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Prevalence and Clinical Correlates of Poststroke Behavioral Dysexecutive Syndrome

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Background—Behavioral dysexecutive syndrome (BDES) is a common phenomenon following stroke. To date, research has focused mainly on individual behavioral symptoms rather than a more comprehensive characterization of goal-directed behavior in stroke survivors. This cross-sectional study evaluated the prevalence and clinical correlates of BDES in Hong Kong stroke survivors.

Methods and Results—A total of 369 stroke survivors were recruited from a regional hospital at 3 months after their index stroke. Patients' demographic and clinical characteristics were extracted from a comprehensive stroke database. BDES was measured with the Chinese version of the Dysexecutive Questionnaire. Four neurocognitive batteries assessed domains of cognitive executive functions. The prevalence of BDES 3 months poststroke was 18.7%. At that time point, the Hospital Anxiety Depression Scale and Mini-Mental State Examination scores and the presence of depression were significant predictors of BDES in a multivariate logistic regression analysis. These parameters remained significant predictors of the Dysexecutive Questionnaire score in a linear stepwise regression analysis and together accounted for 28.5% of the variance. Current depression was predictive of the Dysexecutive Questionnaire score in patients with BDES, with a variance of 9.7%. Furthermore, compared with the non-BDES group, patients with BDES exhibited poor performance–based executive function in the Chinese version of the Frontal Assessment Battery and color trails, arrow, and category fluency tests.

Conclusions—Symptoms of anxiety, current depression, and global cognitive function may be independent predictors of the presence and severity of BDES 3 months poststroke. Stroke survivors with BDES exhibit poor executive functioning, including goal maintenance and semantic memory. (*J Am Heart Assoc*. 2019;8:e013448. DOI: 10.1161/JAHA.119.013448.)

Key Words: anxiety • behavioral dysexecutive syndrome • depression • executive functioning • stroke

Dysexecutive syndrome comprises a group of impaired behavioral (BDES) and cognitive functions. BDES and cognitive dysexecutive syndrome are mainly higher-order executive functions[1] that govern goal-directed actions and adaptive responses in nonroutine, novel, conflicting, or complex situations and tasks.[2] BDES is a common phenomenon in patients with cerebral diseases such as dementia, Parkinson disease, traumatic brain injury, multiple sclerosis, and stroke.[1]

Stroke survivors with BDES commonly present with hypoactivity-apathy, anosognosia, stereotypies, hypoactivity-distractibility, and impaired social behavior[3] that predict functional disability.[3,4] Patients with BDES also exhibit agitation/aggression, euphoria, disinhibition, and irritability, which occurred at frequencies of 27% to 33% in a cohort of 124 stroke patients 2 months after an index stroke.[5] BDES symptoms are present in 1% to 35% in stroke survivors at 1 month to 2 years after the index stroke.[6-8] In 89 stroke survivors the frequency of individual BDES symptoms 3 months after the index stroke ranged from 3% to 35%,[6] and they occurred in 6% to 11% in 51 stroke survivors within 4 weeks of their index stroke[7] and in 1% to 16% in 77 Chinese stroke survivors with white matter hyperintensities within 7 months poststroke.[8]

BDES frequently occurs after stroke, with prevalence rates ranging from 42.1% to 44.2%.[3,9] However, there have been no

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data published about the clinical correlates of poststroke BDES; such correlates may include premorbid personality, stroke severity, global cognitive impairment, executive dysfunction, psychopathology, and poor physical functioning, among others.[4,6-8] Thus, the primary objective of this study was to determine the prevalence and clinical correlates of BDES in a large cohort of stroke survivors. The secondary objective was to examine the cognitive functioning of stroke survivors with BDES.

Methods

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Participants

This project is a substudy of our Neuropsychiatric Disorder in Stroke Registry. The aim of the registry was to examine the phenomenon and neuroimaging correlates of behavioral problems after stroke. A total of 4581 patients with first-ever or recurrent acute ischemic stroke were admitted to the Acute Stroke Unit of the Prince of Wales Hospital between September 2013 and September 2017; 1447 of them received a magnetic resonance imaging scan. All patients with magnetic resonance imaging scan data were screened for study entry using the following inclusion and exclusion criteria. Subsequently, 384 patients underwent initial assessment 3 months after their index stroke (Figure).

The inclusion criteria were (1) Chinese ethnicity; (2) Cantonese as the primary language spoken; (3) age ≥18 years; (4) well-documented acute ischemic stroke occurring within 7 days before admission; and (5) ability and willingness to provide informed consent. The exclusion criteria

were (1) history of epilepsy, head injury, hydrocephalus, intracranial tumor, Parkinson disease, dementia, or any neurological disease(s) other than stroke; (2) history of depression, bipolar affective disorder, schizophrenia, or alcohol/substance abuse/dependence; (3) aphasia, defined as a score of ≥2 on the best language item of the National Institutes of Health Stroke Scale,[10] or auditory impairment; (4) severe cognitive impairment, defined as an Mini-Mental State Examination (MMSE)[11] score of <20; and (5) physical frailty, defined as a physical barrier due to any medical condition precluding attendance at the research clinic. Patients who failed to complete the assessment were also excluded from the evaluation for BDES, resulting in a final study sample of 369 stroke patients (Figure).

