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ORIGINAL COMMUNICATION

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Delirium in the first days of acute stroke

Abstract *Background and Purpose* Delirium is an acute, transient disorder of cognition and consciousness with fluctuating intensity. The aim of this study was to investigate the presence and the risk factors for delirium in the first days after stroke onset. *Patients and methods* We assessed delirium prospectively in a sample of 218 consecutive patients (mean age 57 years) with an acute (≤ 4 days) stroke (28 subarachnoid haemorrhages, 48 intracerebral haemorrhages, 142 cerebral infarcts) and in a control group of 50 patients with acute coronary syndromes with the Delirium Rating Scale (DRS) (cut-off score ≥ 10). *Results* 29 (13 %) acute stroke patients (mean DRS score = 13.2, SD = 2.3) and only one (2 %) acute coronary patient had delirium ($\chi^2 = 5.2$, $p = 0.02$). In nine patients delirium was secondary to stroke without any additional cause, in 10 patients there were also medical complications and in the remaining 10 there were multiple potential causes for delirium. Delirium was more frequent after hemispherical than after brainstem/cerebellum strokes ($p = 0.02$). No other statistically significant associations with stroke locations were found. Medical complications (OR = 4.3; 95 % CI = 1.8 to 10.2), neglect (OR = 3.5; 95 % CI = 1.3 to 9.2), intracerebral haemorrhage (OR = 3.1; 95 % CI = 1.3 to 7.5) and age ≥ 65 (OR = 2.4; 95 % CI = 1.0 to 5.8) were independent factors to the development of delirium in stroke patients. *Conclusion* Delirium was more frequent in stroke than in coronary acute patients. Among stroke patients, delirium was most frequent in older patients, in those with neglect, with medical complications and with intracerebral haemorrhages. These findings indicated that delirium in acute stroke patients 1) is not a non-specific consequence of acute disease and hospitalisation and 2) is secondary to hemisphere brain damage and to metabolic disturbances due to medical complications.

Key words delirium · stroke, acute · haemorrhagic stroke · complications · stroke outcome

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Abbreviations

DRS	Delirium Rating Scale
GCS	Glasgow Coma Scale
NIHSS	Neurological Institute Health Stroke Scale
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition, Text Reviewed
ICH	Intracerebral Haemorrhage
INF	Cerebral Infarct
SAH	Subarachnoid Haemorrhage
SPSS	Statistical Package for Social Sciences
χ^2	Chi-square
OR	Odds Ratios
95 % CI	95 % Confidence Interval
U	Mann-Whitney test
MCA	Middle Cerebral Artery
PCA	Posterior Cerebral Artery

Introduction

Delirium is an acute, transient disorder of cognition and consciousness with fluctuating intensity [1]. Delirium can be a complication of hospitalisation [2] in susceptible patients. It is a marker of risk for dementia and death, even in older people without prior cognitive or functional impairment [3]. Four systematic studies of delirium in acute stroke patients have provided conflicting results concerning the frequency and determinants of delirium [4–7]. None of these studies compared stroke patients with subjects with other acute illnesses, to differentiate between the role of brain lesion, acute illness and hospitalisation in precipitating delirium.

The aim of the present study was to describe the presence of delirium in acute stroke patients, to compare it with acute coronary patients and to analyse the relation between delirium and 1) predisposing/precipitating conditions, 2) clinical/imaging data and 3) functional outcome at discharge.

Patients and methods

Patients

From April 2000 to June 2001 we investigated prospectively the presence, severity and correlates of delirium in consecutive acute stroke patients admitted to a 12-bed Stroke Unit located in the neurology department of a University Hospital. This stroke unit has a catchment area of about 700,000 persons and admits acute (< 24 hours) stroke patients except if: 1) a bed is unavailable, 2) age is > 85 years, 3) there was previous dependency 3) there was a co-morbid diagnosis of cancer, chronic renal failure on dialysis, HIV infection, head trauma or bone fracture.

The inclusion criteria in this study were: 1) an admission diagnosis of cerebral infarct, intracerebral haemorrhage or subarachnoid haemorrhage and 2) psychiatric/psychological assessment performed within 4 days after stroke onset. Alertness was assessed with the Glasgow Coma Scale (GCS). To avoid the confounding effect of aphasia, only the "Ocular" (scored 1 to 4) and "Motor" (scored 1 to 6) responses were added to obtain the GCS score. Patients with a GCS score < 5 on the day of the psychiatric/psychological examination were excluded.

The control group consisted of consecutive acute coronary patients hospitalised in the Coronary Intensive Care Unit of the same hospital with a diagnosis of acute myocardial infarction or unstable angina. Psychiatric/psychological assessment was also performed within 4 days after onset. Concomitant stroke was an exclusion criterion. The remaining exclusion criteria for coronary patients were the same as for stroke patients.

