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Post-stroke alexithymia – a review

Aleksytymia u pacjentów po udarze mózgu – przegląd literatury

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Abstract

Purpose: The goal of this study is a review of the literature on the role of alexithymia among stroke patients, especially assessing its impact on the process of convalescence, psychiatric comorbidity and clinical outcomes.

Views: Organic alexithymia is a common post-stroke complication, which interferes with many aspects of health among stroke survivors, with interleukin-18 having an important role in the appearance and depth of alexithymia. Post-stroke patients suffering from alexithymia are more prone to depression, manifestations of which may differ from the symptoms of this shown by the non-alexithymic post-stroke population. Alexithymia is also the cause of more severe symptoms of stroke itself, as well as more severe symptoms of post-stroke post-traumatic stress disorder. It is often associated with right-hemisphere lesions, but there are findings which show that left brain insult may also be the cause; the explanation is that information transfer from right to left hemisphere causes disturbances in emotional awareness.

Conclusions: Alexithymia plays an important role in the health of post-stroke patients. Assessment of the trait should be considered in their population, since it plays an important role in terms of predicting psychiatric comorbidity and severity of stroke complications, which transfers to treatment choice. Further research is required to examine other post-stroke psychiatric comorbidities associated with alexithymia and to closely determine the response of rehabilitation, including pharmacological treatment and psychological therapy.

Key words: alexithymia, stroke, affective symptoms.

Streszczenie

Cel: Przegląd literatury dotyczący roli aleksytymii u pacjentów po udarze mózgu, a zwłaszcza jej wpływu na proces rekonwalescencji, występowanie innych schorzeń psychiatrycznych i aspekty kliniczne.

Poglądy: Aleksytymia organiczna jest powszechnym powikłaniem u pacjentów po udarze mózgu, które wpływa negatywnie na wiele aspektów zdrowotnych u tych chorych. W pojawieniu się oraz ciężkości aleksytymii znaczącą rolę odgrywa interleukina 18. Pacjenci po udarze mózgu cierpiący z powodu aleksytymii są bardziej podatni na depresję, której objawy mogą się różnić od objawów depresji u pacjentów po udarze mózgu, ale bez aleksytymii. Aleksytymia jest także przyczyną występowania cięższych objawów samego udaru, jak również cięższych objawów poudarowego zespołu stresu pourazowego. Jest powiązana z uszkodzeniami prawej półkuli mózgu. Niektóre badania wskazują, że jej przyczyną mogą być również uszkodzenia w lewej półkuli, co ma związek z przekazywaniem informacji z prawej do lewej półkuli i wywołanymi przez to zaburzeniami świadomości emocjonalnej.

Wnioski: Aleksytymia odgrywa ważną rolę w zdrowieniu pacjentów po udarze mózgu. Należy rozważyć rutynową ocenę tego zaburzenia w tej populacji, gdyż pozwala ono na przewidywanie występowania schorzeń psychiatrycznych oraz ocenę ciężkości powikłań udaru, które to mają wpływ na wybór odpowiedniego leczenia. Konieczne jest przeprowadzenie dalszych badań, aby przeanalizować inne współistniejące choroby psychiatryczne związane z aleksytymią u pacjentów po udarze, a także aby określić odpowiedź na rehabilitację u tych chorych, z uwzględnieniem leczenia farmakologicznego i terapii psychologicznej.

Słowa kluczowe: aleksytymia, udar, zaburzenia afektywne.

INTRODUCTION

In the human population there are persons who are little interested in their own emotional life, and, moreover, are not able to recognize and delineate their states to others. For such an inability the term *alexithymia* was proposed by Sifneos in 1973 [1], and has been further investigated by many researchers. It has been proved that alexithymia is a stable personality trait [2] and is characterized by four different facets: difficulty identifying feelings (DIF), difficulty describing feelings (DDF), restricted imagination including the paucity of fantasies, and externally oriented cognitive style (EOT) [3]. Those deficits are often misinterpreted as somatic complaints [1]. To evaluate the level of alexithymia self-report scales are mainly used, among which TAS-20 (Toronto Alexithymia Scale) is the most widely applied in clinical work. It has been translated to more than 20 languages, with a score of ≥ 61, which reflects the presence of alexithymia. Although TAS-20 is validated and reliable [2, 4], the usage of such instruments imposes limitations on the measurement, with subjectivity being an important flaw.