The study protocol was approved by the Clinical Research Ethics Committee of the Chinese University of Hong Kong. Written informed consent was obtained from all participants on the day of assessment, 3 months after their index stroke.

Collection of Demographic and Clinical Data

Participants' demographic and clinical data were collected by a trained research nurse. The same nurse assessed stroke severity using the National Institutes of Health Stroke Scale[10] and the modified Rankin Scale[12] within 2 days of admission. These data were stored in a stroke registry.

Assessment of BDES

The following assessments were made at a research clinic 3 months after the onset of the index stroke. The timing of this assessment was consistent with that of other studies of neurobehavioral disorders related to stroke.[13,14]

A psychiatrist (W.K.T.) administered the Chinese version of the Dysexecutive Questionnaire (DEX),[15] which comprises 20 items that assess the affective, motivational, behavioral, and cognitive symptoms of BDES.[16] All items are scored on a 5-point Likert scale ranging from "never" to "very often"; higher scores indicate more severe BDES. A cutoff score of 20 defined BDES.[16] This scale has been used to measure BDES in stroke patients[17] and is considered to be reliable[16] and valid.[18] The internal consistency coefficient and test-retest reliability of the DEX are 0.93 and 0.95, respectively.[18]

Assessment of Executive Functions

The assessment of executive functions was administered for all participants recruited from April 1, 2015 onward. A trained research assistant administered an executive cognitive function battery comprising 4 tests to 158 participants at 3 months following the onset of the index stroke, of whom 155 completed the tests. The Chinese version of the Frontal

Assessment Battery was applied previously to evaluate executive functioning in Chinese stroke patients.[19] This test contains 6 items on conceptualization, category (animal) fluency, programming, sensitivity to interference, inhibitory control, and environmental autonomy. The scores range from 0 to 18, with higher scores indicating better executive functioning. The Cronbach α, test-retest reliability, and interrater reliability of the Chinese version of the Frontal Assessment Battery are 0.77, 0.89, and 0.85, respectively.[19]

The Color Trails Test (CTT) was used to measure sustained and divided attention in adults.[20] This test comprises 2 tasks: the first (CTT1) requires respondents to connect the circles in an ascending numbered sequence from 1 to 25, and the second (CTT2) requires the respondents to pay attention to the colors pink and yellow while marking the ascending numbered sequence. The test-retest reliability of the CTT1 and CTT2 are 0.64 and 0.79, respectively.[20] Reaction times, number of errors, near-misses, and prompts were recorded and yielded the interference index score ([CTT1-CTT2]/CTT1).

Participants' ability regarding goal maintenance and verbal inhibition was tested with the Arrow Test.[21] Participants were instructed to respond to a printed word (上 [up] or 下 [down]) in either the "go" or "reverse" condition as quickly and accurately as possible. In the "go" condition, participants were required to read the word as printed, whereas in the "reverse" condition they were asked to respond with the opposite of the printed word; for example, if the printed word was "上 (up)," the correct response would be "下 (down)." Three trials in the "go" condition and 1 in the "reverse" condition were conducted. In addition to the response time, the number of uncorrected and self-corrected errors were also recorded. The interference score was calculated as the time difference between the fourth and third trials.

The Category Verbal Fluency Test tested participants' language, semantic memory and executive functions. This test was previously applied to both healthy and demented Chinese elderly in Hong Kong.[22] Participants were given 1 minute to generate as many items as possible in each of 3 categories in the following order: animals, fruits, and vegetables.[22] The numbers of total, correct, preservative, and intrusive responses for each category were then obtained. The ranges of convergent validity and test-retest reliability for the Category Verbal Fluency Test are 0.44 to 0.64 and 0.45 to 0.67, respectively.[22]

