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WHAT IS STRESS IN EPILEPSY? A CONTENT ANALYSIS AND AN OPEN LETTER TO THE WORLD HEALTH ORGANIZATION (WHO): HIGHLY TIME TO DEFINE STRESS

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Abstract

Aim: Stress is one of the most researched issues in Behavioral Medicine and Health Psychology. The background review illustrated that much peer-reviewed quantitative studies do not define accurately the concept of stress in epilepsy and/or use a different rationale in their definition. This contributes further in major medical and psychological debates and research questions in the last decade of whether stress is 'epileptogenic' and 'seizure triggering' for epileptic patients.

Material and Method: The present qualitative study applied a content analysis on Chapter 5 of World Health Organization's (WHO) first and latest global report on epilepsy -from a Health Psychology point of view-, seeking for (i) a universal definition of stress in epilepsy, (ii) what stressors are more related to 'epileptogenesis' and 'seizure triggering' –if any- and (iii) any proposed stress relief and management strategies to be delivered by psychologists.

Results and Conclusions: Primary and secondary content analysis presented that WHO does not define stress as a single entity, but rather shows an unspecified link with 'social stigma' or 'social stressors'. Moreover, WHO does not show taking leadership in defining stress for research purposes. Lastly, there are some thoughts that although WHO applies the biopsychosocial model in this report, it considers that the 'psycho' part of the model concerns entirely the field of 'psychopathology'.

Keywords: Epilepsy, stress, epileptogenesis, seizure trigger, health psychology.

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INTRODUCTION

According to the first and latest global report on epilepsy published by the World Health Organization (WHO)[1] 'Epilepsy' is a chronic non-communicable brain disease that results mainly in 'recurrent epileptic seizures' defined as *'transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain'* (p.3). Epileptic seizures happen without any warning and result in some loss of awareness/consciousness, while objective medical diagnosis is made through the use of neuroimaging techniques and electroencephalography (EEG).[1]

Regarding 'Stress', the delineation in Health Psychology is based on the physiological response of the neuroendocrine system through the 'Hypothalamic Pituitary Adrenal (HPA) Axis' of the 'Sympathetic Nervous System' (SNS) of the 'Autonomous Nervous System' (ANS), known as the 'fight or flight response'[2] to any stressors as the first stage of the 'General Adaptation Syndrome' (GAS).[3,4] HPA Axis regulates stress and somatic functioning through the production of key hormones, such as cortisol, in order to keep organs in 'fight or flight' response of the SNS or the 'rest and digest' response of the 'Parasympathetic Nervous System' (PNS).[5]

In 'Behavioral Neuroscience' there is much growing evidence that stress 'triggers' particular brain loci -and possibly visa versa- that are associated with particular behaviors such as eating disorders.[6] In Psychology, the most important finding is that stress interplays with emotions in cognitive appraisals.[7] However, stress in 'Behavioral Medicine' has been qualitatively analyzed and given many delineations.[8-13] This is reflected much in present debates regarding what is the role of stress in epilepsy.

Historically, much literature relates epilepsy with mental disorders under the rationale of psychopathology and distress.[14,15] For instance, Diefendorf and Kraepelin[16] and Bleuler[17] supported that untreated epileptic patients could develop bipolar moods, touchiness, fearfulness and anxiety in parallel with anergia, bodily pain, and sleeping disorders. Since the 2000's it has been strongly supported that approximately 50%-60% of epileptic patients develop post-epilepsy mental disorders, of which the most common are depression, anxiety disorders and psychosis.[18-20] A review on neurological and psychiatric comorbidity in epilepsy presented that the prevalence starts as low as 10% for the general epileptic population and escalates as much as 80% in patients with temporal lobe epilepsy (TLE).[18] Bragatti et al. discussed that psychotic depression, depression and anxiety disorders are indeed the most common mental disorders in epilepsy, while the main risk factors include 'neurobiological', 'psychosocial' and 'pharmacological/iatrogenic' factors.[18]

