

# Alexithymia in Neurological Disease: A Review

Lucia Ricciardi, M.D., Ph.D., Benedetta Demartini, M.D., Aikaterini Fotopoulou, Ph.D., Mark J. Edwards, M.D., Ph.D.

**Objective:** Alexithymia has been considered a personality trait characterized by difficulties identifying and describing feelings and an externally oriented thinking style. A high rate of alexithymia is reported among patients with psychiatric and psychosomatic disorders. In this review, the authors examined the literature regarding the prevalence and importance of alexithymia in patients with neurological disorders.

**Methods:** A systematic search of the computerized databases MEDLINE and PubMed was conducted in order to identify papers on alexithymia in neurological disease. Key search terms used included "traumatic brain injury," "head trauma," "head injury," "stroke," "epilepsy," "brain tumor," "multiple sclerosis," "Alzheimer's disease," "Parkinson's disease," "Huntington's disease," "Gilles de la Tourette syndrome," "dystonia," "psychogenic movement disorders," "functional movement disorders," "nonepileptic attacks," and "nonepileptic seizures." These search terms were paired with "alexithymia."

**Results:** Alexithymia seems to be a common feature of neurological disease, with most evidence available for patients with traumatic brain injury, stroke, and epilepsy. However, it is not clear how independent it is from affective disorders such as depression and anxiety, which are themselves very common in neurological conditions.

**Conclusions:** Identification of alexithymia could be relevant for prognosis and therapeutic decisions in patients with neurological disease and is certainly worthy of further study. Tools with which to measure alexithymia and delineation from affective disorders and apathy are important methodological issues for future work.

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The term "alexithymia" was coined in 1973 by Peter Sifneos to describe certain clinical characteristics observed among patients with psychosomatic disorders who had difficulty engaging in insight-oriented psychotherapy.<sup>1</sup> Alexithymia is currently conceptualized as a cluster of cognitive traits, which include difficulty identifying feelings, difficulty describing feelings to others, externally oriented thinking, and limited imaginative capacity. Therefore, people with alexithymia may demonstrate deficiencies in emotional awareness and communication and show little insight into their feelings, symptoms, and motivation.<sup>2</sup> Alexithymia is described as a deficit, an inability, or a deficiency in emotional processing rather than a defensive process.<sup>2</sup>

## ASSESSMENT

Alexithymia is not classified as a mental disorder in DSM-5. The instrument that is most frequently used to measure alexithymia is the 20-item Toronto Alexithymia Scale (TAS-20), a self-report questionnaire.<sup>3</sup> It is composed of 20 items that participants endorse on a 5-point Likert-type scale, ranging from "strongly disagree" to "strongly agree." The total score can range from 20 to 100. A score of 61 or more is taken to be

diagnostic of alexithymia; 52 to 60 indicates "possible" alexithymia; 51 or less indicates the absence of alexithymia. In addition to the total score, three subscores can be calculated which measure distinct factors: "difficulty identifying emotions," "difficulty describing emotions," and "externally oriented thinking" (EOT). Higher scores on the scale are indicative of increased alexithymia.<sup>4</sup>

The TAS-20 has been used extensively in both clinical and nonclinical settings; it has demonstrated satisfactory convergent and discriminant validity, and scores show high agreement with observer ratings of alexithymia.<sup>3</sup>

## PREVALENCE OF ALEXITHYMIA AND ITS ASSOCIATIONS WITH NONNEUROLOGICAL CONDITIONS

The prevalence of alexithymia in the general population is approximately 10%.<sup>5,6</sup> Alexithymia seems to be normally distributed in the population in both genders, consistent with it being a personality dimension. There is some evidence that alexithymia occurs more frequently in men, individuals with advanced age, low educational level, and low socioeconomic status.<sup>7</sup> A high rate of alexithymia (approximately

40%–60%) is reported among patients with psychosomatic disorders<sup>4</sup> and mental health disorders such as anxiety disorders, (prevalence of 13%–58%),<sup>8</sup> depressive disorders (32%–51%),<sup>9</sup> eating disorders (24%–77%),<sup>5</sup> addictive disorder (30%–50%),<sup>6</sup> obsessive-compulsive disorder, (11%–36%)<sup>10</sup> and autism spectrum disorder (40%–60%).<sup>11</sup>

Though there are no longitudinal or prospective studies, such data suggest at the very least a strong association between alexithymia and mental illness.