Methods

Stroke patients were examined whenever possible on the 1st day in the stroke unit by a trained psychologist. A psychiatrist further observed the same patient if a psychiatric disorder was presumed. Previous dementia/cognitive decline and mood disorder, and the acute neuropsychiatric disturbances were assessed during a semistructured interview. The psychologist rated the presence and the severity of the symptoms of delirium according to the Delirium Rating Scale (DRS) [8]. The DRS is a 10-item observational scale that rates "Temporal Onset of Symptoms" (item 1), "Perceptual Disturbances" (item 2), "Hallucinations" (item 3), "Delusions" (item 4), "Psychomotor Behaviour" (item 5), "Cognitive Status During Formal Testing" (item 6), "Physical Disorder" (item 7), "Sleep-wake Cycle Disturbance" (item 8), "Lability of Mood" (item 9) and "Variability of Symptoms" (item 10). Patients were diagnosed as having delirium if they scored ≥ 10 [4] on the DRS and fulfilled the Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition, Text Reviewed (DSM-IV) [1] criteria for delirium. Scoring items 2, 3 and 4 of DRS may require verbal responses and an awake patient. Therefore, patients who had a severe communication disturbance, defined as a score ≥ 2 in the Neurological Institute Health Stroke Scale (NIHSS) item "Best Language" or "Dysarthria", and patients with a GCS score between 5 and 9, were scored zero on these items, unless perceptual disturbance, hallucinations or delusions were reported. The hyperactive variant of delirium was considered if the patient showed "mild restlessness" or "moderate or severe agitation" on item 5 of DRS. The hypoactive variant was diagnosed if on the same item of the DRS he had "a significant withdrawal from the environment".

The following pre-stroke predisposing conditions for delirium [4, 6, 7, 9] were considered: 1) dementia/cognitive decline, defined as a previous medical diagnosis of dementia or of mild cognitive impairment and a history of memory and another cognitive impairment with functional impairment in daily living activities, confirmed by a proxy, 2) alcohol abuse, defined as at least 5 drinks daily, 3) diabetes mellitus, 4) previous mood disorder [10]. Previous mood disorder was diagnosed if the patient had at least once in his lifetime been treated for a mood disorder, has been either prescribed specific medication for these conditions, or used it for more than a month. Thirteen patients were not assessable for previous mood disorder. Medical complications were recorded daily, from admission to the day of interview. They were defined following the methodology of a previous work [11]. Laboratorial values outside the normal range were used as the criteria for electrolyte and other metabolic complications. The cut-off values for uraemia, hyperglycaemia and hypoglycaemia were 35.7, 16.6 and 2.8 mmol/L respectively [4].

We assessed functional outcome at discharge with the Modified Rankin Scale [12, 13]. An unfavourable outcome was defined as a modified Rankin grade ≥ 3 (death or dependency).

Stroke type (subarachnoid haemorrhage (SAH), intracerebral haemorrhage (ICH) and cerebral infarct (INF)) and location [14] were defined based on clinical data and on acute CT/MRI and on a repeated CT if performed. If CT/MRI failed to show an acute lesion, or showed only a silent lesion or an old symptomatic lesion, location was derived from clinical data and grouped as: 1) brainstem/cerebellum, hemispheric or both and 2) left or right hemispheric or both (Fig. 1).

The presence and severity of delirium in the control group was assessed as previously described for stroke patients, using the DRS and the DSM-IV criteria for delirium.

Statistics

Data were analysed in the SPSS version 10. Chi-square (χ^2) (Yates correction when necessary) or Fisher's exact test, odds ratios (OR) and 95 % confidence interval (95 % CI) were used to test bivariate associations between the presence of delirium and its type (hypoactive or hyperactive), age (< 65 or ≥65 years), gender and educational level (0–9 or ≥10 years of school, according with the minimal number of mandatory years of schooling in Portugal), clinical symptoms and signs (neglect, aphasia, hemiparesis), predisposing and precipitating conditions (previous stroke, dementia/cognitive decline, previous mood disorder, alcohol abuse, diabetes, medical complications) for delirium, type (INF, ICH, SAH) and location of stroke (brainstem-cerebellum or hemispheric; hemispheric, left or right; hemispheric, deep or superficial; superficial, anterior or posterior; deep, lacune, striatocapsular or thalamic infarcts) and modified Rankin grade at discharge (0–2 or ≥3). The Mann-Whitney test (U) was used to measure differences in DRS scores between two conditions of a categori-

cal variable. For multivariate analysis we used backward stepwise logistic regression, entering all the variables with a $p < 0.15$ on bivariate analysis.

A p-value ≤ 0.05 was considered statistically significant.