Much attention has also been drawn upon 'Psychogenetic Non-Epileptic Seizures' (PNES) as a condition in which patients -exposed by objective EEG feedback- experience pseudo-epileptic seizures, resulting in some loss of awareness, without having epilepsy.[21,22] According to Bendadis up to 30% of visiting patients, who think they had suffered from their first epileptic episode, in neuro-epileptic centers in the USA are diagnosed with PNES.[23] Similarly, Perez and LaFrance's review discuss about an identical percentage -of which 80% consists of women- and that is diagnosed with PNES although the estimated prevalence is 0.00033%.[24] Perez and LaFrance continue that PNES is strongly related with prior mood disorders such as anxiety disorders, depression, post-traumatic stress and personality disorders.[24] Nowadays, it seems that neurological and psychiatric conditioning in epilepsy is clearly divided. PNES symptomatology in literature requires the existence of prior mental conditions without any pathology in the 'Central Nervous System' (CNS), while epilepsy results in mood disorders after its pathological development.

Regarding 'epileptogenesis' and stress, Gelisse et al. reported that only 22 out of 4,618 focal epileptic patients had experienced within the last months a major life changing events before their first epileptic episode, although that more than 50% of epileptic patients report 'stress' as the 'etiopathology' and 'seizure trigger' in epilepsy.[25] A recent meta-analysis on the prognostic, diagnostic and predictive biomarkers on epilepsy included cognitive and behavioral biomarkers in its research questions.[26] Amongst all 30 biomarkers summarized for the study, it was not discussed the role of Neuropeptide Y (NPY) as the specific biomarker related to stress management and treatment target,[27] although its role against stress is known since the 1980's.[28] On the contrary, Aguiar et al. in a literature review discussed that 'oxidative stress' may increase the likelihood of epileptic seizures

and that 'chronic oxidative stress' may have an essential role in epileptogenesis.[29] In another review, it was strongly supported that oxidative stress should be treated against epileptic seizures activity, cognitive impairment and neuronal loss in epilepsy combined with proper anti-seizure medication.[30] Again, Salim's review presented that 'emotional stress' affects the immune system and ANS through oxidative stress.[31] Furthermore, Wulsin et al.[32] showed that HPA Axis is hyperactive in TLE patients and that HPA Axis dysfunctioning in these patients may be due to abnormal connectivity with the limbic system, providing possible implications on the interplay of NPY, amygdala and the hippocampus as a stress relief mechanism.[27] Lastly, a current review reported that 'types of stress' are indeed 'seizure triggers', while the review included one study in which 'loss of child' was discussed as epileptogenic.[33]

Consequently, the obvious outcome is that stress plays a significant role in epilepsy. However, there are much different definitions of stress. Although almost all studies underline the significance of stress there are almost no studies defining stress. Additionally, the interplay between emotions and stress in epilepsy is exclusively communicated as 'depression' and 'anxiety' although there is evidence that these conditions concern hyperactivity of the HPA Axis in GAS on chronic stress.[27] Lastly, there is not any stressors' taxonomy, such as incompetence to deal with situation -based on self-efficacy[34,35] and locus-of-control[36] theories-, to prevent 'epileptogenesis', 'seizure triggering' and 'distress'.

Under this rationale, this study will perform a content analysis,[37] as a qualitative analysis of the surrounding meaning after locating the words related to 'stress', on WHO's report for epilepsy, named *EPILEPSY A public health imperative*.[1] It was considered that it may provide answers upon what is the common language and meaning of the word 'stress' and 'stressors' in the case of epilepsy as an internationally accepted reference for defining and explaining medical conditions.

METHOD

The present study intends to give a primary understanding on how stress is related to epilepsy.