Several studies have found an association between alexithymia and a wide range of medical conditions, including asthma, allergies, essential hypertension, cancer, myocardial infarction, angina pectoris with coronary spasm, diabetes, and inflammatory bowel disease.<sup>4</sup> These studies have controlled for the presence of depression and anxiety, which were not found to be a confounding factor.

### **PATHOPHYSIOLOGY OF ALEXITHYMIA**

Multiple factors, both neurobiological and environmental, have been suggested as pathophysiologically significant for the development of alexithymia; nevertheless all studies regarding the pathophysiology of alexithymia have been conducted on small samples of patients and the results (perhaps unsurprisingly in view of this) have often been conflicting.

Functional MRI (fMRI) has been used as a tool to investigate the pathophysiology of alexithymia. Wingbermühle and colleagues<sup>12</sup> found reduced blood-oxygenation-level-dependent (BOLD) responses to external emotional stimuli and reduced activity during imagery of emotional states, in the limbic and paralimbic areas. In contrast, Craig and colleagues<sup>13</sup> found increased BOLD responses in somatosensory and sensorimotor regions, including the insula using a similar paradigm. In addition BOLD responses in the medial, prefrontal, and insula cortex were reduced when people with alexithymia were involved in social tasks compared with healthy controls.<sup>14</sup>

It has also been suggested that an interhemispheric functional disconnection is relevant to alexithymia so that emotional information from the right hemisphere is not properly transferred to the language regions in the left hemisphere.<sup>15</sup> Another neuropsychological model suggests that alexithymia may be related to a dysfunction of the anterior cingulate cortex.<sup>16</sup>

### **ALEXITHYMIA IN NEUROLOGICAL DISEASE**

In this review, we focus specifically on the association between neurological disease and alexithymia in order to clarify two main questions: 1) Is alexithymia common in patients with neurological disease? This is potentially important from a clinical point of view because the presence of alexithymia could have prognostic implications and affect suitability and response to different types of treatment. 2) Does the nature of the neurological conditions in which alexithymia is a common feature give any clues as to the pathophysiological mechanism of alexithymia?

### **METHODS**

A systematic search of computerized databases MEDLINE and Pubmed was conducted in order to identify papers on alexithymia in neurological disease of central nervous system. Key search terms used included “traumatic brain injury,” “head trauma,” “head injury,” “stroke,” “epilepsy,” “brain tumor,” “multiple sclerosis,” “Alzheimer’s disease,” “Parkinson’s disease,” “Huntington’s disease,” “Gilles de la Tourette syndrome,” “dystonia,” “psychogenic movement disorders,” “functional movement disorders,” “nonepileptic attacks,” and “nonepileptic seizures.” These search terms were paired with “alexithymia.” Only articles published in peer-reviewed journals in English were included. All study designs were included. As a first review on alexithymia in neurological conditions, we also included studies without control group in order to have a global view on this topic. Manual searches of references of retrieved articles identified additional studies, which were also included in the review. We only included those studies where alexithymia was measured in patients with central nervous system diseases, including those studies where such patients were used as a control group for comparison with patients with functional/psychogenic neurological symptoms (e.g., epilepsy and nonepileptic seizure patients). We only included those studies which used TAS-20 as assessment scale and which considered a TAS-20 score of 61 or more as indicative of alexithymia.

### **RESULTS**

Our initial searches retrieved 46 articles. After abstract review and removal of duplicates, we were left with 40 articles that met our review criteria.

The available literature on alexithymia in neurological diseases is summarized in the data supplement accompanying the online version of this article.

#### **Alexithymia and Traumatic Brain Injury (TBI)**

TBI is the most common cause of brain damage and when severe is usually characterized by focal damage superimposed on more diffuse white-matter and brain-stem damage. Changes in emotional and social behavior are common and debilitating consequences of TBI, and are a major source of disability.

Koponen and colleagues<sup>17</sup> evaluated the prevalence of alexithymia in 54 TBI patients and 54 healthy controls and investigated whether any characteristic of TBI including severity and the presence, laterality, or location of contusions on MRI, might be associated with the score on the TAS-20. They also evaluated the influence of a concomitant axis I and II psychiatric disorders on alexithymia in these patients. Authors confirmed that alexithymia was significantly higher in patients with TBI than in HC (31.5% versus 14.8%), but there was no association found with any clinical features of the TBI such as location of focal damage or severity. However, 15/17 alexithymic patients had a psychiatric disorder (most commonly

anxiety disorders and personality disorders), and a significant association was observed for the presence of both axis I and axis II psychiatric disorders and higher TAS-20 total scores.

