and cognitive DES can present separately.[5,6] Behavioural DES (BDES) is a common condition following stroke, with a prevalence of 42.1% to 44.2%.[5,6]

To the best of our knowledge, there are few structural brain imaging studies of BDES or behavioural symptoms in stroke. These studies identified associations between BDES/behavioural symptoms and infarcts in the right hemisphere,[7] anterior capsule,[8] thalamus,[8] insular,[9] and white matter hyperintensities.[10] However, these studies were limited by small sample size,[7-10] biased sampling (from clinical trial samples),[10] inclusion of subjects with current psychiatric diagnoses,[7] lack of standardised assessment of BDES,[7-10] executive function,[7,9,10] or detailed radiological examination.[7,9]

The primary objective of this study was to evaluate the prevalence and predictors of BDES and its clinical, neuropsychological, and magnetic resonance imaging (MRI) correlates in a cohort of Hong Kong stroke survivors. The secondary objective was to determine the clinical course of BDES.

Methods

A total of 4581 patients with first-ever or recurrent acute ischaemic stroke were admitted to the Acute Stroke Unit of Prince of Wales Hospital between September 2013 and September 2017. Of whom, 1447 received MRI, and 384 of whom participated in the initial 3-month assessment.

The inclusion criteria were Chinese ethnicity, Cantonese as the primary language, age of ≥18 years, right-handedness, acute first ischaemic stroke occurring within 7 days before admission, and informed consent given. The exclusion criteria were a history of epilepsy, head injury, hydrocephalus, intracranial tumour, Parkinson disease, dementia, or other non-stroke neurological disease; a history or current diagnosis of depression, bipolar disorder, schizophrenia or alcohol/substance abuse/dependence; aphasia, defined as a score of ≥2 on the best language item of the National Institutes of Health Stroke Scale (NIHSS)[11], or auditory impairment; dementia, defined as a Mini-Mental State Examination (MMSE)[12] score of <20; contraindications for MRI such as a pacemaker in situ, physical frailty or severe claustrophobia; physical frailty; and recurrence of stroke prior to the 3-month assessment. Duplicate subjects and those who failed to complete the assessment were excluded from the analysis. Finally, 369 stroke patients and

237 healthy controls were included.

At 3 months after the onset of the index stroke, a trained research assistant blind to the stroke patients' radiological data administered the Chinese version of the Dysexecutive Questionnaire, which contains 20 items that assess the affective, motivational, behavioural, and cognitive symptoms of BDES using a 5-point Likert scale ranging from 'never' to 'very often', with higher scores indicating more severe BDES. A cutoff of 20 indicates the presence of BDES.

The demographic and clinical data of stroke patients were collected by a research nurse. The same nurse also assessed patients' stroke severity using the NIHSS and degree of disability in daily activities using the modified Rankin Scale within 2 days of admission. The research assistant administered an executive cognitive function battery (the Chinese version of the Frontal Assessment Battery, Colour Trails Test, Arrow Test, and Category Verbal Fluency Test) 3 months after stroke, and the MMSE, Barthel Index, the anxiety subscale of the Hospital Anxiety Depression Scale, 15-item Geriatric Depression Scale at the baseline and follow-up assessments. Healthy controls attended one assessment interview where the same research assistant administered the Dysexecutive Questionnaire, Geriatric Depression Scale, MMSE, and the executive cognitive function battery.

MRI was performed using a 3.0-T MRI system (Philips Achieva 3.0T, X Series, Quasar Dual MRI System) within 7 days of the index admission. An experienced neuroradiologist blind to the subjects' psychiatric diagnoses and BDES status assessed the MRI images. The number, volumes, and locations of acute infarcts and the number of old infarcts were evaluated. The number of lacunae, the number and location of cerebral microbleeds, and the Fazekas white matter hyperintensity score were recorded. Voxel-based lesion-symptom mapping was performed.

To examine the determinants of BDES, we compared demographic and clinical variables between the stroke and healthy control groups and between the BDES and non-BDES groups using the *t*-test, χ^2 test, Fisher's exact test, or Mann-Whitney *U* test, as appropriate. MRI variables in the BDES and non-BDES groups were also compared. Bonferroni adjustment was applied to multiple statistical comparisons of MRI variables. Multivariate logistic regression (forward Wald mode) was performed to determine the predictors of the presence of BDES at 3 months after the index stroke. A paired-sample *t*-test was applied to investigate differences in the stroke patients' clinical characteristics between the first and follow-up assessments. Analyses of covariance adjusted for age and education level were conducted to compare the performance of all groups on the cognitive battery. Two types of voxel-based lesion-symptom mapping analysis were conducted.

Results

The final sample (n=369) consisted of 236 (64%) men. The mean age of the sample was 66.5±9.8 years and the mean years of education was 7.7±4.4 years. The mean NIHSS score on admission was 4.0±3.9.

