### Relation among Psychopathological Symptoms, Neuropsychological Domains, and Functional Disability in Subacute Poststroke Rehabilitation

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> Background: Neuropsychiatric disorders are commonly observed in patients following a stroke. Among 30%-60% of poststroke patients suffer from depression and anxiety (18%-25%). Some authors suggest an association between psychological symptoms and lesions in specific brain areas. In particular, lesions in left frontal cortex and left basal ganglia are frequently associated with poststroke depression and with comorbidity of anxiety and depression, whereas isolated anxiety symptoms are frequently observed after right hemispheric lesions. *Methods:* We investigated the relationship between depressive symptoms and anxiety in patients with subacute stroke and lesion side, motor disability, and cognitive impairment. We enrolled 100 patients undergoing a rehabilitative program within 1-3 months after a first-onset stroke. Results: Our patients presented mild to moderate depressive and anxious symptoms after stroke. In the comparison between patients with right and left lesions, during subacute poststroke phase, we did not find a specific link between existence of psychiatric symptoms and lesion side. However, in left lesion, depression correlated with age and alteration in delayed memory and attention, whereas memory deficit influenced anxiety symptoms. On the contrary, in right lesion, depressive symptoms were associated with attention ability, whereas anxiety was related to memory and attention. Depression and anxiety were not related to degree of neurological and functional deficits. Conclusions: The comorbidity between stroke and psychopathological disorders has been recognized as syndrome and should be diagnosed early and treated in order to improve the quality of life of patients and caregivers, and to improve rehabilitative process. Key Words: Anxiety-depression-disability-neuropsychology-stroke. © 2017 National Stroke Association. Published by Elsevier Inc. All rights reserved.

#### Introduction

Psychological symptoms, such as distress, depression, anxiety, and post-traumatic stress disorder, are commonly observed in patients following a stroke.<sup>1</sup> Among 30%-60% of all patients with stroke suffer from poststroke depression<sup>2</sup> and anxiety (18%-25%).<sup>3</sup>

Alterations in emotional aspects are associated with worse outcomes and are related to poor quality of life, social isolation, impaired activities of daily living, and decrease in functional independence, in participation, and functional ability.<sup>4</sup> Moreover, anxiety, and, in particular, depression, are associated with a higher mortality rate.<sup>5</sup>

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In addition, psychopathological symptoms have a negative impact on patient participation in the rehabilitative process. Considerable symptom overlap exists between anxiety and depressive disorders. Indeed numerous studies have shown a high comorbidity of anxiety disorders with major depression in stroke survivors.6 Clinical data regarding the causes of anxiety and depression following stroke are controversial. Psychological symptoms after stroke are often described as reaction to clinical consequences, such as motor disability and limitations in daily life.<sup>7</sup> Other authors instead suggest that they are associated with lesions in specific brain areas, and, presumably, subsequent changes in neurotransmitters.8 In particular, lesions in left frontal cortex and left basal ganglia are frequently associated with poststroke depression9 and to comorbidity of anxiety and depression, whereas isolated anxiety symptoms are frequently observed after right hemispheric lesions.<sup>10</sup> The severity of psychiatric symptoms should be related to hemispheric side of brain lesion, and their etiology and prevalence could vary during the recovery periods.<sup>11</sup> Therefore, different pathogenic models have been proposed to explain the high prevalence of mood alterations.<sup>12</sup>

In this study we evaluated the prevalence of depressive symptoms and anxiety in subacute stroke patients undergoing a rehabilitative program and the association to lesion side, motor disability, and cognitive impairment.

#### Materials and Methods

This study included patients who were admitted to a rehabilitative program within 1-3 months after a firstonset stroke. Between 2015 and 2016, 100 stroke patients (50 hemorrhagic and 50 ischemic) were consecutively recruited at the IRCCS (Istituto di Ricerca e Cura a Carattere Scientifico) Centro Neurolesi "Bonino Pulejo."

All patients gave written consent to the study and minor subjects' consents were signed by legal guardians. The study protocol was approved by the Local Ethics Committee according to the Declaration of Helsinki. Patients affected by severe aphasia, agnosia, neglect, and significant cognitive impairment or psychiatric history were excluded. Demographic and clinical characteristics, such as gender, age, education were also collected (Table 1).

All patients underwent magnetic resonance imaging examination to identify lesion location.

The neuropsychological evaluation was assessed by using Repeatable Battery for the Assessment of Neuropsychological Status (RBANS).<sup>13</sup> The RBANS is a brief, individually administered test measuring attention, language, visuospatial/constructional abilities, and immediate and delayed memory. It consists of 12 subtests, with 5 index scores and a total score.

Beck Depression Inventory (BDI-II) and Hamilton Rating Scale for anxiety (HAM-A) were used to assess anxiety and depressive symptoms.

Table 1.	Socio-demographic characteristics of patients with	th
rigl	(n = 56) and left lesion $(n = 44)$ (frequency)	

	Right lesion	Left lesion	<i>P</i> -value
Patients	56	44	
Sex			
Women	27 (48.21)	20 (45.45)	
Men	29 (51.78)	24 (54.54)	
Age (mean $\pm$ SD)	$58.17 \pm 13.20$	$60.6 \pm 11.2$	.48
Education	$11.61\pm2.60$	$12.9 \pm 4.63$	.26
(mean ± SD)			
BDI-II (median)	18	14	.14
(I-III quartile)	(14.0-26.25)	(13.75-20.5)	
HAM-A (median)	17	16	.63
(I-III quartile)	(12.0-21.0)	(12.75-21)	
FIM (median)	83.5	113.5	.17
(I-III quartile)	(71.5-105.25)	(66.75-119)	
Total score	74	77	.53
RBANS			
(median)			
(I-III quartile)	(70.7-84-2)	(69.7-86.2)	

Abbreviations: BDI-II, Beck Depression Inventory; FIM, Functional Independence Measure; HAM-A, Hamilton Anxiety Rating Scale; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; SD, standard deviation.

The BDI-II measures the severity of depressive symptoms and includes 21 items concerning different symptom domains, with 4 possible answers describing symptoms of increasing severity associated with a score from 0 to 3. The maximum total score is 63 where 0-13 indicates minimal depression, 14-19 mild depression, 20-28 moderate depression, and above 29 severe depression.<sup>14</sup>

The HAM-A measures the severity of anxiety symptoms. The scale consists of 14 items, each defined by a series of symptoms, and measures both psychic anxiety (mental agitation and psychological distress) and somatic anxiety (physical complaints related to anxiety). Each item is scored on a scale of 0 (not present) to 4 (severe), with a total score range of 0-56, where below 17 indicates mild severity, 18-24 mild to moderate severity, and 25-30 moderate to severe.<sup>15</sup>

The Functional Independence Measure scale was used to assess physical and cognitive disability.<sup>16</sup> Items are scored on the level of assistance required for an individual to perform activities of daily living. The scale includes 18 items, of which 13 items are physical domains and 5 items are cognition items. Each item is scored from 1 to 7 based on level of independence, where 1 represents total dependence and 7 indicates complete independence.

#### **Statistical Analysis**

Quantitative variables were expressed as mean  $\pm$  standard deviation, and the differences were assessed using independent sample *t* test. A nonparametric analysis was

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