Wood and colleagues<sup>18</sup> evaluated 121 TBI patients and compared them with 52 orthopedic patients in terms of TAS-20 and of a complete neuropsychological test battery in order to evaluate the presence of alexithymia and its relationship to injury severity, neuropsychological ability, and affective disorder. They showed a higher prevalence rate of alexithymia in TBI patients than in orthopedic controls (57.9% versus 15.4%) and that higher scores on the TAS-20 were associated with poorer cognitive performance (verbal and sequencing abilities).

Henry and colleagues<sup>19</sup> conducted a behavioral study involving 28 patients with TBI and 31 healthy subjects. The MRI was performed in 18/28 patients and showed bilateral injuries in 10 and focal unilateral lesions in the remaining 8. In 50% of these 18 patients, lesions specifically involved the frontal lobes. Authors investigated the differences in levels of alexithymia in TBI patients and healthy subjects on the three dimensions of TAS-20 and evaluated whether alexithymia was related to deficits in executive functions, mood disorders (depression and anxiety) and quality of life (QoL). They confirmed that alexithymia was commoner in TBI patients than in healthy controls (32.1% versus 12.9%) but there was no difference in the three sub scores when analyzed separately. However, TBI patients were more depressed than healthy controls, and this was not controlled for in the assessment of alexithymia.

Becerra and colleagues<sup>20</sup> described a 21-year-old patient with a TBI, resulting mainly in bilateral parietal and frontal damage, who presented with a syndrome substantially similar to alexithymia. They introduced the term “organic” alexithymia referring to a condition of acquired alexithymia that shares some aspect of the primary alexithymia but it might be considered different from it. Ho and colleagues<sup>21</sup> described a 46-year-old lady with occipital lobe damage after a severe childhood TBI. She had a high alexithymia score (TAS-20: 63) and low empathy score (EQ 16), and the authors suggested that she had ‘organic’ alexithymia, and speculated about a possible causative role of the visual cortex for this phenomenon.

A recent study evaluated the frequency of suicidal ideation following TBI and its relationship with alexithymia as well as with depression, hopelessness, and worthlessness in 105 TBI patients comparing them with healthy controls. TBI patients were more alexithymic (61% versus 6.5%) and more depressed ( $p=0.0005$ ) than the control group, they had higher frequency of suicidal ideation (33%), hopelessness (84.8%), and worthlessness (61%) as measured by means of the BDI. Those patients reporting suicidal ideation were more depressed than those patients without suicidal ideation (74% versus 24%), and they had higher scores on the TAS-20, largely dependent on higher scores on the “difficulty identifying emotions” subscale.<sup>22</sup>

Williams and colleagues studied the relationship between alexithymia and emotional empathy in 64 TBI patients

and 64 healthy controls and they confirmed a higher alexithymia and lower emotional empathy in these patients compared with healthy controls and also showed an inverse relationship between alexithymia and emotional empathy in TBI although it was not possible to disclose the real nature of this relationship.

Along the same line, Neumann and colleagues<sup>23</sup> explored whether TBI patients, being more alexithymic, might be also be more likely to have problems understanding others’ emotions and assuming others’ points of view. They investigated the relationship between alexithymia, affect recognition (both voice and face) and empathy in 60 patients with moderate to severe TBI and in 60 healthy controls. They found a significantly higher proportion of those with TBI were alexithymic than healthy controls, they had poorer facial and vocal affect recognition ( $p\leq 0.001$ ) and lower empathy scores. They concluded that alexithymia, especially externally oriented thinking is associated with reduced affect recognition and cognitive empathy and suggested that those patients who have a tendency to avoid thinking about emotions are more likely to have problems understanding others’ emotions and assuming others’ points of view.

An important issue is whether the presence of alexithymia might be associated with worse outcome from TBI. This has been assessed by Williams and colleagues<sup>24</sup> with regard to social and family life in 47 patients following TBI and their partners in order to evaluate the quality of their personal relationships and satisfaction with marital life after the occurrence of TBI from both the patient’s and the partner’s point of view. They evaluated whether the presence of alexithymia in the patients might influence these aspects. Partners reported significantly more relationship problems than patients; in addition, partners of alexithymic patients reported poorer scores than partners of nonalexithymic ones in a scale assessing some relationship factors including satisfaction, consensus, cohesion and expression of affection.