The prevalence of alexithymia in the general population, according to different studies, varies from 5.2% to 17% [5-8], with most researchers indicating that men not only score higher in the measures of the trait, but that it is also more common among them than it is among women [5-11]. It is debatable if such sex differences, especially regarding EOT facet, are due to cultural impacts and gender role socialisation [12, 13] or some other factors. The linkage between ageing and alexithymia shows discrepancies, with some studies showing no associations [5] while others suggest that alexithymia increases with age [6, 7, 11], and yet others that it decreases [4, 14]. The incremental rise in alexithymia with age has been explained by the poor physical health of older people and differences in upbringing and cultural environment among them and the young population, which leads to disparate coping styles regarding their affects, with a strong correlation between aging and alexithymia shown in the study by Mattila *et al.* [11]. On the other hand, very low correlations were observed regarding no association of linkage of alexithymia and age as well as alexithymia decreasing with age [5, 14].

Alexithymia is associated with language deficits and, as observed in many psychiatric and somatic conditions, its presence should be taken into account while a choosing proper form of treatment and therapy, with psychodynamic therapy being an inappropriate form of treatment for such patients [15]. It also plays an important role in prognosis and therapeutic decisions for patients with neurological diseases, and its prevalence among stroke survivors is a common feature [16].

THE "ORGANIC ALEXITHYMIA" CONCEPT AND ITS OUTCOMES

The concept of splitting alexithymia on the basis of its derivation appeared early in the literature, and the terms "primary" and "secondary" emerged consequently [17], later to be complemented with the term "normative", which encompasses the differences in alexithymia between men and women posited to be caused by traditional masculine role socialization [12].

Primary alexithymia refers to a stable personality trait that is developed in early childhood and early adult years [18], with some causes of it being psychic trauma [19], negative attachment experiences [20] and genetic factors [9], such as genetic polymorphism of the 5-HT transporter-linked promoter region [21].

Secondary alexithymia, on the other hand, is a result of events that occur in the life course, both of psychological significance (e.g. adult trauma) or chronic medical illness, with its foundation lying in psychological and somatic (organic) causes [18]. Therefore, secondary alexithymia is a consequence of a disease, and while it might be serving as a defence mechanism to help in coping with stress and highly emotional events [22], it also can be a result of a brain injury (both direct and indirect insults to the brain) that leads to damage of the regions of the nervous tissue responsible for emotional processing in the right hemisphere [23, 24]. Therefore, the term "organic alexithymia" has been introduced for such nervous tissue aftermath insults, and was described in a detailed way in 2002 by Becerra *et al.* [24], and although it had been used before in 1990 by Savard and Andermann [25], its widespread use among researchers began with Becerra's and his colleagues' descriptive work.

Regarding brain structures and the damage to them responsible for the occurrence of secondary alexithymia, a few of them seem to play a decisive role. In their work on neurobiological underpinnings of alexithymia, Meza-Concha *et al.* [26] reviewed multiple papers concerning alexithymia and its neurobiological coordinates, mentioning damage to such structures as the amygdala, anterior cingulate cortex (ACC), anterior insula (AI), prefrontal cortex (PFC), cerebellum, and processes of abused interhemispheric connections being responsible for the occurrence of the trait. Patrikelis *et al.* [27], who also reviewed multiple papers regarding alexithymia's neurobiological coordinates, conclude that insulting the anterior cortical midline structures like the aforementioned ACC, AI and medial prefrontal cortex (mPFC) can possibly play key roles in secondary alexithymia, as these structures take part in regulating various processes of our emotional life. Through regulating the interoceptive processing (receiving and transforming bodily states into feelings), AI regulates the conscious self-awareness of emotions [28]; ACC regulates the process of interoceptive awareness and