Assessment of Global Cognitive Function, Mood Symptoms, and Functioning

The research assistant also administered the following instruments at 3 months following the onset of the index
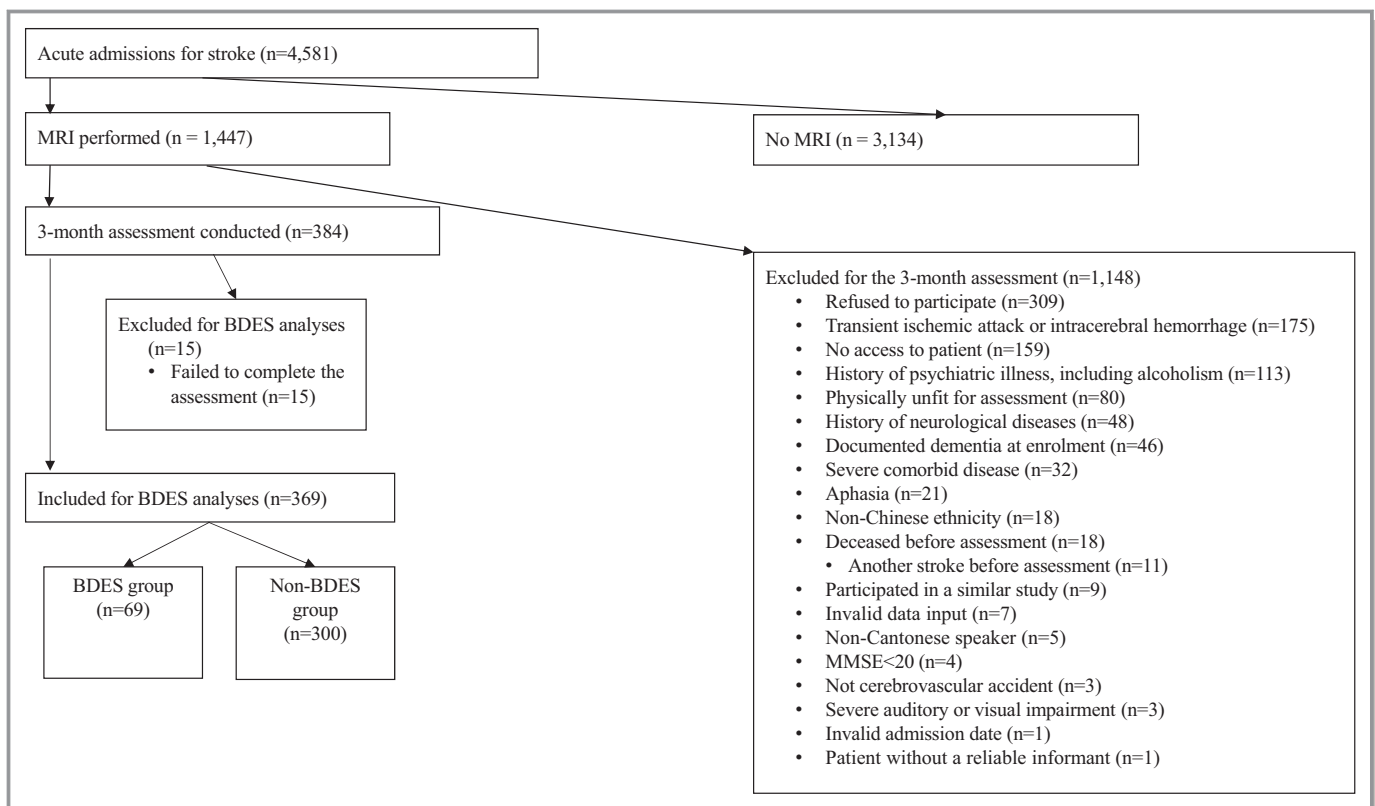
Figure. Recruitment and follow up diagram of the study. BDES indicates behavioral dysexecutive syndrome; MMSE, Mini-Mental State Examination; MRI, magnetic resonance imaging.

stroke. Global cognitive functioning was evaluated with the Cantonese version of the MMSE.[11] This test has Cronbach α and test-retest reliability of 0.86 and 0.78, respectively, and an interrater reliability (intraclass correlation) of 0.99.[11]

The modified version of the Barthel Index (BI)[23] assessed the extent of participants' disability in daily functioning. The BI covers 10 items: personal hygiene, bathing, feeding, toileting, stair climbing, dressing, bowel control, bladder control, ambulation or wheelchair use, and chair-bed transfer. The total scores range from 0 to 20; higher scores indicate more independent level of self-care. The BI has a high level of internal consistency (Cronbach α=0.94).[24]

Anxiety was assessed with the anxiety subscale of the Hospital Anxiety Depression Scale (HADSA).[25] The response to each item was scored on a Likert scale ranging from 0 to 3: 0="not at all"; 1="occasionally"; 2="quite often"; and 3="very often indeed." The response to each item was based on the relative frequency of anxiety symptoms over the past week. This scale has excellent sensitivity and specificity of 80% and 90%, respectively, as well as an overall misclassification rate of 12% and positive and negative predictive values of 67% and 95%, respectively.[25]

The Chinese version of the 15-item Geriatric Depression Scale (GDS)[26] was employed to assess depressive symptoms. The GDS exhibits good psychometric properties, and it has been used to evaluate depressive symptoms in adults.[27] The Cronbach α and test-retest reliability of the GDS were 0.89 and 0.85, respectively.[27] Current depression has been defined as a GDS score of ≥7.[28]

Statistical Analyses

Statistical analyses were performed with SPSS Statistics, Version 24 (IBM Corp, Armonk, NY). The Kolmogorov-Smirnov test was initially applied to test the normality of all variables. Demographic and clinical variables were compared between the BDES and non-BDES groups with the χ^2 test, Student t test, Mann-Whitney U test, or Fisher exact test, as appropriate. Pearson and Spearman correlations were used to examine the correlates of the DEX score. Variables that were identified as significant in the abovementioned univariate analyses were included in multivariate logistic regression and stepwise linear regression analyses to identify the predictors of BDES and the DEX score, respectively. The levels of significance in the univariate and multivariate analyses were set at P values of <0.01 and <0.05, respectively.