One study on 83 TBI patients underlined that alexithymia might potentially act translating emotional distress into a somatic experience. In this study, alexithymia, measured by the TAS-20 score, was associated with an increased tendency to somatize distress after TBI.<sup>25</sup> The authors speculated that individuals who have difficulties in identifying and recognizing sensations of emotional distress from bodily sensations such as pain or discomfort may interpret emotional distress as physical sensations translating it into somatic experience and expressing them in the form of physical symptoms.

In patients with mild TBI, Wood and colleagues<sup>26</sup> studied whether alexithymia, anxiety, and psychological distress might predict the occurrence of postconcussional (PC) symptoms in the acute recovery stage of mild TBI in 61 patients. The presence of anxiety and depression did predict the occurrence of PC, but the presence of alexithymia did not.

Finally Wood and colleagues<sup>27</sup> examined the relations among coping styles, alexithymia, and psychological distress following TBI in 71 patients with TBI. They found that difficulty identifying feelings was a significant predictor for psychological distress; they concluded that early screening for alexithymia following TBI might identify those most at risk of

developing maladaptive coping mechanisms. This could assist in developing early rehabilitation interventions to reduce vulnerability to later psychological distress.

### Alexithymia and Stroke

After stroke, patients frequently present with behavioral, emotional, and affective disturbance. Several studies have attempted to evaluate the role of lesion lateralization in patients with right-hemisphere stroke lesions compared with left-hemisphere ones in generating emotional processing deficits.<sup>28</sup>

In this context, a number of studies have assessed the prevalence of alexithymia in patients with stroke trying to clarify whether the presence of alexithymia might be related to any clinical characteristic such as lesion laterality or location. Spalletta and colleagues<sup>29</sup> conducted a study on 48 stroke patients in order to test the hypothesis that right brain damage (RBD) contributes to the development of alexithymia (total TAS-20 score or TAS subscale score) more than left brain damage (LBD). They authors concluded that alexithymia is more frequent in patients with RBD and that the right hemisphere might be involved in the neurobiological mechanism of some features of alexithymia.

In a separate study, the same authors investigated the relationship between different forms of unawareness including anosognosia for motor impairment, sensory neglect, and alexithymia (conceptualized as unawareness of emotions) in 50 right hemispheric stroke patients. The authors suggest that “unawareness” in all its different forms such as anosognosia for motor impairment, neglect, and alexithymia in patients with a right hemispheric stroke is a multifaceted phenomenon and that despite the frequent comorbidity of these different types of unawareness, they are independent each other and there are patients who suffer from just one pure form.<sup>30</sup>

More recently, Wang and colleagues<sup>31</sup> investigated whether alexithymia might be involved in the development and maintenance of post-traumatic stress disorder (PTSD) and psychiatric comorbidity following stroke. Thirty percent of the patients presented had PTSD as defined by this scale 1 month after stroke and 23.1% after 3 months. Alexithymia was associated with increased severity of poststroke PTSD and psychiatric comorbidity in the short-term (after 1 month) but at the 3 months poststroke evaluation, this association was no longer significant after adjusting for PTSD, psychiatric comorbidity, physical disability, and time from the stroke occurrence. Authors suggest that an alexithymic trait might influence psychological outcomes acutely after the stroke but not in the long term, and that PTSD could develop in response to alexithymic characteristics.

Cravello and colleagues<sup>32</sup> evaluated the effect of venlafaxine and fluoxetine on alexithymia severity in patients with post-stroke depression in an open label randomized study on 50 patients with first-event stroke and poststroke depression. They showed that patients treated with venlafaxine had a greater reduction in TAS-20 score than patients treated with fluoxetine even when correcting for baseline Hamilton Rating Scale for Depression (HAM-D) score. Despite the several limitations of the study, mainly the open label design, the small sample size and the lack of a correlation to stroke characterizes, authors

suggest that drugs acting on both noradrenergic and serotonergic systems can improve emotional awareness in patients with post stroke depression.

### Alexithymia and Epilepsy

A small number of studies have investigated the prevalence of alexithymia in people with epilepsy, but most of these have focused on prevalence of alexithymia in patients with psychogenic nonepileptic seizures (PNES) and have used patients with epilepsy and healthy controls as comparison groups. PNES are events resembling epileptic attacks, but lacking their characteristic clinical and electrophysiological features.