Results

Presence and severity of delirium in stroke patients (Table 1) and controls

From 231 consecutive acute admitted stroke patients, 220 complied with the study inclusion and exclusion criteria. In two cases, the assessment could not be completed. Included and excluded patients had similar age (≥65 years: 31 %/15 %; 95 % CI = –12 % to 2 %; $\chi^2 = 1.45$, $p = 0.23$, $t = 1.49$, $p = 0.14$) and gender (Male: 60 %/39 %; 95 % CI = –9 to 4 %; $\chi^2 = 2.26$, $p = 0.13$). We studied 218 patients, with a mean age of 57.3years (SD = 13, range 24 to 86) and a median of 4 years of education (22 % ≥10 years of school). Thirty-three exhibited a moderate/severe communication disturbance on NIHSS and 12 had a GCS between 5 and 9. The distribution by stroke type and location is depicted in Fig. 1. The median of the DRS of the whole stroke sample was 4 (mean DRS score = 4.9, SD = 4.0). The frequency of predisposing and precipitating conditions for delirium is shown in Table 1. Forty-seven patients (22 %) had a medical complication during their first days of hospitalisation, predominantly infections (n = 26).

Twenty-nine (13.3 %) of the stroke patients had delirium with a DRS mean score of 13.2 (SD = 2.3, range 10 to 19) (Table 2).

We assessed delirium in 50 acute coronary patients. Thirty-eight (76 %) were men and 12 were women with a mean age of 59.1 years (60 % were less than 65 years old) and a median of 4 years of education (35 % ≥10 years of school). Six (12 %) patients had medical complications. Thirteen (26 %) patients had previous mood disorder, 4 (8 %) patients had a history of dementia/cognitive decline, 6 (12 %) had alcohol abuse and 14 (28 %) had diabetes.

Only one acute coronary patient had delirium (DRS score = 14). Delirium was more frequent ($\chi^2 = 5.23$, $p = 0.02$; OR = 7.5, 95 % CI = 56.6 to 1) and severe ($U = 4084$, $p = 0.005$, mean DRS difference = 1.76, 95 % CI = 2.6 to 0.89) in stroke than in acute coronary patients.

Some of the baseline variables were not similarly distributed in stroke and in coronary patients. Acute coronary patients were more often males ($\chi^2 = 4.65$, $p = 0.03$), had a higher educational level ($t = 2.06$, $p = 0.04$) and a lower frequency of alcohol abuse ($\chi^2 = 12.10$, $p = 0.001$) than stroke patients. There was no difference in the proportions of patients with medical complications between the two groups ($\chi^2 = 2.05$, $p = 0.15$). We performed a backward stepwise logistic regression with: delirium as the dependent variable and stroke/coronary, medical complications, dementia/cognitive decline, age (< 65 or ≥65 years), alcohol abuse, diabetes and educational level (0–9 or ≥10 years of school) as predictors. The best regression logistic model retained medical complications (OR = 5.3; 95 % CI = 2.3 to 12.0), stroke (OR = 5.6; 95 % CI = 0.7 to 43.5) and low education (OR = 3.5; 95 % = 0.8 to 15.7) as explanatory variables for delirium (Nagelkerke $R^2 = 0.20$).

Delirium in stroke patients: influence of stroke type, location, predisposing and precipitant conditions

Delirium was most frequent and severe after intracerebral haemorrhage and in patients with hemispheric strokes. Increasing age, GCS ≤ 9 points and neglect were also associated with a higher frequency and severity of Delirium. DRS mean score was higher in patients with lower education, with previous dementia/cognitive decline, with aphasia and with hemiparesis (Table 1). Delirium was most frequent and DRS scores were higher in patients with medical complications. Overall in nine patients delirium was secondary to stroke without any additional cause, in 10 patients there were also medical complications and in the remaining 10 there were multiple potential causes for delirium (stroke; medical complications, diabetes, alcohol abuse and previous cognitive impairment) (Table 2).

Delirium was more frequent after right (16 %) than left hemispherical (8 %) infarcts, but the difference of proportions (8 %; 95 % CI = –5 % to 23 %) did not reach the significance level (Fig. 1, Table 1). Only one patient with a lacunar infarct developed delirium (Table 2: patient n° 21). The most common lesions in delirious patients were deep haematomas and large right middle cerebral artery (MCA) infarcts. A few patients had lesions located in other sites (caudate, thalamus) and territories (posterior cerebral artery – PCA). Table 3 shows that although lesions in such anatomical sites were associated with increased odds of delirium, there were many "negative" cases (i. e. cases with similar site damage and no delirium) and the confidence intervals were wide, owing to the small number of subjects with lesions in each location.

Backward stepwise logistic regression analysis was performed entering all variables with $p < 0.15$ on bivariate analysis (Table 1). The final model (Nagelkerke $R^2 = 0.26$) retained medical complications (OR = 4.3; 95 % CI = 1.8 to 10.2), neglect (OR = 3.5; 95 % CI = 1.3 to 9.2), intracerebral haemorrhage (OR = 3.1; 95 % CI = 1.3 to 7.5) and age ≥65 (OR = 2.4; 95 % CI = 1.0 to 5.8) as independent risk factors for delirium. This model had a 50 % sensitivity value and a 97 % specificity.