Results

The final sample comprised 369 patients with acute ischemic stroke. Patients in the study sample had significantly higher National Institutes of Health Stroke Scale scores than the excluded patients (4.0±3.9 versus 2.8±4.7, P<0.001), but no significant differences in sex, age, and MMSE scores at admission were found between the 2 groups. The study sample had male predominance (64%), a mean age of 66.5±9.8 years, and a mean educational attainment of 7.7±4.4 years. The mean National Institutes of Health Stroke Scale score at admission was 4.0±3.9 (Table 1, Tables S1 and S2, Figures S1 and S2).

Prevalence and Clinical Correlates of BDES Status at 3-Month Follow-Up

The mean DEX score of the entire sample was 11.2±8.8. Sixty-nine (18.7%) of the 369 participants were diagnosed with BDES. There were no significant differences between the BDES and non-BDES groups in terms of age, sex, education level, history of hypertension, hyperlipidemia, diabetes mellitus, stroke, ischemic heart disease, or the severity of stroke at admission (Table 1). The BDES group had significantly higher GDS and HADSA scores. At the 3-month follow-up, a larger proportion of patients were diagnosed with depression in the BDES group than in the non-BDES group (53.6% versus 14.0%). Additionally, BDES patients had significantly lower MMSE and BI scores.

Strong correlations were observed between the HADSA and GDS scores (r=0.538, P<0.001) and the GDS score and current depression (r=0.841, P<0.001). Accordingly, the GDS scores were removed from subsequent regression analyses.

Four demographic and clinical variables (BI, HADSA, MMSE scores, and current depression at 3-month follow-up) were entered into the multivariate logistic regression analysis models (forward Wald mode). These models identified the HADSA score, current depression, and MMSE score as significant predictors of BDES at 3 months after the index stroke (Table 2).

Correlates of the DEX Score at 3-Month Follow-Up

The DEX score correlated positively with current depression and with the HADSA, GDS, and BI scores but negatively with the MMSE score. Borderline significant correlations were found between the DEX score and education, history of hyperlipidemia, and modified Rankin Scale score (Table 3).

The severity of depressive symptoms and current depression correlated positively with the DEX score in the BDES group. The severity of anxiety symptoms at 3 months exhibited a borderline significant correlation with the DEX score.

The results of the multivariate stepwise linear regression model are shown in Table 4. Seven demographic (education

Table 1. Demographic and Clinical Characteristics of BDES and Non-BDES Stroke Patients

	All Stroke Patients (n=369)	BDES Group (n=69)	Non-BDES Group (n=300)	BDES Group Versus Non-BDES Group
	Mean±SD or n (%)	Mean±SD or n (%)	Mean±SD or n (%)	P Value
Age, y*	66.5±9.8	65.7±10.5	66.7±9.6	0.534
Sex, female†	133 (36.0)	33 (47.8)	100 (33.3)	0.024
Education, y‡	7.7±4.4	6.9±3.6	7.9±4.6	0.134
Hypertension†	191 (61.2)	36 (54.5)	155 (63.0)	0.210
Diabetes mellitus†	80 (25.6)	16 (24.2)	64 (26.0)	0.769
Hyperlipidemia†	90 (28.8)	23 (34.8)	67 (27.2)	0.225
Ischemic heart disease§	17 (5.4)	1 (1.5)	16 (6.5)	0.136
History of stroke	28 (9.0)	8 (12.1)	20 (8.1)	0.314
DEX score‡	11.2±8.8	24.9±5.1	8.1±6.0	<0.001
NIHSS total score on admission‡	4.0±3.9	4.5±4.5	3.9±3.7	0.277
NIHSS total score >7 on admission†	33 (8.9)	8 (12.1)	25 (10.0)	0.624
BI score at 3MFU‡	18.7±1.8	17.9±2.1	18.9±1.6	<0.001
mRS score at 3MFU‡	1.2±0.8	1.4±0.8	1.2±0.8	0.040
HADSA score at 3MFU‡	2.0±3.1	4.5±4.4	1.4±2.4	<0.001
GDS score at 3MFU‡	4.0±3.5	6.6±3.7	3.4±3.2	<0.001
Current depression at 3MFU†	79 (21.4)	37 (53.6)	42 (14.0)	<0.001
MMSE score at 3MFU‡	26.8±2.4	25.6±2.4	27.0±2.3	<0.001

3MFU indicates 3-month follow-up; BDES, behavioral dysexecutive syndrome; BI, Barthel Index; DEX, Dysexecutive Scale; GDS, Geriatric Depression Scale; HADSA, Hospital Anxiety Depression Scale (Anxiety subscale); MMSE, Mini-Mental State Examination; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.
*Student t test.
†Pearson chi-squared test.
‡Mann-Whitney U test.
§Fisher exact test.

level) and clinical (history of hyperlipidemia, BI, MMSE, modified Rankin Scale, and HADSA scores, and current depression) variables at the 3-month follow-up were entered into the whole-sample model. Current depression and the MMSE, HADSA, and BI scores were significant predictors of

Table 2. Multivariate Logistic Regression (Forward Wald Mode) of Demographic and Clinical Determinants of BDES at 3-Month Follow-Up (n=369)

	OR (95% CI)	P Value	Nagelkerke R^2
BI score at 3MFU			0.300
HADSA score at 3MFU	1.184 (1.083-1.295)	<0.001	
Current depression at 3MFU	4.055 (2.060-7.983)	<0.001	
MMSE score at 3MFU	0.805 (0.705-0.906)	<0.001	

3MFU indicates 3-month follow up; BDES, behavioral dysexecutive syndrome; BI, Barthel Index; HADSA, Hospital Anxiety Depression Scale (Anxiety subscale); MMSE, Mini-Mental State Examination; OR, odds ratio.

the DEX score, accounting for 28.5% of the variance. The model was a significant predictor of the DEX score [F(3, 274) =37.807, $P<0.001$].