The intention was created after the understanding that popular -based on Google Trends- free public web sources of information on medical issues -such as 'National Institutes of Health (NIH)', 'KidsHealth', 'WebMD', 'MedlinePlus', 'Drugs.com', 'NHS Direct', 'NetDoctor' and 'MayoClinics'- presented with unclear and confusing language the role of stress or stress related issues -and occasionally excluded it at all- in epilepsy and epileptic seizures.

Thereinafter, the researcher performed a background review in peer-reviewed studies, of which most are included in the introduction section, and indeed the initial hypothesis of confusing language was qualitatively confirmed.

After, WHO's foresaid report on epilepsy[1] was retrieved in order to answer the following questions.

1. How is 'stress' defined in epilepsy?
2. What 'stressors' are more related to epilepsy?
3. Are there any proposed strategies for stress management and stress reduction for epileptic patients?

The full report was downloaded in pdf form from WHO's official website. Then, the researcher searched for the word 'stress' on the text of 171 pages using the 'CTRL+F' button. It was initially considered that there would be some other words that would had been highlighted, such as '**stress**es', '**stress**ful' and 'di**stress**', or meanings, such as '**stress** management' and 'di**stress**ful situation' and which were intended to be included in the analysis.

All results were found in '*CHAPTER 5 The social response: misconceptions and stigma in epilepsy*' (p. 67-77). Consequently, the whole chapter was included in the analysis for a comprehensive understanding to answer the 3 research questions, while the rest WHO's report was excluded.

There was a primary analysis in order for the researcher to understand the meaning of the highlighted/spotted stress related words and phrases from their surrounding content. Then a secondary analysis took place on the whole chapter with a view for the entire concept of stress to be understood.

Due to the outcome, the researcher considered that question 1 and 2 have one answer.

Finally, the questions were answered and the study was conducted.

RESULTS

Primary analysis

After applying the 'CTR+F' button, 3 spots that contained 'stress' were highlighted and are as follows: '*stresses*', '*distress*', '*stress*'. The first analysis aimed to give a primary understanding on what the detected words are determined by WHO.

The first word 'stresses' was detected in the following sentence:

Further stresses and stigmatization can occur to those who are elderly (p.72)

The above sentence continues the meaning of the previous two sentences in which WHO discuss that epileptic people deal with five particular social conditions. The prior content is as follows:

Globally, stigmatized people with epilepsy are more likely to have lower self-esteem and quality of life, greater social isolation, poorer psychological health and worse epilepsy control. The burden of stigma, however, is greatest for people who live in low-income, less developed settings, and for this reason, stigma contributes to social and economic morbidity (p.72)

Using the phrase '*the burden of stigma*' and continuing in the next sentence using '*further phrases and stigmatization*', WHO provides a first understanding that stigma and stress interplay, co-exist or are co-morbidities. Qualitatively there is a schematic progression from stigmatization in epilepsy to particular social discrimination which is defined in continuum as 'stressors'.

The second word 'distress' was detected in the following sentence.

The psychological distress, failure of adjustment and coping, and self-perceived stigma contribute to poor quality of life (p.75)

The use of '*psychological distress*' works as an umbrella term for depression and anxiety. This is shown by the previous content:

Stigmatization and discrimination lead to worsening of psychological well-being, resulting in greater stigmatization than experienced before. Stigma is associated with higher levels of depression and anxiety. (p.75)

Consequently, the meaning of 'distress' is presented as a psychological phenomenon that includes anxiety and depression and works as a vicious cycle in epilepsy.

The third word 'stress' was detected in the next sentence:

In addition to personal impact, the family and care partners of people with epilepsy also experience increased burden and stress, and poorer family functioning. (p.75)

This explains in a more systemic manner that epilepsy affects also the family.