Table 1 Presence of delirium, DRS scores and types of delirium

Variables	n	Delirium n = 29	No delirium n = 189	p (Chi-square)	OR (95 % CI) (Chi-Square)	DRS (median)	p (U)	Hyperactivity n = 14	Hypoactivity n = 15	p (Fisher's test)
Demographic										
Gender Male	130	17	113	0.90	0.95 (0.4 to 2.1)	4.0	0.66	6	11	0.14
Age < 65	150	15	135	**0.03**	0.4 (0.2 to 0.9)	3.0	**0.02**	6	9	0.47
Educational Level 0–9	164	24	140	0.06	3.9 (0.9 to 17)	2.0	**0.0001**	13	11	1.0
Assessment Day										
1	56	5	51			2.0		4	1	
2	66	8	58			2.0		4	4	
3	50	8	42	0.48		2.0	0.84*	2	6	0.26**
4	46	8	38			2.0		4	4	
Clinical signals and symptoms										
Neglect	33	11	22	**0.0001**	4.6 (1.9 to 11.1)	7.0	**0.002**	5	6	1.0
Aphasia	44	8	36	0.29	1.6 (1.7 to 3.9)	4.0	**0.0001**	3	5	0.68
Hemiparesis	154	24	134	0.51	2 (0.7 to 5.4)	2.0	**0.03**	9	13	0.22
GCS										
5–9	12	6	6			8.0		2	4	
10	206	23	183	**0.0001**	8 (2.4 to 26.7)	2.0	**0.0001**	12	11	0.65
Predisposing and precipitating conditions										
Previous Stroke	40	5	35	0.86	0.9 (0.33 to 2.6)	4.0	0.94	2	3	1.0
Dementia/Cognitive Decline	7	2	5	0.94	2.7 (0.5 to 14.8)	4.0	**0.02**	1	0	1.0
Alcohol Abuse	83	7	76	0.24	0.5 (0.2 to 1.2)	2.0	0.32	2	5	0.39
Diabetes Mellitus	41	6	35	0.94	1.1 (0.4 to 3.0)	2.0	0.75	3	3	1.0
Previous Mood Disorder	40	1	39	0.09	0.1 (0.0 to 1.0)	2.0	0.48	1	0	1.0
Medical Complications	47	16	31	**0.0001**	6.3 (2.7 to 14.3)	4.0	**0.0001**	6	10	0.27
Stroke type										
Subarachnoid Haemorrhage	28	3	25			3.5		3	0	
Intracerebral Haemorrhage	48	13	35	**0.006**		5.5	**0.0001***	4	9	0.08**
Cerebral Infarct	142	13	129			3.0		7	6	
Stroke Location										
Brainstem-Cerebellum	51	2	49			1.0		0	2	
Hemispherical	136	24	112	**0.02**	0.2 (0.0 to 0.8)	2.0	**0.001**	11	13	0.49
Hemispherical										
left	71	11	60			2.0		6	5	
right	63	13	50	0.74	0.7 (0.3 to 1.7)	2.5	0.22	5	8	0.68
Hemispherical										
deep	53	11	42			2.0		6	5	
superficial	48	11	37	0.79	0.9 (0.3 to 2.3)	3.0	0.33	3	8	0.39
Superficial										
anterior	24	6	18			3.5		1	5	
posterior	24	5	19	0.73	0.8 (0.2 to 3.0)	2.0	0.50	2	3	0.55
Deep										
Lacune	10	1	9			2.0		0	1	
Striatocapsular	33	8	25	0.61		2.0	0.61*	5	3	0.39**
Thalamic	16	3	13			2.5		2	1	

* Kruskal-Wallis; ** Yates Correction

Table 2 Demographic and clinical data of delirious patients (N = 29)

