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## Quality of Life and Psychiatric Aspects in Epilepsy

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### 1. Introduction

Epilepsy is a chronic disorder characterized by a spontaneous tendency for recurrent seizures which affects major aspects of a patient's life, including cognitive, behavioral, psychological and social functioning (Foldvary & Wyllie, 1999). It has been reported that cumulative lifetime risks for epilepsy and for any unprovoked seizure are 3.1% and 4.1% respectively in industrialized countries. Estimates of annual incidence of epilepsy are reported as high as 43 cases per 100,000 of the population in so-called developed countries, and are almost double this figure in the developing world (McHugh & Delanty, 2008). Another estimation points out that there are 50 million people who have epilepsy in the world (WHO 2001, Leonardi & Ustun, 2002). It was suggested that more than 80% of people with epilepsy live in developing countries, where the condition remains largely untreated (ILAE/IBE/WHO Annual Report, 1999; Meinardi et al., 2001).

### 2. Quality of life and psychiatric aspects in epilepsy

The science of health related quality of life (HRQOL) measurement rapidly evolved during the 1980s and 1990s within general health and in all medicine disciplines. (Tulsky & Rosenthal 2002). Despite a substantial increase in the number of published articles in recent years, research in the literature regarding the quality of lives of epileptic patients is relatively limited (Aydemir et al., 2004; Birbeck 2002). One of the most important reasons why HRQOL has become so important for those who engaged in epilepsy is related with well known characteristics of this disorder. Its chronic nature, presence of unexpected, intractable and/or frequent seizures, stigma and side effects of the antiepileptic drugs are some of these characteristics among others.

Epileptic patients experience various problems due to this disorder which will result in a lower quality of life. Seizure frequency, side effects of the antiepileptic drugs, psychological comorbidity and stigma are the factors which are associated with the severity of the disease and these factors may cause an important impact on life quality of epileptic patients.

Previous researches regarding quality of life (QOL) in epilepsy yielded contradictory results (Jacoby 1994; Leidy et al., 1999). Although most reports in this field share a common message emphasizing the negative effects of epilepsy on patients' HRQOL, there are still some other

studies which reported that this disease has little or no effect on epileptic patients' QOL (Jacoby 1994; Leidy et al., 1999). Some authors suggested that the impact of epilepsy might be minimal if the disease is well controlled and HRQOL of patients in this condition would be nearly the same as those of healthy controls (Jacoby 1994; Leidy et al., 1999). On the other hand, epileptic patients living in Europe and North America were reported to have significant impairment in HRQOL (Stavem et al., 2000; Buck et al., 1999). This discrepancy in reported results may well be related to methodological issues and/or cultural differences. However, one can easily notice that especially in studies conducted with larger samples it was found that HRQOL is decreased in patients with epilepsy (Baker et al., 2005; Baker et al., 1997).

Baker et al. reported that epilepsy has the potential to negatively affect different aspects of what is called "quality of life" (Baker et al., 2005). The authors collected data from 3889 patients with epilepsy from 10 different countries. In this multicenter survey it was concluded that the most commonly reported complaints interfering with daily living activities were nervousness, headaches and tiredness. Respondents in this study reported that their disease and its treatment had a significant impact on their HRQOL. Short Form-36 (SF-36) was used in Baker et al.'s study and patients scored significantly lower in domains such as physical and social functioning, energy and vitality (Baker et al., 2005).

In another multicenter (European) study again conducted by Baker et al. in 15 countries in Europe, data from more than 5000 patients were investigated and it was concluded that epilepsy had a negative effect on patients' social and psychological well-being (Baker et al., 1997). Argyriou et al. studied the impact of epilepsy on the psychological health and HRQOL of patients suffering from mild epilepsy in a rural area of southeastern Greece and reported that HRQOL of their patient sample was obviously affected while their psychological health remained nearly unaffected (Argyriou et al., 2004). Kutlu et al. investigated the HRQOL, anxiety and depression states of patients with epilepsy (PWE) (Kutlu et al., 2010). The SF-36 health survey scores were significantly lower in all subscales in PWE compared with the control group. Total scores for Beck Depression Inventory (BDI) were significantly higher in epilepsy patients. Hamilton anxiety scale were also found to be significantly increased in the epilepsy group. It was concluded that epilepsy significantly interferes with QOL and psychologic health of patients. In the patient group relationship between the seizure frequency and vitality was found to be statistically significant (Kutlu et al., 2010).

Women with epilepsy of childbearing age were reported to be at high risk of depression. Factors associated with depression include lack of occupation, the presence of an underlying disabling condition (with treatment), and the severity of epilepsy. Compared with the general population depressed women have greater impairment of HRQOL with epilepsy, which reflects the physical, social and emotional implications of the disease (Beghi et al., 2004).