The primary analysis resulted into the ideas that (i) stress and stigma are identical or cannot be separated due to their interaction in a vicious cycle, (ii) stigma outcomes are actually 'social stressors', and that (iii) distress defines the psychological phenomena, leaving not much space for 'positive psychological phenomena' such as resilience,[38] post-trauma growth[39] as a 'positive personal change' form,[40] self-efficacy,[34,35] locus-of-control,[36] Sense-of-Coherence (SOC)[41] and Salutogenesis.[41,42]

Secondary Analysis

The analysis continued by applying content analysis to the whole Chapter 5 under the consideration of answering the research questions and after the first analysis outcome.

Secondary analysis showed that WHO considers that stigma is divided into two types: '*Felt (internalized) stigma*' and '*Enacted (institutionalized) stigma*' (p.69) similarly to theories of intrinsic and extrinsic stressors.[41,42] The difference between them is that the one is a product of inner decisions, i.e. '*people with epilepsy often make a decision about whether they will conceal their illness or not*' (p.69), which results in negative psychological phenomena, i.e. '*Keeping one's status of epilepsy a secret reduces the opportunities for enacted stigma but can cause substantial internal conflict and increased levels of social anxiety and felt stigma*' (p.69). On the contrary, the second type of stigma refers to social welfare, access to services and quality of interpersonal relationships, i.e. '*Respondents [...] reported barriers for people with epilepsy at the country level of difficulty in finding jobs, restriction at school, for marriage and children, social isolation by community, as well as discrimination by family and relatives*' (p.69).

After defining the two types of stigma, WHO proceeds to 4 thematic schemas. Firstly, WHO gives some attention to 'factors' that can predict stigma and include *'culture, demographics, illness-related and psychosocial factors'* (p.70). The most important finding that is linked to the research questions is that WHO clearly states '*Higher levels of felt stigma are associated with a reduced sense of self-efficacy, poor epilepsy outcomes and seizure severity*' (p.70) which gives some more support on the idea that stress is defined as a 'social stressor' in the name of stigma.

Secondly, WHO discusses about 'social misconceptions' on epileptic patients that result in stigma. WHO makes clear that these misconceptions depend from local cultures and result in labels such as '*crazy*' and '*possessed by demons*' (p.70). Much attention is given to support these misconceptions which are presented both to '*the general public*' and in people with authority in social services such as '*health care providers*' and '*teachers*' which lead to stigma (p.71).

Thirdly, WHO presents the '*consequences of stigma*' (p.72). Due to stigma, epileptic people tend to present '*lower self-esteem and quality of life, greater social isolation, poorer psychological health and worse epilepsy control*' (p.72). Then, the consequences are analyzed in 6 schemas which include 'marriage', 'driving legislation' as a sense of self-competence to travel for various aspects of life, 'insurance', 'school' in which WHO states that '*Removal from school or denial of access to school for a child due to epilepsy, because of their epilepsy, has lifelong impacts on the development of social, emotional and vocational skills*' (p.73), 'income and employment' in which WHO supports that globally there is some link to unequal opportunities and overall poorer quality-of-life which are measured in terms of psychological wellbeing, i.e. '*Stigmatization and discrimination lead to worsening of psychological well-being, resulting in greater stigmatization than experienced before*' (p.74).

Finally, WHO presents some solutions in the part '*Cultural approaches to reducing stigma*' (p.75-76). The first step is to reduce 'felt or internalized stigma' with 'counseling' and 'individual and group interventions', 'i.e. '*Counselling, individual and group interventions that develop resiliency in people with epilepsy have been shown to reduce stigma*' (p.75). It is noteworthy, that the use of the word 'resiliency' against stigma provides some concrete support that stigma is a stressor since resilience in Health Psychology has to do with stress, stressors, emotions, anxiety, depression, anger, adaptation, cognition and the immune system.[43] To proceed, according to WHO 'institutionalized stigma' will be reduced if the general population will be more informed on epilepsy, i.e. '*Studies show that people with less knowledge about epilepsy, or without personal contact with someone with epilepsy, have poorer attitudes*' (p.75). Thus, close people to epi-

leptics, policy makers, authority and influential figures in all social domains will adapt better attitudes. It is also proposed that by the time of the first diagnosis, patients and family members must be informed for the condition, i.e '*Providing people with epilepsy and their family with information about their disease at the time of diagnosis is a strategy for increasing disclosure rates.*' (p.76)

The secondary analysis provided the final answers to the research questions, which are given and discussed below.