mediates the appearance of emotional arousal, and along with mPFC regulates the limbic structures involved in generating emotions [27]. Papers reviewed in abovementioned studies on finding the damage to exact brain regions responsible for alexithymic traits were mostly based on careful examination of neuroimaging, including MRI, fMRI, PET and others. Worth mentioning is the fact that activation of the AI, ACC and mPFC is linked to, among other things, altruistic behaviour, empathic concern and perspective taking [29].

Organic alexithymia is common in many neurological conditions (e.g. various forms of dementia, stroke, epilepsy, traumatic brain injury, Parkinson's disease) due to alterations to the brain regions responsible for emotional awareness, mainly in the right hemisphere [16]. It coexists with cognitive impairment and is considered by some to be more resistant to treatment than other forms of alexithymia [30]. Worth mentioning is the classification of alexithymia based on clinical history, as proposed by Messina and colleagues [18], who stated that responses to treatment and outcomes in patients with organic alexithymia are better than in those suffering from the primary nature of the trait, but it must be underlined that authors emphasise the fact that this was based on the research studies and personal experience of one of them. Moreover, as underlined in their research, the involvement of the brain structures responsible for alexithymia (both primary and organic) cannot be used to differentiate the origin of the trait, and instead clinical symptoms and outcomes should be applied to distinguish one from another, with further research focusing on this subject required. Taking the above into consideration, clinical decisions regarding patients suffering from organic diseases should be examined with caution, depending on whether alexithymia derived from primary cause and has existed beforehand in such a patient, or is an acquired trait due to a brain illness and/or insult.

In their paper, Ricciardi *et al.* [16] suggested that alexithymia among patients with neurological diseases might be a manifestation of right hemispheric denial syndrome, as there is no control over the overall denial style in TAS-20. They also stressed that alexithymia is hard to distinguish from other subjective facets which concern feelings and that it might resemble aprosodic deficit, which is an inability to recognise and express affective or emotional information carried by the voice, which features, among other things, pitch, tone, rate and loudness, with emotional prosody being almost fully functional [31-33]. Alexithymia, on the other hand, is a global cognitive-affective deficit that concerns emotional awareness, diminished interest of one's own emotional life, and a paucity of fantasies.

Riccardi *et al.* suggest that such knowledge should be taken into consideration when assessing the trait among the aprosodic population. Their conclusion regarding the aforementioned issues is that TAS-20 should be contextually evaluated for patients suffering from various forms of neuropsychological deficits and that further researchers should consider switching to a more objective evaluation scale (i.e. Alexithymia Provoked Response Questionnaire).

ALEXITHYMIA AMONG STROKE SURVIVORS

A small number of studies show a linkage between alexithymia and psychiatric comorbidity following stroke. Among them is one from Wang *et al.* [34], who examined ninety patients (78 of them completing the study) with stroke, looking at associations of post-stroke alexithymia with post-traumatic stress disorder (PTSD) and psychiatric comorbidity. They discovered that at approximately 1 month after the stroke, alexithymia was positively correlated with severity of PTSD and psychiatric comorbidity, with DIF having the strongest association. They also found (controlling for variables of PTSD, physical disability, psychiatric comorbidity and the time elapsed since the occurrence of the stroke) that alexithymia was not associated with the aforementioned after three months following stroke, therefore, its influence over time disappeared. In another study of psychiatric comorbidity and alexithymia following stroke Hung *et al.* [35] investigated the role of alexithymia in post-stroke depression (PSD). 285 patients were enrolled in the study, with 93.3% completing it. The authors proved that higher levels of the alexithymia at the baseline of occurrence of the stroke, especially the difficulty in identifying emotions, were predictive factors for PSD in the next six months.