N	Age	Gender	DRS	Delirium Type	Stroke type	Left/ Right	CT-Lesion	Neglect	Aphasia	Hemiparesis	GCS (A, B)	Mood Disorder	Previous Dementia	Alcohol Abuse	Diabetes	Medical Complications	Modified Rankin Grade
1	83	Female	14	Hyperactive	INF	Right	MCA total	1	0	1	10	0	0	0	1	GI bleeding	3
2	44	Female	18	Hyperactive	INF	Right	Occipital	1	0	1	10	0	0	0	1	Seizure	3
3	71	Male	19	Hyperactive	ICH	Right	Capsulolenticular	1	0	1	9	0	0	1	0	0	5
4	62	Male	11	Hypoactive	ICH	Right	Capsulolenticular	1	0	1	10	0	0	1	0	Respiratory infection, fever	4
5	84	Male	13	Hyperactive	INF	Left	No lesion	0	0	1	10	0	1	0	0	Uremia	4
6	53	Female	15	Hypoactive	ICH	Left	Frontal	0	1	0	9	0	Down's syndrome	0	0	Respiratory infection	6
7	57	Female	13	Hypoactive	ICH	Right	Capsulolenticular	1	0	1	10	0	0	0	1	0	4
8	51	Female	16	Hyperactive	ICH	Left	Thalamic-capsulolenticular	0	1	1	10	0	0	0	0	Uremia	4
9	63	Male	15	Hypoactive	ICH	Left	Capsulolenticular	0	1	1	10	0	0	1	0	Respiratory infection, alcohol withdrawal, GI bleeding	4
10	66	Female	13	Hyperactive	ICH	Left	Capsulolenticular	0	1	1	7	1	0	0	0	Respiratory infection	6
11	63	Male	14	Hypoactive	INF	Right	MCA total	1	0	1	9	0	0	0	0	Fever, uremia	5
12	59	Male	10	Hypoactive	INF	Right	Fronto-Temporo-Parietal	1	0	1	10	0	0	0	0	0	4
13	60	Male	12	Hyperactive	INF	Left	Occipital; Thalamus	0	0	1	10	0	0	0	0	0	3
14	72	Male	11	Hypoactive	ICH	Left	Temporal	0	1	1	10	0	0	1	1	0	2
15	68	Male	12	Hyperactive	ICH	Right	Capsulolenticular	1	0	1	10	0	0	1	1	Respiratory infection	5
16	33	Female	12	Hypoactive	ICH	Left	Frontal	0	1	1	10	0	0	0	0	Seizure	3
17	69	Male	18	Hyperactive	INF	Right	Caudate	0	0	1	10	0	0	0	0	0	2
18	71	Female	14	Hyperactive	INF	Left	No lesion	0	1	0	10	0	0	0	0	0	2
19	77	Female	11	Hypoactive	INF	Right	MCA cortical	1	0	1	10	0	0	0	0	0	4
20	79	Male	13	Hypoactive	ICH	Right	Thalamus	0	0	1	9	0	0	0	0	Fever, hypoxemia	5
21	76	Male	12	Hypoactive	INF	Right	White Matter	1	0	1	10	0	0	0	0	Fever	1
22	67	Male	12	Hypoactive	INF	Bilateral	Cerebellum	0	0	1	10	0	0	0	0	Respiratory infection	4
23	50	Male	12	Hyperactive	SAH			0	0	0	10	0	0	0	0	0	0
24	53	Female	17	Hypoactive	ICH	Left	Temporo-Parieto- Occipital	0	1	1	9	0	0	0	1	Hyponatremia	3
25	40	Female	12	Hyperactive	INF	Left	Striatocapsular	1	0	1	10	0	0	0	0	0	3
26	65	Female	15	Hyperactive	SAH (ACA aneurysm)			0	0	0	10	0	0	0	0	0	2
27	80	Male	10	Hypoactive	INF	Right	Cerebellum	0	0	1	10	0	0	1	0	Asthma	3
28	54	Female	11	Hyperactive	SAH (AComA aneurysm)			0	0	0	10	0	0	0	0	0	3
29	58	Male	12	Hypoactive	ICH	Right	Temporal	0	0	1	10	0	0	1	0	0	1