Of the 369 patients, 69 (18.7%) were diagnosed with BDES. In the multivariate logistic regression, predictors of the presence of BDES at 3 months post-stroke were the anxiety subscale score of the Hospital Anxiety Depression Scale (odds ratio [OR]=1.184, 95% confidence interval [CI]=1.083-1.295, P<0.001), presence of current depression (OR=4.055, 95% CI=2.060-7.983, P<0.001), and MMSE score (OR=0.805, 95% CI=0.705-0.906, P<0.001). After adjusting for multiple testing, no significant differences in any MRI characteristics were observed between the BDES and non-BDES groups. Similarly, the voxel-based lesion-symptom mapping analysis yielded no significant results.

The mean score of the Chinese version of the Frontal Assessment Battery was significantly lower in the BDES group than in the non-BDES group (10.1±2.5 vs 12.8±2.4, P=0.001). The BDES group made significantly more errors and nearly missed responses and required more prompts during the Colour Trails Test, compared with the non-BDES group (errors: 4.9±4.9 vs 0.6±1.7, P<0.001; nearly-missed responses: 6.2±7.3 vs 0.6±2.5, P<0.001; prompts: 7.2±7.4 vs 1.1±2.8, P<0.001). The time required to complete trail 2 in the Colour Trails Test was significantly longer in the BDES group than in the non-BDES group (215.0±80.4 vs 162.5±76.8 seconds, P=0.040).

In the Category Verbal Fluency Test, the BDES group made significantly more intrusion responses (1.4±1.8 vs 0.4±1.0, P<0.001) and fewer total correct responses (33.0±11.3 vs 41.3±10.6, P=0.025) than the non-BDES group. In the Arrow Test, the BDES group had a significantly longer mean response time than the non-BDES group (47.5±27.1 vs 24.6±10.5 seconds, P<0.001). The BDES group also had a significantly higher mean interference score than the non-BDES group (104.6±101.0 vs 24.8±36.2, P<0.001).

Of the 69 patients with BDES at the 3-month follow-up, 44 (63.8%) attended a second follow-up at a mean of 40 (range, 9-52) months after the index stroke. At the second follow-up, no patients presented with BDES, and the mean Dysexecutive Questionnaire score significantly decreased from 25.8±5.7 at 3 months to 2.2±3.2 (P<0.001). The 174 (58%) patients without BDES at the 3-month follow-up attended a second follow-up at a mean of 37.6 (range, 13-55) months after the index stroke. At the second follow-up, no patient had developed BDES,

and the mean Dysexecutive Questionnaire score significantly decreased from 8.1±6.1 at 3 months to 2.0±2.1 (P<0.001). Participants in both groups showed significant decreases in modified Rankin Scale score and Geriatric Depression Scale score and an increase in Barthel Index score (all P<0.001).

Discussion

BDES was identified in 18.7% of the stroke patients 3 months after the index stroke. Predictors of BDES at the 3-month follow up in patients with ischaemic stroke were a higher level of anxiety symptoms, the presence of current depression, and poor global cognitive functioning. BDES correlated with poor executive function (cognitive deficits) related to conceptualisation, category verbal fluency (information generation), motor programming, sensitivity to interference, inhibitory control, environmental autonomy, and semantic memory. Our results showed that BDES does not have a late onset and runs an acute course. Previous studies found that different behavioural and neuropsychiatric symptoms were associated with specific cognitive domains.

The prevalence of BDES in the current study (18.7%) is lower than that in previous studies (42.1%–44.2%).[5,6] The inconsistency may be attributable to the methodologies used. Different inclusion criteria for participants' level of impairment, global cognitive functioning, and the status of the stroke survivors were used, and the assessment time and measurement of BDES were also incompatible.

Our results were consistent with previous findings on mood symptoms[13-16] and impaired global cognitive functioning,[10,17,18] as correlates of individual neuropsychiatric symptoms. The literature associates DES with disruptions of the fronto-subcortical circuits.[8,19,20] However, our study did not find any association between lesion location and BDES.

Our results demonstrated that all stroke patients who presented with BDES at 3 months post-index event had recovered from BDES at 40 months. Furthermore, no delayed onset of BDES was observed at the 38-month follow up. The prevalence of BDES decreased from 18.7% at 3 months to none in the follow-up assessment. Previous longitudinal studies showed recovery of behavioural[7] and neuropsychiatric[21] symptoms in some patients 12 to 15 months after the index stroke. There are mixed findings on the late onset of neuropsychiatric symptoms after stroke, for instance, 17.4% of participants remained symptom-free for 1 year, whereas 10.8% had delayed onset of fatigue at 6-month follow-up.[22]

The main limitation of this study is the potential for selection bias. A relatively small proportion of the original cohort of ischaemic stroke patients was examined, and this may limit the generalisability of our findings. Although the present study investigated the course of BDES over 38 months, the change between the first and second assessment remained unclear. Furthermore, patients with previous stroke were included, and pre-existing infarcts may have contributed to the development of BDES.

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Disclosure

The results of this research have been previously published in:

1. Tang WK, Lau CG, Liang Y, et al. Prevalence and clinical correlates of poststroke behavioral dysexecutive syndrome. J Am Heart Assoc 2019;8:e013448. doi:10.1161/JAHA.119.013448

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