Bossu *et al.* investigated the association between disease outcome, alexithymia, depression and serum levels of pro-inflammatory cytokine interleukin-18 (IL-18) among stroke survivors. The findings of their study were that the IL-18 level increases specifically in patients with post-stroke alexithymia, and does not increase in healthy subjects and non-alexithymic patients. Also, a positive correlation was found between levels of cytokine and the trait, especially among patients with right brain damage (RBD). Moreover, alexithymic patients had more severe stroke in the acute phase than those who were non-alexithymic, with IL-18 not being correlated with stroke severity. The authors point to the clinical usage of their findings, proposing IL-18 as a factor of emotional awareness disturbances among stroke survivors [36]. Their study was later extended to the one conducted by Sacchinelli *et al.*, which showed that among healthy subjects there is a significant correlation between IL-18 levels and the alexithymic facet of having difficulties identifying feelings [37].

In 2001 Spalletta and colleagues conducted a study examining the effects of laterality and gender regarding alexithymic features in forty-eight post-stroke patients.

Patients with right brain damage (RBD) were more prone to develop alexithymia than those with left brain damage (LBD). Analysis of the data showed that only describing and identifying feelings, not the EOT facet, could distinguish patients with RBD and LBD, which leads to the conclusion that some – but not all – aspects of alexithymia are connected to the right hemisphere. The study also confirmed a previously reported discovery that alexithymia and depression are distinctive dimensionally, although alexithymia is a risk factor for post-stroke depression. Regarding gender differences, men with RBD scored higher on TAS-20 than men with LBD, but this observation did not apply to women, among whom both groups had high level of alexithymia [23].

In 2006 the same researchers examined fifty patients with a first-ever stroke diagnosis and a diagnosis of major depressive disorder towards alexithymia. Eighteen of them, with lesions more frequent in right hemisphere, proved to have alexithymia, as validated with TAS-20. Subjects were administered antidepressant therapy (sertraline or fluoxetine), and reassessed after eight weeks of treatment. The data collected showed that among non-alexithymia patients no significant changes were evident, but that among patients with alexithymia the decline in severity of the trait, unconnected to response to depression, was observed both with the identifying and describing of feelings, but not with the EOT facet. Surprisingly, the cognitive impairment measured by MMSE (Mini Mental State Examination) improved only in patients without alexithymia. The authors presume this was because of the low EOT facet interfering with cognitive recovery [38]. Similar conclusions regarding alexithymia and its treatment come from the study by Cravello *et al*., who found that both fluoxetine and venlafaxine lower alexithymia among patients with post-stroke depression, the latter being more effective than the former, which leads to the further conclusion that not only serotonergic, but also adrenergic transmission prove to have an impact on alexithymia among post-stroke patients [39].

Limitations of Spalletta's *et al.* studies were small groups of participants and exclusion of individuals with aphasia, which might back up the RBD as an important factor of organic alexithymia, since the patients with acquired language problems due to LBD embracing language areas would have been rejected, so further evaluation of the results should be conducted.

Using PET and self-report scales (including TAS-20), Paradiso *et al*. examined the effects of middle cerebral artery (MCA) stroke on emotional activity in neural areas distant from the insult. After the stroke, the anterior cingulate cortex (ACC) showed decreased neural activity, which resulted in reduced emotional awareness, thus inducing alexithymia among subjects. Moreover, the EOT facet did not decline in stroke subjects, so the findings were consistent with those by Spalletta *et al.* [38]. The authors stress that presentation of depression might be altered among alexithymic patients, therefore proper instructions should be given to such patients and their families concerning observing symptoms for the assessment of the hedonic tone of situations [40]. The sample of this study was relatively small (6 stroke subjects and 12 healthy volunteers), so further research is needed to confirm the findings.