One recent study has investigated the relationship between alexithymia, epileptic focus side, and handedness in patients with temporal lobe epilepsy. The authors studied 105 temporal lobe epilepsy patients, 52 with a left-sided focus and 53 with a right-sided one, assessing them for depression, anxiety, alexithymia, and psychopathological symptoms. They showed that alexithymia score was not associated with handedness and focus laterality but that it was associated with psychopathological variables (such as depression, anxiety, and somatization). This study had several methodological limitations, such as the lack of a control group of epileptic patients with a different focus or, generalized epilepsy and the lack of a control group of healthy controls. Also, they did not distinguish between secondary epilepsy and idiopathic epilepsy, thus, making it difficult to determine whether alexithymia might be related to a functional or a structural disconnection of brain areas.<sup>33</sup>

Chung and colleagues<sup>34</sup> published two studies on the same population of 71 epileptic patients with PTSD following epileptic seizure and psychiatric comorbidity, and they analyzed the relationship between alexithymia and the severity of them. They showed that 81% of patients met the criteria for PTSD. When considering alexithymia, 41% of epileptic patients had high level of alexithymia and a regression analysis showed that DIF subscale of TAS-20 predicted postepileptic seizure PTSD and psychiatric comorbidity in these patients. They suggested that the severity of PTSD and comorbid psychiatric symptoms is strongly related to the level of difficulty that people with epilepsy experience in processing and “getting in touch” with their internal feelings and emotions. Once more these studies’ limitations do not clarify the meaning of alexithymia in epilepsy, however, authors confirm the existing literature on the link between alexithymia, PTSD, and chronic medical illness.<sup>35</sup>

Focusing on alexithymia as a diagnostic indicator for developing PNES, Tojek and colleagues<sup>36</sup> assessed 25 patients with PNES and 33 patients with epileptic seizures on stressful life events and psychosocial risk factors for somatization as well as on alexithymia (TAS-20). They found that both groups of patients had a higher level of alexithymia (30%) than that reported for community norms, and that PNES patients had more stressful negative life events, greater somatic symptoms, greater anxiety, and depression than the epileptic patients. This study did not use a control group of healthy subjects. Also, the



authors reported only the results of overall TAS-20 scores, not considering the examination of the three subscales of TAS-20, moreover PNES patients had higher level of anxiety and depression and the potential confounding effect of these two affective features was not analyzed.

In the attempt to go beyond the limitations of the previous study, Bewley and colleagues<sup>37</sup> conducted a study where PNES were compared with both patients with epilepsy and healthy controls in terms of alexithymia. They identified as alexithymic 90.5% of PNES patients, 76.2% of epilepsy patients, and 14.3% of healthy controls. They revealed significant differences between PNES and healthy controls groups and between epilepsy and healthy controls groups; in contrast no significant difference was observed between PNES and epilepsy patients. However, no significant differences were found between the three groups on total alexithymia scores when anxiety and depression were controlled for. When analyzing the single subscales, PNES patients had significantly higher score in DIF subscale than healthy controls even when depression was controlled for and significantly higher score in DDF than healthy controls when anxiety was controlled for. No significant difference between PNES and epilepsy patients in alexithymia, depression, and anxiety were detected. Therefore, authors concluded that alexithymia was not useful as a diagnostic indicator for PNES.

On the contrary, comparing PNES and ES in terms of alexithymia, early childhood trauma and immature defensive styles, Kaplan and colleagues<sup>38</sup> showed on a sample of 94 patients with PNES and 81 patients with epilepsy a significant difference in TAS-20 total score and subscale DIF with PNES patients being more alexithymic. However, the lack of investigation of the potential confounding role of psychiatric comorbidities in these patients limits the conclusions that can be drawn from this study.

Aiming to study emotional dysregulation, alexithymia, attachment, and psychopathology in patients with PNES and epilepsy, a recent study assessed 43 patients with PNES and 24 with epilepsy. This found no differences in terms of all these domains. However, when performing a cluster analysis, a cluster of 11 patients with PNES was identified, with high levels of both emotional dysregulation and alexithymia compared with a second cluster of the remaining PNES patients and epilepsy patients who scored higher in tests for anxiety, depression, and somatization. This suggested that there might be different subgroups of patients with PNES with distinct psychological profiles.<sup>39</sup>

Myers and colleagues<sup>40</sup> also studied the prevalence of alexithymia in patients with PNES and with epileptic seizures, showing that 37% and 29%, respectively, were alexithymic, but there was not a significant difference between these two groups of patients. The same group, in the attempt to identify psychological factors that might play a role in triggering and maintaining PNES, studied 66 patients with PNES and 35 patients with epilepsy. They reported that the prevalence of alexithymia to be 36.9% in PNES and 28.6% in patients with epilepsy, a nonsignificant difference. Regarding PNES patients, they showed a significant positive correlation between alexithymia and

heightened symptoms of anxiety, autonomic hyperarousal, intrusive experiences, dissociation, and defensive avoidance.<sup>41</sup>

### Alexithymia and Multiple Sclerosis

Only a small number of studies in the English language have investigated the prevalence of alexithymia in patients with multiple sclerosis (MS).<sup>42-45</sup> An Italian study aiming to determine the prevalence of alexithymia in a sample of 58 MS patients, observed a prevalence of 13.8%, which is not different from the prevalence usually reported in the healthy population.<sup>42</sup> However, they reported higher levels of fatigue and depression in alexithymic patients compared with nonalexithymic ones.