0 Absence; *1* Presence; *MCA* Middle Cerebral Artery; *GI* Gastro intestinal

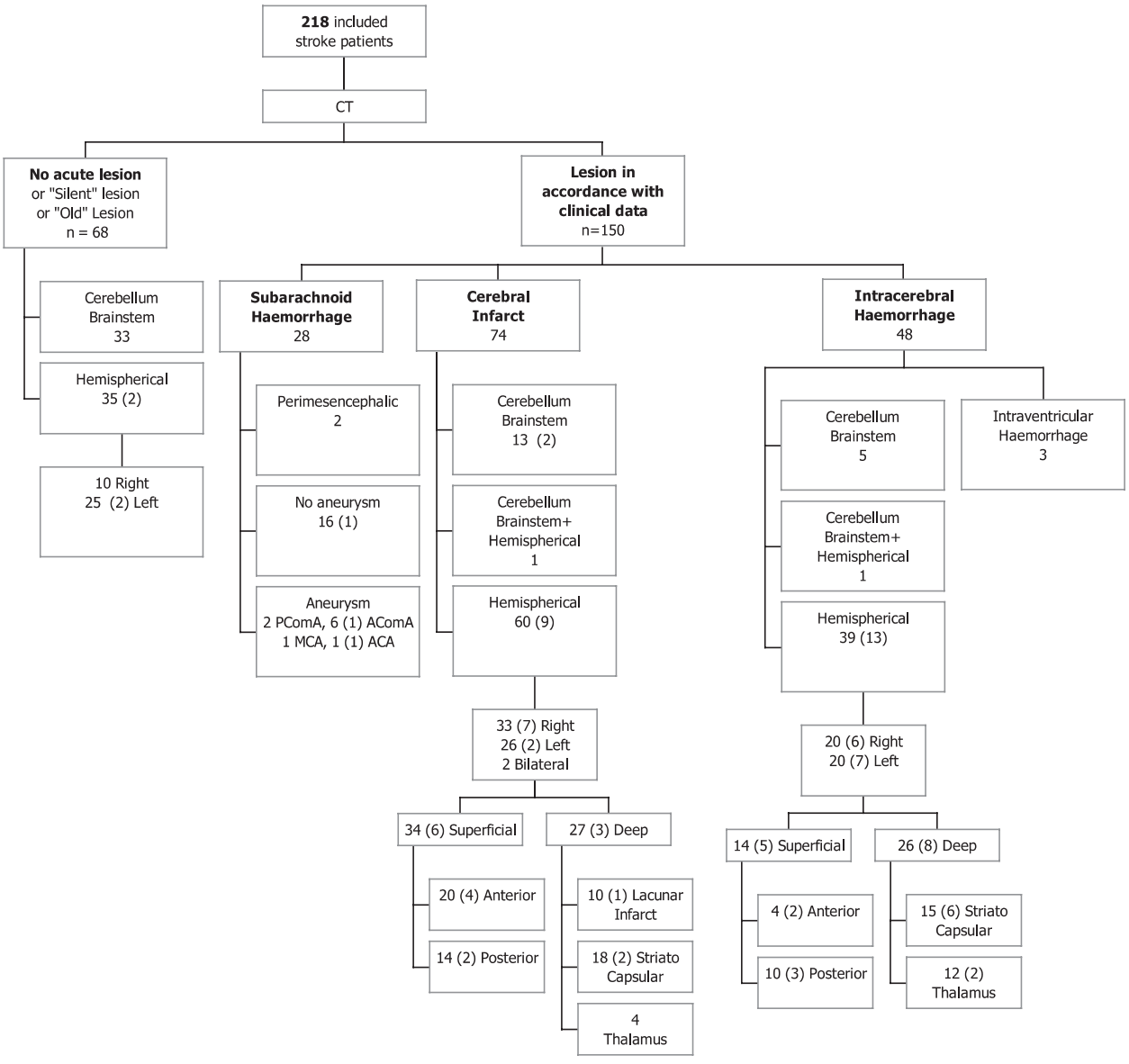

Fig. 1 Clinical and CT/MR features
(n) Number of delirious patients

Table 3 Focal forms of delirium

	n	Delirium	OR	95% CI
MCA right infarct	16	4	2.4	0.7 to 7.9
PCA infarct	7	2	2.7	0.5 to 14.8
Caudate infarct	2	1	6.7	0.4 to 110.4
Thalamic haemorrhage	12	2	1.3	0.3 to 6.4

Delirium profile (Fig. 2) and hyper/hypoactive subtypes (Tables 1 and 2)

A consistent profile on the individual items of the DRS was found in the 29 delirious patients. DRS items "Cognitive Status", "Psychomotor Behaviour", "Sleep-wake Cycle Disturbance" and "Variability of Symptoms" were frequently disturbed, while "Liability of Mood", "Perceptual Disturbances", "Hallucinations" and "Delusions" were infrequently scored. High scores on items "Temporal Onset of Symptoms" and "Physical Disorder" were related to the acute onset of delirium and its relation with a physical disorder.

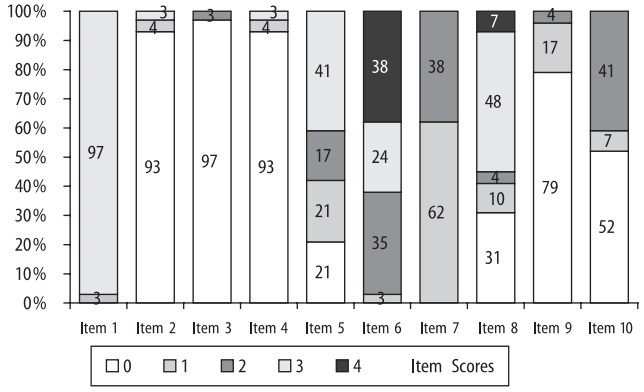

Fig. 2 Distribution of scores (in %) in each item of DRS, for delirious patients (N = 29) (**DRS** *Item 1:* Temporal Onset of Symptoms; *Item 2:* Perceptual Disturbances; *Item 3:* Hallucinations; *Item 4:* Delusions; *Item 5:* Psychomotor Behaviour; *Item 6:* Cognitive Status During Formal Testing; *Item 7:* Physical Disorder; *Item 8:* Sleep-wake Cycle Disturbance; *Item 9:* Lability of Mood; *Item 10:* Variability of Symptoms. Each item can be scored 0 to 2, 3 or 4. DRS score can range 1 to 32)

Of the 29 delirious patients, 15 (52 %) were hypoactive, while 14 (48 %) were hyperactive. Delirium was hyperactive in all the 3 delirious SAH patients. No other associations between delirium type and stroke location and characteristics were found.