In their recent study (2020), Hobson *et al*. examined the question of whether organic alexithymia was somehow determined by acquired language problems among chronic stroke patients. A sample of 118 patients was included, both with and without post-stroke language difficulties, and to overcome the problem of language-impaired patients self-reported data was supervised by a trained speech and language therapist. The research concluded that while patients with self-reported communication difficulties were prone to alexithymia, those with language-impairment and non-impairment that were tested with behavioural measures showed no difference in alexithymia levels. The authors emphasize the point that such results might be the cause of less sensitivity in behavioural measures than self-report tools. They also point out that future research is needed concerning short-term language impairments as being the cause of alexithymia, as they conducted their research at 6 months or later post-stroke. Contradictory to previously mentioned studies, they found that both RBD and LBD were the same risk factors for acquiring alexithymia [41]. Similarly, Paradiso *et al*. found, in their study of subjects with left basal ganglia stroke, that compared to healthy subjects patients with LBD scored higher on TAS-20. To explain this phenomenon they proposed that activity changes in the right hemisphere following LBD might help explain such observations [42]. There have also been studies which suggested that alexithymia appears due to the poor transfer of emotional information from right hemisphere to language regions in the left hemisphere [43-45].

DISCUSSION

Alexithymia is a common clinical problem among stroke survivors [23, 35, 36, 38, 39, 41]. Its occurrence among this population of patients is associated with elevated levels of interleukin-18 [36] and damage to brain structures which lie in the right hemisphere, mainly the anterior cingulate cortex (ACC), anterior insula (AI) and prefrontal cortex (PFC) [23, 26, 27], though insults to left hemisphere can also play an important, yet still not fully understood role [41, 42]. Alexithymia has a positive correlation with the severity of post-stroke PTSD [34] and is a predictive factor for depression in stroke survivors [35]. Venlafaxine, fluoxetine and sertraline should be considered for lowering the degree of alexithymia among post-stroke depression population, but little evidence is available so far [38, 39].

The papers mentioned have some limitations, which should be undoubtedly taken into consideration in further research. The exclusion of patients who have suffered from communication issues, especially those with LBD, makes studies less precise and does not show how many patients really suffer from post-stroke alexithymia and how LBD and language difficulties can affect the prevalence of the trait in this population; this is the case with the papers by Wang *et al.*, Spalletta *et al.*, Hung *et al.* [23, 34, 35, 38]. Hobson *et al.* [41] tried to overcome that problem through the oversight of a trained speech and language therapist in the assessment of the trait, yet their sample consisted of patients who had a stroke 6-months prior to the screening, thus some of their symptoms may have partially resolved and other vascular changes might develop [42].

Small sample size, as well as limitations on the type of stroke included, are factors that should make the studies by Hung *et al.*, Spalletta *et al.*, Bossu *et al.*, Cravello *et al.* and Paradiso *et al.* [23, 35, 36, 38-40] considered as preliminary, with stronger evidence embracing the broader range of locations of the lesions and choice of treatment is needed to confirm their findings. Another important thing that future researchers should take into consideration is the involvement of interhemispheric transfer in the role of alexithymia, bearing in mind that patients with communication difficulties should also be enrolled in such studies. Only a few studies have shown that LBD can also play an important role in the occurrence of the trait [41, 42], which can lead to the conclusion that abnormal information transfer between hemispheres is underestimated in research following organic alexithymia among stroke survivors, even though it seems to play an important role in the explanation of its origins.

CONCLUSIONS

Alexithymia is a prevalent issue among stroke-survivors. The ubiquitous assessment of the trait in this population ought to be considered, as alexithymia plays an important role in psychiatric comorbidity and severity of the stroke itself, and might indirectly interfere with the rehabilitation process [23]. Pharmacological treatment might help lower the alexithymia levels in post-stroke subjects, but there is little data on which drugs are preferable. The possible choice of psychotherapy should be adopted with caution, as psychodynamic therapy is contraindicated against patients with alexithymia. Further research is required to examine alexithymia's outcomes among patients with left brain stroke damage, its impact on other post-stroke psychiatric comorbidities, and to closely determine the best options for rehabilitation, pharmacological treatment, and psychological therapy.

Conflict of interest/Konflikt interesu

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