A study based in France, aiming to determine the predicting factors of depression in MS patients found that depression was associated with alexithymia. They reported a prevalence of alexithymia of 23.2% in 115 patients.<sup>43</sup>

Prochnow and colleagues<sup>44</sup> evaluated in a broader way the emotional processing deficits in 35 MS patients and 61 healthy controls, assessing their performance on tests of facial affect recognition (Ekman-60-Faces test and Perceptual Competence of Facial Affect Recognition) and alexithymia. The patients with MS were more alexithymic than healthy controls (25.7% versus 16.4%) and more impaired in both facial affect recognition tasks. More specifically, MS patients recognized less accurately than controls the emotions fear, surprise, anger, and sadness, whereas they did not differ from healthy controls on recognition of disgust and happiness.

Recently, Chahraoui and colleagues<sup>45</sup> conducted a study to investigate the course of alexithymia over a period of 5 years and its relationship with anxiety and depression in 62 patients with MS. They observed a prevalence of 30% of alexithymia in this population of patients with MS, and this proportion remained stable over the two time points studied. They confirmed the relation between alexithymia and both anxiety and depression, however, a multivariate logistic regression analyses showed that alexithymia was more strongly associated with anxiety.

Methodological issues, mainly the lack of a control group of healthy subjects and the lack of any correlation with the disease characteristics, limit the majority of these studies. An unanswered question is whether alexithymia is associated with MS lesions in specific areas of the central nervous system, indeed, all the studies refer to the expanded disability status scale (EDSS) as a measure of disease severity but they do not take into account factors such as the number and site of lesions or the lesion load.

### Alexithymia and Parkinson's disease

There has been increasing interest in nonmotor symptoms of Parkinson's disease, and in this context, recent studies have investigated the relationship between alexithymia and PD.

Costa and colleagues<sup>46</sup> assessed 70 PD and 70 healthy controls with TAS-20 and showed that there was a higher prevalence of alexithymia in PD (21.4% compared with 10% in healthy controls). When individual subscales were assessed, PD patients only differed from healthy controls with respect to the subscale "difficulty describing feelings." The same patients

were evaluated with a battery of tests assessing verbal episodic memory, executive functions, abstract reasoning, visual-spatial, and language abilities in order to determine any link between alexithymia and neuropsychological deficit in PD. Those patients with higher scores on the TAS-20 had poorer performance in tasks requiring the analysis of visual-spatial stimuli, speculating that, because the right hemisphere is known to be specifically involved in processing visual-spatial information, the relationship found between alexithymia and performance on right hemisphere functioning-dependent tasks in PD patients could reflect a more basic involvement of the right hemisphere in the modulation of some facets of alexithymia.<sup>47</sup>

The relationship between alexithymia and severity of depression in PD has been studied; one study on 58 patients showed a prevalence of 20.7% of alexithymia and of 20.7% of major depression. Patients with a diagnosis of major depression were more alexithymic than nondepressed ones. The results of a regression analyses demonstrated that higher scores on a self-report measure of depression predicted high scores on the overall alexithymia score as well as the DIF and DDF sub scores of the TAS-20. Thus, the authors suggested that the severity of depression might predict alexithymia in PD patients.<sup>48</sup> In contrast, Assogna and colleagues<sup>49</sup> suggested that alexithymia is a depression-independent phenomenon in PD patients and may be associated with the disease process. This discrepancy might be due to the different setting of the two studies, one evaluating hospitalized patients and the other outpatients and to the methodological differences (one study has no control group, the other has a control group of patients with different somatic medical conditions; none has a control group of healthy subjects).

Poletti and colleagues<sup>50</sup> have conducted a number of studies on newly diagnosed, untreated (de novo) PD patients. In one study, on 42 de novo PD and 30 healthy controls, they reported no difference in prevalence of alexithymia in de novo PD (24%) and healthy controls (17%) suggesting that dopamine depletion that precedes the clinical motor onset does not impact on alexithymia.