DISCUSSION

Regarding research questions 1 and 2, stress, as a unique entity, is unclearly defined. There is much confusion on whether stigma is stress or stress related and WHO's rationale is far away from debates whether stress is 'epileptogenic' and 'seizure triggering'. Another idea is that WHO considers stigma to be a stressor – and the only one presented in the report- of societal background or that stress is 'social stress'.

It is assumed that WHO wants to discuss that 'social stress/stigma' derives on 'how' the epileptic patient would present the illness to themself and to the surroundings -family and society-; and what the surroundings will respond to the patient in a sense of family affairs –e.g. marriage- and social discrimination –e.g. job opportunities- that will altogether distress the person and his family.

It seems that WHO uses the biopsychosocial model of illness.[44,45] However, while the 'bio' part is covered by epilepsy, the 'psycho' part is entirely covered by distress. This implies that epilepsy predicts accurately depression and anxiety in epileptic patients, while WHO does not consider the 'positive psychological phenomena' in the 'psycho' part. For instance, 'resilience' against the illness may increase self-efficacy,[34,35] sense-of-control,[36] SOC[41] and produce the most for salutogenesis[42] for overall increase in 'quality-of-life' for the patient and the surroundings. It seems that there is an attempt to enclose the 'psycho' part into the frame of 'psychopathology' and to expel the positive phenomena to the 'socio' part of epilepsy, probably considering the positive phenomena as 'psychosocial' that can be communicated in the report as 'stigma'.

Lastly, WHO's report does not seem to take any effort to lead

and define 'stress' for research in epilepsy, but rather adapts a more 'prudent' flow of meanings in the content. The report reflects accurately the lack of a universal definition of stress in epileptic studies. Consequently, the outcome of the present study is consistent to the studies included in the background review and from which there is a clear lack of universal definition of stress.

Regarding research question 3, WHO supports that 'intrinsic stigma' –which probably is a result of emotional cognitive appraisal that results in stress- can be dealt with counseling and individual and group interventions. It is again unclear if the term 'counseling' and 'interventions' includes psycho-education and psychotherapy or behavior-change interventions on -for instance- healthy eating and physical exercise. The only in text support -which is again not directly manifested- is that people with epilepsy, their family and the public should be informed of epilepsy which probably implies that there should be psycho-education by the time of diagnosis, community and public interventions.[46] Furthermore, WHO supports that 'extrinsic stigma' -which probably refers more to 'conceptual stressors' of the social establishment such as laws, education and welfare- may be decreased by educating people with significant influence on emotions and emotional development, personal belongingness, self-efficacy and personal control over the situation of the epileptic patients. Such people are teachers, lawmaker, employers and the beloved ones. This includes mostly interventions at community and public level.[46] However, this is the interpretation coming from Health Psychology and these interventions and campaigns have nothing to do with stress as a neuroendocrinological response[47] –for which purpose the study took place-, but rather to decrease stigma.

Limitations

The present study uses qualitative research methods, thus there is a high risk of subjectivity in the outcome. Furthermore, the report, the illness and stress are seen from a point of view that reflects the rationale concerning Health Psychology. Lastly, content analysis was applied only on Chapter 5, and therefore it is proposed for any future study to include the whole report.

CONCLUSIONS

The analysis presented that WHO does not define stress as a single entity, but rather 'blend' it with 'social stigma/stressors'. Therefore, the research questions could not be directly addressed. Furthermore, there is no action on defining stress for research purposes. Finally, it is debatable whether WHO includes any positive psychology theories to the biopsychosocial model, since it may consider that the 'psycho' part of the model includes only 'psychopathology'.

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