In an analysis of the BDES group, 2 clinical variables (current depression and severity of anxiety symptoms) were added to a stepwise linear regression model for analyzing the BDES group. Current depression was a significant predictor of the DEX score, accounting for 9.7% of the variance [F(1, 57) =7.196, $P=0.010$].

Executive Functions in Patients With BDES at 3-Month Follow-Up

The BDES group had a significantly lower Chinese version of the Frontal Assessment Battery score compared with the non-BDES group. During the CTT, BDES participants had a significantly greater number of errors and near-misses and required more prompts compared with their non-BDES counterparts. The BDES group also needed a significantly longer time to complete CTT2. In the Category Verbal Fluency Test, BDES participants had a significantly greater total

Table 3. Correlations Between Sociodemographic and Clinical Information, and DEX Score at 3-Month Follow-Up

	All Stroke Patients (n=369)		BDES Group (n=69)	
	r	P Value	r	P Value
Demographic characteristics				
Age, y*	−0.028	0.586	<0.001	0.999
Sex, male†	0.044	0.400	−0.029	0.811
Education, y†	−0.126	0.017	0.067	0.588
Clinical characteristics				
Hypertension‡	−0.042	0.464	0.012	0.924
Diabetes mellitus‡	−0.011	0.853	0.135	0.305
Hyperlipidemia‡	0.101	0.087	−0.151	0.249
Ischemic heart disease‡	−0.059	0.321	−0.118	0.370
NIHSS total score on admission‡	0.009	0.883	−0.180	0.168
NIHSS total score of >7 on admission‡	−0.031	0.598	−0.143	0.276
BI score at 3MFU‡	0.270	<0.001	0.080	0.542
mRS score at 3MFU‡	0.113	0.055	−0.023	0.863
HADSA score at 3MFU‡	0.377	<0.001	0.293	0.023
GDS score at 3MFU‡	0.443	<0.001	0.305	0.018
Current depression at 3MFU‡	0.428	<0.001	0.333	0.009
MMSE score at 3MFU‡	−0.336	<0.001	−0.175	0.180

3MFU indicates 3-month follow up; BDES, behavioral dysexecutive syndrome; BI, Barthel Index; DEX, Dysexecutive Scale; GDS, Geriatric Depression Scale; HADSA, Hospital Anxiety Depression Scale (Anxiety subscale); MMSE, Mini-Mental State Examination; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.
*Pearson correlation.
†Spearman correlation.
‡Adjusted for age, sex, and education.

Table 4. Multiple Linear Regression (Stepwise) Analyses

	β	P Value
DEX score in the whole sample at 3-month follow-up (n=369)		
Education, y	…	…
Hyperlipidemia	…	…
mRS score	…	…
BI score at 3MFU	−0.497	0.039
Current depression at 3MFU	6.751	<0.001
MMSE score at 3MFU	−0.940	<0.001
HADSA score at 3MFU	0.553	0.001
Model		
P	<0.001	
R^2 (adjusted)	0.285	
DEX score in the BDES group at 3-month follow-up (n=69)		
Current depression at 3MFU	3.584	0.010
HADSA score at 3MFU	…	…
Model		
P	0.010	
R^2 (adjusted)	0.097	

3MFU indicates 3-month follow up; β, unstandardized β coefficient; BDES, behavioral dysexecutive syndrome; BI, Barthel Index; DEX, Dysexecutive Scale; HADSA, Hospital Anxiety Depression Scale (Anxiety subscale); MMSE, Mini-Mental State Examination; mRS, modified Rankin Scale.

number of intrusions and fewer total correct responses than the non-BDES participants. In the Arrow test, BDES participants had significantly longer response times compared with the non-BDES participants. Furthermore, the interference score was significantly higher in the BDES group than in the non-BDES group (Table 5).

Discussion

Prevalence and Predictors of BDES

In this study, the 18.7% frequency of poststroke BDES is considerably lower than the rates of 42.1% to 44.2% reported in the literature.[3,9] This variation may be due to differences in the demographic and clinical characteristics of the study samples and the instruments used. The discrepancy between the results reported by an earlier study[3] and the present study might be explained by differences in the severity of stroke and the level of global cognitive functioning between the 2 study samples; whereas in the earlier study[3] the severity of stroke was not measured, the current study included only stroke survivors with relatively minor impairment. Another study,[9] which reported the prevalence of BDES at 44.2% in 156 stroke patients, conducted structured interviews with the Behavioral Dysexecutive Syndrome Inventory, whereas the current study administered a validated self-reported inventory to assess BDES. Furthermore, only 24% of patients in the earlier investigation[9] had ischemic stroke, whereas the rest of patients suffered from cerebral hemorrhage, cerebral venous thrombosis, and ruptured aneurysm of the anterior communicating artery.