The same authors investigated the association between alexithymia and clinical motor subtypes in the same cohort of 42 de novo PD patients. Patients who presented with postural instability and gait disorders as main clinical characteristics were more alexithymic than PD patients with other motor subtypes. Patients with different motor predominant subtypes did not differ for depressive symptoms.<sup>51</sup>

The same authors also investigated whether and how alexithymia may influence decision making under conditions of uncertainty, assessed by means of the Iowa Gambling Task, in de novo PD patients. Alexithymic subjects outperformed the nonalexithymic in a sub-block of Iowa gambling task, suggesting that alexithymia might modulate decision making under uncertainty and that it might be associated with faster learning to avoid risky choices and the negative feedback with which these choices are more frequently associated.<sup>52</sup>

A recent study investigated 91 PD patients (89 on dopaminergic medication) evaluating alexithymia, impulsivity,

depression, anxiety, and behavioral inhibition, and their relationship with the development of impulsive-compulsive disorders (common behavioral disorders in PD). They suggested that alexithymia contributes to the development of these disorders even independently from impulsivity, depression and anxiety.<sup>53</sup>

### Alexithymia and Dystonia

Primary focal dystonia is a movement disorder characterized by involuntary muscle contractions and abnormal postures, whose pathophysiology is related to abnormalities in striato-thalamo-cortical circuitry.<sup>54</sup> Blepharospasm and cervical dystonia (CD) are the most common forms of focal dystonia. Recent studies suggest that motor symptoms in dystonia patients are accompanied by a wide variety of nonmotor features, including neuropsychiatric ones, especially on the anxiety spectrum.<sup>55</sup>

Gündel and colleagues<sup>56</sup> assessed if alexithymia might be a risk factor for exacerbation of abnormal postures and maximum range of motion in patients with CD. They concluded that high-alexithymic patients showed a generally increased level of tonic, sympathetic arousal in all the conditions, suggesting that this autonomic arousal might represent a permanent state of “internal alarm” in high-alexithymic patients.

### Alexithymia and Huntington’s Disease

One study<sup>57</sup> was identified that has assessed alexithymia in Huntington’s Disease (HD) as part of a wider study on emotional processing. The study, which compared 13 HD patients with mild motor impairments and 13 controls matched for age and gender, suggested impairment both in recognition and in expression of facial emotions in HD patients. However, the prevalence of alexithymia in HD patients was not significantly different compared with the control group.

## DISCUSSION

With this review, we have attempted to draw together current data on alexithymia in patients with neurological disease. Alexithymia was a concept developed with respect to a group of patients with psychosomatic symptoms, but the underlying aspects of brain function, which might be broadly termed “emotional processing,” clearly have a wider relevance.

Most data are available for patients with TBI: in those with TBI, 30% to 60% are found to be alexithymic. However, there does not appear to be any clear relationship between clinical variables such as severity and lesion location and the presence or absence of alexithymia. This suggests a possible relationship between alexithymia and other common counterparts of TBI, in particular affective disorders such as depression. There are also well-known associations between TBI and alcoholism,<sup>58</sup> which itself may be an independent risk factor for alexithymia, and is one which is not generally controlled for in studies of TBI and alexithymia. Only one study has specifically assessed the impact of alexithymia on behavioral outcome and found some evidence of a negative impact of alexithymia.<sup>24</sup>

While TBI is commonly associated with both focal and diffuse injury, stroke typically produces more discrete lesions, which might give more insight into anatomical associations between brain damage and alexithymia. In the few studies available, there does appear to be right hemisphere predominance for stroke associated with alexithymia. This would be consistent with the greater role for the right hemisphere in emotional processing.<sup>28</sup>

Although most studies of alexithymia and epilepsy have been motivated by the study of alexithymia in PNES and have used patients with epilepsy as a control group, they have revealed surprisingly high levels of alexithymia in patients with epilepsy. This has not been correlated with any clinical outcomes, and nor has there been study of those with epilepsy who also have PNES, and whether alexithymia might be a risk factor for this common clinical association.

Only very limited study has taken place of alexithymia in patients with movement disorders, despite the large existing literature on (other) emotional processing deficits and psychiatric comorbidity in these patients.