Delirium and stroke outcome

134 (61 %) acute stroke patients were independent at discharge (modified Rankin grade = 0–2) and 84 (39 %) were dependent or died (modified Rankin grade = 3–6). The presence of delirium was associated with an increased risk of unfavourable outcome ($\chi^2 = 19.47$, $p = 0.0001$, OR = 6.44, 95 % CI: 2.61 to 15.88), as 76 % (22) of the delirious patients and only 33 % (62) of the non-delirious patients had an unfavourable outcome.

Discussion

In the present study 13 % of stroke patients had delirium contrasting with only 2 % of acute coronary patients, indicating that delirium could be a consequence of hemispheric brain damage and not a non-specific consequence of acute disease and hospitalisation. Among stroke patients delirium was associated with intracerebral haemorrhages, older age, neglect and medical complications. Delirium had a negative influence on the outcome.

This study included some innovative features, such as the comparison of stroke patients with an acute non-encephalic vascular control group and the assessment of all consecutive stroke patients. In order to decrease selection bias that could lead to an underestimation of the frequency of delirium, we enrolled aphasic patients and those who were not fully alert. In fact, delirium was more severe in aphasic and non-fully alert patients. Assessment was performed as soon as possible, decreasing the confounding effect of medical complications.

The main limitations of our study are 1) lack of a formal prestroke cognitive assessment, 2) lack of a systematic repeated CT or MR in all patients, 3) no systematic analysis of the possible role of previous and current medication [15], 4) admission bias towards young and middle age stroke patients, and 5) a high percentage of haemorrhagic stroke. The results of this study might only be generalised to a middle age stroke population with a comparable prevalence of haemorrhages.

The presence of delirium is lower in this study than in those previously reported in literature (15 % to 48 %) [4–7]. Differences between studies may be due either to the use of different criteria and assessment instruments for delirium, or to differences in case mix, in the mean age of the samples and in the prevalence of previous dementia/cognitive decline. In two prior studies [6, 7], instruments other than DRS were used. Increasing age is a predisposing condition for delirium and younger patients are also less likely to suffer from prestroke cognitive impairment or dementia. The age-related loss of cholinergic reserve and the focal loss of acetylcholine in the nucleus basal of Meynert may be the reasons why delirium is more common in older individuals and in patients with dementia [16]. Hénon et al. [4] and Gustafson et al. [6] identified pre-existing cognitive decline as an important predisposing factor for acute confusional state. Respectively, 11.6 % and 81.6 % of their delirious patients had previous cognitive decline [4, 6], while we found only 7 %. It is possible that if we had assessed pre stroke cognitive status with a specific instrument [4], we could have detected a few more cases of prestroke cognitive impairment. It is possible that our study underestimates the prevalence of delirium, because of the younger mean age and lower frequency of dementia in its sample.

Our study disclosed that delirium was more frequent after haemorrhagic and hemispherical strokes. The number of patients with lesions on each specific site was small, decreasing statistical power and limiting the ability to confirm the reported relations between delirium and strokes involving the caudate, thalamus, right MCA territory and PCA infarcts [5, 9, 17–19]. Less than a third of stroke patients with right MCA or PCA infarcts developed delirium, indicating either individual susceptibility, subtle anatomical differences between infarcts, or the need for additional predisposing/precipitant conditions to unchain delirium.

Left hemineglect was significantly associated with delirium. The right hemisphere is dominant for sustained attention [20]. In neglect there is both a defect of alerting, of non-lateralized non-spacial sustained attention and of lateralized spatial attention [21]. Such ne-

glect-related attention deficit probably plays an important role in delirium, since the inability to focus, sustain and shift attention is a key feature of delirium.

All previous systematic studies of delirium in stroke exclude SAH. We detected delirium in 11 % of SAH patients. Based on a review of medical records, Reijneveld et al. [22] found acute confusional state as a presenting feature in 1.4 % of aneurysmal SAH. Global ischaemia at onset due to sudden increase in intracranial pressure, hydrocephalus and intracerebral haematoma are likely mechanisms contributing to delirium in acute SAH. Reijneveld et al. [22] related delirium to initial global ischaemia, although the majority of their patients had hydrocephalus, intraventricular haemorrhages or frontal haematoma. One of our cases also had an intrahemispheric basofrontal haematoma. The cingulum, frontal projections from the thalamus, the septal area and the Meynert nucleus are likely to be damaged by basofrontal haematomas. Both in our and Reijneveld et al.'s series [22] delirious SAH patients were hyperactive. Orbitofrontal and mesial temporal lobe dysfunction may account for the hyperactivity.