In this study, current depression, higher number of anxiety symptoms, and poor global cognitive functioning were predictors of poststroke BDES at the 3-month follow up. Poststroke depression also predicted the severity of BDES at 3 months after the index stroke. To the best of our knowledge, no study has reported data on predictors of the presence and severity of poststroke BDES.

In this study 53.6% of patients in the BDES group had current depression. Previous reports have not discussed the

Table 5. Executive Functioning of BDES and Non-BDES Groups at 3-Month Follow-Up

	BDES Group (n=14)	Non-BDES Group (n=141)	BDES Versus Non-BDES
	Mean±SD	Mean±SD	P Value*
CFAB Score	10.1±2.5	12.8±2.4	0.001
Color Trial Test			
Time in CTT1, s	79.0±29.8	77.2±38.3	1.000
Time in CTT2, s	215.0±80.4	162.5±76.8	0.040
Interference index	1.8±0.8	1.6±4.4	1.000
Total time, s	293.9±100.4	239.7±108.9	0.240
Total error	4.9±4.9	0.6±1.7	<0.001
Total near-misses	6.2±7.3	0.6±2.5	<0.001
Total prompts	7.2±7.4	1.1±2.8	<0.001
Category fluency test			
Total correct	33.0±11.3	41.3±10.6	0.025
Total response	35.7±9.7	43.0±10.9	0.068
Total perseveration	1.8±1.5	1.5±1.5	1.000
Total intrusion	1.4±1.8	0.4±1.0	<0.001
Arrow test			
Average time, s	47.5±27.1	24.6±10.5	<0.001
Interference score	104.6±101.0	24.8±36.2	<0.001

BDES indicates behavioral dysexecutive syndrome; CFAB, Chinese version of Frontal Assessment Battery; CTT1, trial 1 in Color Trial Test; CTT2, trial 2 in Color Trial Test.
*Adjusted for age and education level.

prevalence of poststroke depression in patients with BDES after stroke.[5,17] A recent study examined the prevalence of symptoms of depression, anxiety, euphoria, and disinhibition in stroke but did not investigate their possible correlates,[5] and another study assessed BDES but did not evaluate mood symptoms.[17] In a cross-sectional and correlational study of male stroke survivors, more depressive symptoms were found to correlate with more severe behavioral symptoms of impulsiveness and planning, measured with the Barrat Impulsiveness Scale.[29] Studies of dementia[30] and traumatic brain injury[31] suggested that an abnormal level of serotonergic activity may explain the relationship between depression and aggression. Neural structure characteristics in the frontal cortex, hippocampus, and striatum associated with both depression and dysexecutive deficits after traumatic brain injury may account for the robust correlation between depression and DEX.[32]

In contrast to an earlier report[6] that found no correlation between BDES and anxiety symptoms, anxiety symptoms were predictive of BDES in the present study. This inconsistency could be explained by the differences in methodology, particularly the instruments—Neuropsychiatric Inventory

global score and Hamilton Rating Scale for Anxiety versus DEX and HADSA—and the way of collecting information—behavioral symptoms reported by caregivers versus self-reported data.

Anxiety was an independent predictor of poststroke fatigue during the acute phase.[33] Poststroke anxiety at 1 month predicted fatigue at the 6- and 12-month follow-ups.[34] These findings led to a hypothesis that anxiety and fatigue have overlapping pathomechanisms in stroke-related brain damage.[33] Further, anxiety is related to other neuropsychiatric dysexecutive symptoms via enhanced amygdala activation, which is associated with increases in anxiety and impulsive and aggressive behavior in patients with traumatic brain injury.[35]

Impaired global cognitive functioning is known to correlate with BDES,[6] and impaired global cognitive functioning is both a correlate[8,13,36] and a predictor[37] of neuropsychiatric symptoms of stroke, including apathy, impulsivity, and euphoria. Higher caregiver-reported apathy was predictive of impaired global cognitive functioning in 408 stroke patients.[37] Moreover, any neuropsychiatric symptoms were found to be associated with poor global cognitive functioning in 77 stroke patients.[8] Two studies[13,36] compared global cognitive functions between apathetic and nonapathetic stroke patients within 1 and 6 months after the index stroke, and both observed more impaired global cognitive functioning in the former group.