Where does this leave the concept of alexithymia and its relevance to patients with neurological disease? It does appear that alexithymia is a quite common counterpart of neurological disease, but it is not certain how well it is separated from affective disturbance, which is itself very common in those with neurological disease. The studies reviewed here do suggest that alexithymia cannot be completely subsumed within affective disorders such as depression. However, it is still not apparent whether knowing that a patient is alexithymic is useful in terms of making treatment or prognostic decisions. We do not know if alexithymia precedes disease onset and, therefore, might act as an important mediator for developing comorbid psychiatric symptoms such as depression and anxiety. In some patients, alexithymia may well be related to the disease process itself and therefore forms part of the disease burden of the neurological disease itself. In addition, one could propose that alexithymia might in some people be a way to cope with psychological distress resulting from chronic illness.

There is a further important methodological challenge regarding the concept and measurement of alexithymia, namely the validity of using a self-report questionnaire to assess a disorder characterized by an inability to identify one's own emotional state can be called into question. This issue may be magnified in TBI patients where damage to the rostral prefrontal cortex is very common, a region associated with implicit emotion generation.<sup>57</sup> In one study reported above, self-rated degree of alexithymia did correlate with objective ratings, but clearly this important measurement issue needs to be taken into account when judging data related to alexithymia. It is also an important consideration that some patients (perhaps most often those with functional neurological symptoms, also known as conversion disorder) may be unwilling to consider the relevance of emotional and psychological issues to their physical symptoms, as this might imply that their physical symptoms are "not real."

Moreover, when evaluating patients by means of the TAS-20, there is no control for an overall denial style in answering the questionnaire. One cannot, therefore, exclude that alexithymia might be a manifestation of a right hemispheric denial syndrome. This idea would be supported by the few available studies showing a right hemisphere predominance for stroke associated with alexithymia, supporting the hypothesis of alexithymia as an element of anosognosia for emotional stimuli. However, the study by Spalletta and colleagues<sup>30</sup> investigated the relationship between anosognosia for motor impairment, neglect, and alexithymia in patients with right hemispheric stroke as different expressions of unawareness, and concluded that these different forms of unawareness are independent factors although they are often present as comorbidities in patients with a stroke.

Another issue is that when considering a complex field such as the emotional one, it is very hard to differentiate different facets of subjective experience of one's own feelings, with concepts such as alexithymia, abulia, apathy, and anhedonia hard to distinguish from one another, in particular with the use of self-report assessment scales in clinical populations.

Alexithymia might, in some respects, resemble aprosodic deficit observed after brain damage. However, although alexithymia expresses a diminished subjective experience of one's own feelings, aprosodia refers to a testable deficit in the perception and expression of affect associated with language and communication, in which internal feelings are usually preserved. In this regard, we encourage investigating in future studies the relationships between aprosodia and self-reports of alexithymia (i.e., evaluating alexithymia in patients with aprosodia in the context of neurological disorders such as TBI). This could be potentially useful in grounding a rather ephemeral concept such as alexithymia to specific brain areas lesions or dysfunction in particular networks. We also encourage future studies on alexithymia in neurological disorders, aiming to contextually evaluate the self-report TAS-20 as a subjective assessment and a more objective evaluation scale: the Alexithymia Provoked Response Questionnaire. This could be useful to go beyond some important limitations of the studies considered here and to give a more objective evaluation of alexithymia in clinical populations.

Finally, another methodological limitation of our review might be the inclusion of studies without control groups. This might be taken into account in further reviews on this topic.

However, despite these issues, there are reasons to pursue further study of alexithymia in patients with neurological disease. Not only does it appear to be a prevalent issue for these patients, but rehabilitation, which is a common treatment for patients with neurological disease, might be more effective if alexithymic features of patients are taken into account. This might be particularly the case for psychological treatments such as cognitive-behavioral-therapy and psychodynamic psychotherapy. We believe that assessment of alexithymia may be a useful addition to the neuropsychological assessment of patients with neurological disease. Future research should focus on how the identification of alexithymia in

particular, over and above other neuropsychological assessments can predict prognosis and response to specific treatments.

#### AUTHOR AND ARTICLE INFORMATION

From the Sobell Dept., UCL Institute of Neurology, Queen Square, London, United Kingdom (LR, BD, MJE); Dept. of Clinical and Experimental Medicine, University of Messina, Messina, Italy (LR); Dept. of Psychiatry, San Paolo Hospital and University of Milan, Milan, Italy (BD) and Division of Psychology and Language Sciences, CEHP Research Dept., University College London, London, United Kingdom (AF).

Send correspondence to Dr. Edwards; e-mail: m.j.edwards@ucl.ac.uk.

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