Delirium in acute stroke can be caused by a medical complication of stroke, by substance intoxication or withdrawal, by the stroke itself or by multiple causes. Alcohol withdrawal was not a frequent cause of delirium in our study. Our results confirmed that stroke and its medical complications, mostly infections, are the most common precipitants of delirium [4, 6].

Delirium is a frequent complication of acute stroke and is associated with poor outcome. This justifies a systematic approach to its detection, prevention, pharmacological and non-pharmacological management [23, 24].

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References

1. American Psychiatric Association (2002) Delirium, Dementia and Amnestic and Other Cognitive Disorders. Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Reviewed. Washington. DC, American Psychiatric Press, pp 153–180
2. Inouye SK (2001) Delirium: a barometer for quality of hospital care. Hosp Pract 36:15–18
3. Rockwood K, Cosway S, Carver D, Jarrett P, Stadnyk K, Fisk J (1999) The risk of dementia and death after delirium. Age Ageing 28:551–556
4. Hénon H, Lebert F, Durieu I, Godefroy O, Lucas C, Pasquier F, Leys D (1999) Confusional state in stroke. Relation to preexisting dementia, patient characteristics, and outcome. Stroke 30:773–779
5. Mori E, Yamadori A (1987) Acute confusional state and acute agitated delirium. Occurrence after infarction in the right middle cerebral artery territory. Arch Neurol 44:1139–1143
6. Gustafson Y, Olsson T, Eriksson S, Asplund K, Bucht G (1991) Acute confusional states (delirium) in stroke patients. Cerebrovasc Dis 1:257–264
7. Gustafson Y, Olsson T, Asplund K, Hägg E (1993) Acute confusional state (delirium) soon after stroke is associated with hypercortisolism. Cerebrovasc Dis 3:33–38
8. Trzepacz PT, Baker RW, Greenhouse J (1988) A symptom rating scale for delirium. J Psychiatry Res 23:89–97
9. Ferro JM, Caeiro L, Verdelho A (2002) Delirium in acute stroke. Curr Opin Neurol 15:51–55
10. American Psychiatric Association. Mood Disorders (2002) Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Reviewed. Washington DC, American Psychiatric Press, pp 345–428
11. Pinto AN, Melo TP, Lourenço ME, Leandro MJ, Brázio A, Carvalho L, Franco AS, Ferro JM (1998) Can a clinical classification of stroke predict complications and treatments during hospitalisation? Cerebrovasc Dis 8:204–209
12. Rankin J (1957) Cerebral vascular accidents in patients over age 60. Scott Med J 2:200–215
13. Bamford JM, Sandercock PAG, Warlow CP, Slattery J (1989) Interobserver agreement for the assessment of handicap in stroke patients. Stroke 20:828
14. Tatemichi TK, Foulkes MA, Mohr JP, Hewitt JR, Hier DB, Price TR, Wolf PA (1990) Dementia in stroke survivors in the Stroke Data Bank Cohort. Prevalence, incidence, risk factors and computed tomographic findings. Stroke 21:858–866
15. Han L, McCusker J, Cole M, Abrahamowicz M, Primeau F, Élie M (2001) Use of medications with anticolinergic effects predicts clinical severity of delirium symptoms in older medical inpatients. Arch Intern Med 161:1099–1105
16. Tune LE, Egeli S (1999) Acetylcholine and Delirium. Dement Geriatr Cogn Disord 10:342–344
17. Brust JCM, Caplan LR (2001) Agitation and delirium. In: Bogousslavsky J, Caplan LR (eds) Stroke syndromes. 2nd Edition. Cambridge, Cambridge University Press, pp 222–231
18. Horenstein S, Chamberlain W, Conomy J (1962) Infarctions of the fusiform and calcarine regions with agitated delirium and hemianopsia. Trans Am Neurol Assoc 92:85–89
19. Devinsky O, Bear D, Volpe BT (1988) Confusional state following posterior cerebral artery territory infarction. Arch Neurol 45:160–163
20. Pardo JV, Fox PT, Raichle ME (1991) Localization of a human system for sustained attention by positron emission tomography. Nature 349:61–64
21. Heilman KM, Watson RT, Valenstein E (1993) Neglect and related disorders. In: Heilman KM, Valenstein E (eds) Clinical neuropsychology. New York, Oxford University Press, pp 279–336
22. Reijneveld JC, Wermer M, Boonman Z, van Gijn J, Rinkel GJE (2000) Acute confusional state as presenting feature in aneurysmal subarachnoid haemorrhage: frequency and characteristics. J Neurol 247:112–116
23. Cole MG (1999). Delirium: effectiveness of systematic interventions. Dement Geriatr Cogn Disord 10:406–411
24. Inouye SK, Bogardus ST, Charpentier PA, Leo-Summers L, Acampora D, Holford TR, Cooney LM Jr (1999) A multicomponent intervention to prevent delirium in hospitalised older patients. N Engl J Med 340:669–676