Executive Functioning in BDES

In this study, patients with BDES exhibited poor performance-based executive functioning suggestive of an association of poststroke BDES with impairments in conceptualization, verbal categorical fluency (information generation), motor programming, sensitivity to interference, inhibitory control, environmental autonomy, and semantic memory. This finding agrees partly with some[38-40] but not all[41] cross-sectional studies that focused similarly on specific cognitive domains. Self-reported impulsivity was found to be associated with deficits in cognitive inhibitory control,[39] and stroke patients with neuropsychiatric symptoms exhibited the poorest cognitive performance in terms of attention, executive function, and information processing.[40] Furthermore, neuropsychiatric symptoms predicted poor verbal fluency performance in stroke patients.[38] In the present study poor performance on the CFVT was associated with BDES. Patients with both frontal lesions and BDES exhibited significantly worse performance in dual-task coordination (ie, simultaneous memory span and tracking task performance) but not in verbal fluency, compared with patients with frontal damage without BDES.[41]

Certain behavioral disorders are thought to result from underlying cognitive impairment.[32] Neuropsychiatric

symptoms have been associated with a decline in executive functioning; the behavioral and cognitive aspects of executive functions are correlated.[39,42] Furthermore, hypoactivity within the apathy/abulia domain of BDES was predictive of the cognitive executive indices on the Cognitive Dysexecutive Battery.[43]

This study has limitations, most notably a selection bias and limited generalizability of the findings. First, only a relatively small proportion (369 out of 4581) of the original cohort of ischemic stroke patients participated in the study. Only patients who received a magnetic resonance imaging examination were deemed eligible to participate. Due to a lack of resources, magnetic resonance imaging examinations were conducted in patients with mild/moderate stroke. Second, the final sample had a mild/moderate stroke. Third, around 300 eligible patients refused to participate. The above recruitment bias might have contributed to the low prevalence of BDES and male predominance in the final sample. Furthermore, cognitive tests were not performed among participants recruited before April 2015, and about 60% of the participants refused or were unable to complete the cognitive batteries. Another limitation was that ≈20% of the participants had a history of previous stroke, the effects of which may have also contributed to the development of BDES.

Conclusions

BDES was common in this cohort of stroke survivors at 3 months after the index stroke and could be predicted by anxiety symptoms, current depression, and poor cognitive functioning. BDES correlated with poor executive functioning in the areas of conceptualization, category fluency, and motor programming.

The psychological burden of BDES on stroke patients should not be underestimated. The early identification of this condition is crucial, as behavioral changes can increase tension between patients and their caregivers and can affect the prognosis of stroke. Further longitudinal studies are warranted to explore the course of BDES and its effects on cognitive functioning and stroke patients' quality of life.

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Disclosures

None.

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SUPPLEMENTAL MATERIAL

Table S1. Testing for normality in BDES group.

		Age	Years of education	DEX score	NIHSS total score on admission	BI Score at 3MFU	mRS score at 3MFU	HADSA score at 3MFU	GDS score at 3MFU	MMSE score at 3MFU
N		69	67	69	66	69	69	69	69	69
Normal Parameters[*],[†]	Mean	65.74	6.836	25.0580	4.50	17.91	1.36	4.48	6.58	25.57
	Std. Deviation	10.511	3.5658	5.06105	4.466	2.140	.804	4.371	3.656	2.422
Most Extreme Differences	Absolute	.084	.183	.180	.186	.270	.355	.224	.129	.158
	Positive	.084	.160	.180	.183	.165	.355	.224	.122	.085
	Negative	-.081	-.183	-.159	-.186	-.270	-.254	-.153	-.129	-.158
Test Statistic		.084	.183	.180	.186	.270	.355	.224	.129	.158
Asymp. Sig. (2-tailed)		.200[‡],[§]	.000[‡]	.000[‡]	.000[‡]	.000[‡]	.000[‡]	.000[‡]	.006[‡]	.000[‡]

DEX=Dysexecutive Scale; NIHSS=National Institutes of Health Stroke Scale; BI=Barthel Index; mRS=modified Rankin Scale; HADSA=Hospital Anxiety Depression Scale (Anxiety subscale); GDS=Geriatric Depression Scale; MMSE=Mini-Mental State Examination; 3MFU=3-month follow up.

[*]. Test distribution is Normal.
[†]. Calculated from data.
[‡]. Lilliefors Significance Correction.

Table S2. Testing for normality in non-BDES group.

		Age	Years of education	DEX score	NIHSS total score on admission	BI Score at 3MFU	mRS score at 3MFU	HADSA score at 3MFU	GDS score at 3MFU	MMSE score at 3MFU
N		302	293	302	250	302	301	299	302	302
Normal Parameters[*,†]	Mean	66.65	7.945	8.1093	3.86	18.88	1.15	1.40	3.42	27.03
	Std. Deviation	9.608	4.5875	5.99595	3.720	1.645	.753	2.456	3.194	2.341
Most Extreme Differences	Absolute	.047	.125	.108	.149	.248	.349	.291	.160	.171
	Positive	.035	.125	.108	.144	.248	.349	.291	.160	.102
	Negative	-.047	-.087	-.088	-.149	-.224	-.278	-.285	-.142	-.171
Test Statistic		.047	.125	.108	.149	.248	.349	.291	.160	.171
Asymp. Sig. (2-tailed)		.200[‡,§]	.000[‡]	.000[‡]	.000[‡]	.000[‡]	.000[‡]	.000[‡]	.006[‡]	.000[‡]

DEX=Dysexecutive Scale; NIHSS=National Institutes of Health Stroke Scale; BI=Barthel Index; mRS=modified Rankin Scale; HADSA=Hospital Anxiety Depression Scale (Anxiety subscale); GDS=Geriatric Depression Scale; MMSE=Mini-Mental State Examination; 3MFU=3-month follow up.

*. Test distribution is Normal.
†. Calculated from data.
‡. Lilliefors Significance Correction.
§. This is a lower bound of the true significance.

Figure S1. Visualizing results in BDES group.

DEX=Dysexecutive Scale; NIHSS=National Institutes of Health Stroke Scale; BI=Barthel Index; mRS=modified Rankin Scale; HADSA=Hospital Anxiety Depression Scale (Anxiety subscale); GDS=Geriatric Depression Scale; MMSE=Mini-Mental State Examination; 3MFU=3-month follow up.
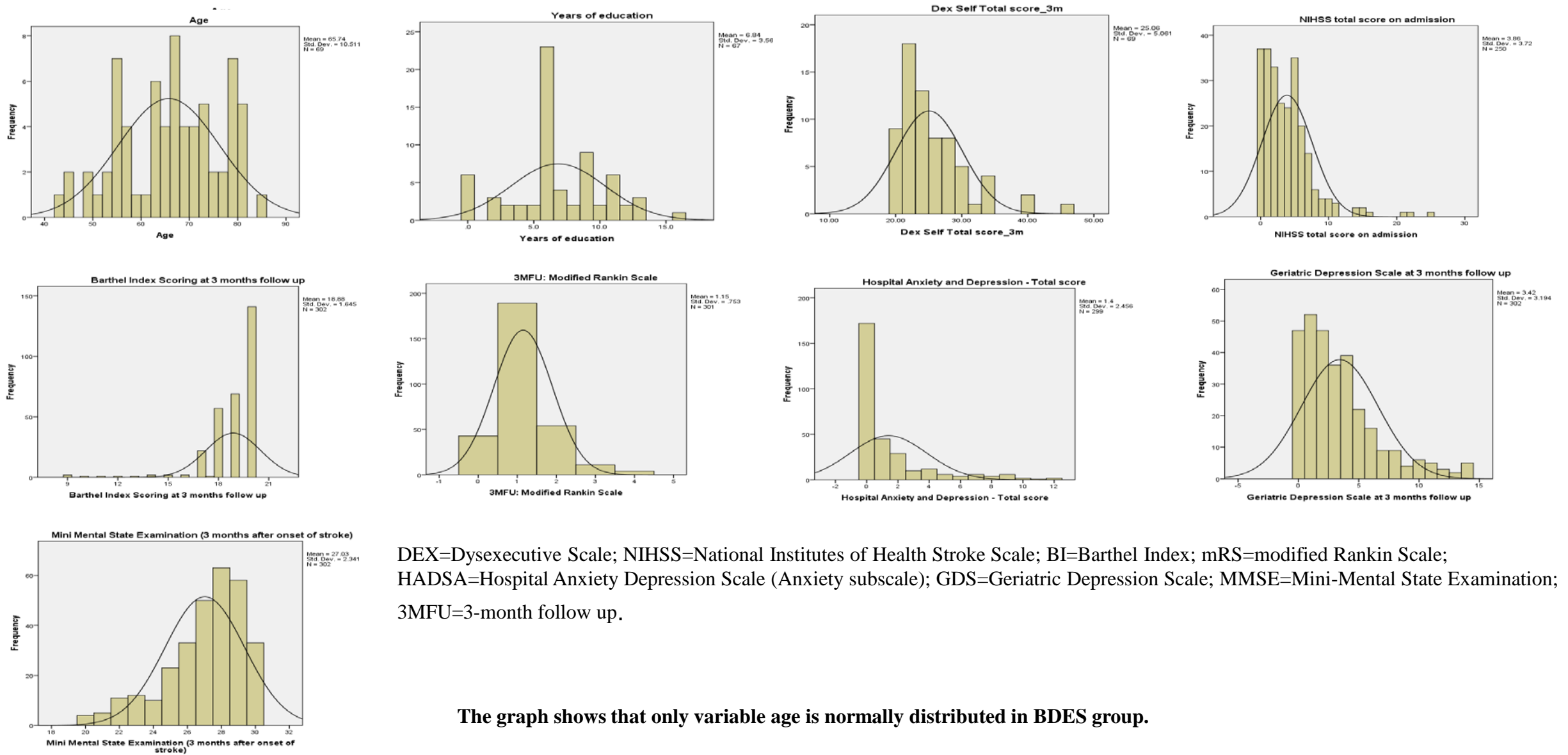
The graph shows that only variable age is normally distributed in BDES group.

Figure S2. Visualizing results in non-BDES group.

DEX=Dysexecutive Scale; NIHSS=National Institutes of Health Stroke Scale; BI=Barthel Index; mRS=modified Rankin Scale; HADSA=Hospital Anxiety Depression Scale (Anxiety subscale); GDS=Geriatric Depression Scale; MMSE=Mini-Mental State Examination; 3MFU=3-month follow up.

The graph shows that only variable age is normally distributed in BDES group.