Several comorbid psychiatric problems accompany the clinical picture in epilepsy. According to Kanner depression is the most common comorbid psychiatric disorder in patients with epilepsy though it remains underrecognized and undertreated (Kanner, 2003). According to Devinsky, seizures by definition change behaviour (Devinsky, 2004). Behavioural disorders are perhaps the most common and serious complications in epilepsy. For patients with difficult to control epilepsy, depression makes a greater contribution to impaired quality of life than seizure frequency (Devinsky, 2004). In an extended review reported by Gaitatzis et al. it was pointed out that 6% of people with epilepsy in the general population appears to suffer from a psychiatric disorder while this rate increases to 10-20% in patients with temporal lobe and/or refractory epilepsy (Gaitatzis et al., 2004). In general 30% of PWE suffer from depression, 10-20% from anxiety, 2-7% psychosis, 1-2% from personality disorders (Gaitatzis et al., 2004). On

the other hand, fear of seizures seems to play a very important role in psychiatric aspects of this disease. Newsom-Davis et al, stated that after an experience of a generalized epileptic seizure, a subsequent and anticipatory fear may well be seen in the sufferer (Newsom-Davis et al.,1998). Authors also underlined that there is a sufficient evidence in the literature suggesting that epileptic patients commonly fear death and or brain damage resulting from their seizures (Newsom-Davis et al.,1998). Furthermore there is a strong association between the degree of psychopathology and the intensity of patients fears.

To qualify as a specific phobia, the Diagnostic and Statistical Manual IV requires that the following criteria are met: (a) a marked and persistent fear is excessive or unreasonable and cued by the presence or anticipation of a specific object or situation; (b) exposure to the phobic stimulus provokes an immediate anxiety response; (c) the person recognizes that the fear is excessive or unreasonable; (d) the phobic situation is avoided or endured with intense anxiety or distress; and (e) avoidance, anxious anticipation, or distress in the feared situation interferes significantly with the person's normal routine, occupational functioning or social activities or relationships (Newsom-Davis et al.,1998; DSM-IV, 1994).

It is very well known that one of the most important features of epilepsy is stigma. De Boer et al. reviewed the global burden and stigma of epilepsy (De Boer et al., 2008). The authors stated that people with disabilities are among the most vulnerable in any society. Hidden disabilities such as epilepsy leads to even a greater vulnerability. Epileptic people may fear going outside their homes unaccompanied and they also fear what people might think of them if they were to have a seizure in public. Inevitably this leads to social isolation and participation restriction in the community.

In a recent study reported by Kanner et al. it was demonstrated that patients with subsyndromic depressive episodes (SSDEs), major depressive episodes (MDEs), anxiety disorders, and mixed MDEs (or SSDEs) with anxiety disorder(s) have a significantly worse quality of life than asymptomatic patients (Kanner et al., 2010). Authors also suggested that the comorbid occurrence of mixed MDE/anxiety disorders (particularly in the presence of more than one type of anxiety disorder) and SSDE/anxiety disorder yielded a worse impact on HRQOL than the occurrence of anxiety disorders alone. Another important finding of this study was that the comorbid occurrence of depressive and anxiety disorders have been found to have significant clinical implications beyond their impact on HRQOL which include:

1. An increased suicidal risk.
2. A worse course and poorer response to treatment of a depressive disorder
3. An increased risk of MDE recurrence. types of anxiety increased the probability of a new depressive episode.
4. An increased risk of failure to achieve a seizure-free state following an anterotemporal lobectomy in patients with pharmacoresistant temporal lobe epilepsy (Kanner et al., 2010).

Literature survey reveals enough evidence regarding the negative impact of mood disorders and anxiety symptoms on the quality of life of patients with epilepsy (PWEs) (Perrine et al., 1995; Gilliam, 2002; Cramer et al., 2003; Boylan et al., 2004; Johnson et al., 2004; Loring et al., 2004; Tracy et al., 2007). Symptoms of depression and anxiety are independently associated with reduced HRQOL; psychiatric comorbidity explains more variance in HRQOL than the combined groups of clinical seizure or demographic variables (Johnson et al., 2004). A study with a large sample included 435 PWEs aiming to investigate the relative impact of mood and anxiety symptoms as well as social and seizure related variables on HRQOL (Tracy et al., 2007); the presence of depressive symptoms was the strongest predictor of the composite

and subscales of the Quality of Life in Epilepsy instrument used (QOLIE-31). In none of the cases did the severity of symptoms of depression interact significantly with the other variables, suggesting that its effect on HRQOL was direct and not mediated by other factors. In other studies conducted on patients with pharmacoresistant temporal lobe epilepsy (TLE), symptoms of depression were found to be the strongest independent predictors of poor quality of life but (unexpectedly) not the seizure frequency or severity (Perrine et al., 1995; Gilliam, 2002; Boylan et al., 2004). All of the mentioned studies relied on screening instruments identifying symptoms of depression and anxiety, but did not generate psychiatric diagnoses of mood or anxiety disorders, based on predetermined diagnostic criteria, such as those suggested by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV-TR, 2000). The lack of a DSM-IV-TR diagnosis does not invalidate the significance of the data cited earlier. Studies on primary mood disorders emphasised the relatively high prevalence and significant clinical impact of subsyndromic forms of depressive disorders (Van Praag et al., 2004). Whether subsyndromic depressive episodes (SSDEs) differ from major depressive episodes (MDEs) or anxiety disorders in their impact on HRQOL of PWEs is yet to be established. The purpose of van Praag et al.'s study was to test the following four hypotheses:

1. Patients with SSDEs, MDEs, and anxiety disorders have worse HRQOL than asymptomatic patients,
2. The more severe forms of depressive episodes (e.g., MDEs) have a greater negative impact on HRQOL measures than SSDEs,
3. Depressive and anxiety disorders do not differ in their impact on HRQOL,
4. Comorbidity of MDEs and anxiety disorders, but not of SSDEs and anxiety disorders, has a worse impact on HRQOL than MDEs and anxiety disorders alone (Van Praag et al., 2004).

According to Winter, self-esteem is the most important part of the ego, which is also the most important factor contributing to psychosocial well-being (35). The most important determinants of self-esteem are (1) what we think of ourselves, as a reflection of what the people we care about think of us; (2) how we evaluate ourselves in comparison to other people; and (3) our ability to reach a positive outcome concerning issues that are important to us (Winter, 1996). Literature survey reveals contradictory data regarding the correlation between epilepsy and self-esteem (Winter, 1996; Reeve & Lincoln, 2002; Lee et al., 2008). Gauffin et al. studied self-esteem, and sense of coherence in a group of young adults with epilepsy and compared the results with those obtained five years earlier (Gauffin et al., 2010). The authors found that there was a decline in both sense of coherence and self-esteem overtime in young adults with epilepsy. On the other hand Lee et al. reported that epilepsy in general has little impact on overall self-esteem in adolescents (Gauffin et al., 2010).

As it was mentioned above several comorbid psychiatric problems such as depression, anxiety, psychosis and personality disorders accompany the clinical picture in epilepsy. One should also bear in mind the important role of antiepileptic drugs (AEDs) in psychopathology of epilepsy (Mula & Monaco, 2009). Mula and Monaco have drawn attention to the risk benefit ratio of AED usage in epilepsy. Possible adverse effects of AEDs include behavioural problems and psychiatric disorders. According to the authors it is often difficult to determine which psychopathological manifestations are due to the drug therapy and which may be due to the characteristics of epilepsy disease itself. Mula and Monaco concluded that the most commonly reported psychiatric adverse effects of AEDs are non-specific behavioral problems (Mula & Monaco, 2009). Among specific psychiatric diagnoses, depression is the most commonly reported. Psychosis is much less frequent.



In a study which investigated the sociodemographic and clinical factors associated with depression in epilepsy it was reported that, depressed subjects with epilepsy were significantly less likely to be married or employed and more likely to report comorbid medical problems and active seizures in the past 6 months (Thompson et al., 2009). Another important conclusion of this study was, when adjusted for all other variables, subjects with epilepsy reporting lamotrigine use were significantly less likely to be depressed compared to those not reporting lamotrigine use (Thompson et al., 2009).

In a review covering 35 years of research specifically devoted to QOL in adult epilepsy, Leone et al. classified the questionnaires used in epilepsy according to validation, diffusion of use and specificity of domains characteristics (Leone et al., 2005). The authors concluded that questionnaires covering all three aspects (Washington Psychosocial Seizure Inventory (WPSI), Epilepsy Surgery Inventory 55 Survey (ESI-55), Quality of Life in Epilepsy Inventory (QOLIE-89), QOLIE-31, QOLIE-10, Liverpool Batteries) should be preferred when planning a QOL study in epilepsy. However those covering only two aspects (SF-36, The Side Effect and Life Satisfaction (SEALS) inventory, Epilepsy Psychosocial Effects Scale (EPSES), Performance, Sociodemographic aspects, Subjective evaluation/estimation questionnaire (PESOS), Quality of Life Assessment Schedule (QOLAS) could also be useful in selected situations or may become a first-choice instrument in the future, after more widespread use or complete validation (Leone et al., 2005). On the other hand Wiebe et al. aimed to determine the minimum clinically important change, and small medium, and large changes in broadly used epilepsy specific and generic HRQOL instruments and found that QOLIE-89, QOLIE-31, SF-36, SF-36 physical composite score and HUI-III (health utility index mark III) differentiated between no change and minimum important change with precision (Wiebe et al., 2002). Birbeck et al. in their study evaluating ability of HRQOL measures to detect change overtime in people with epilepsy, suggested that SF-36 yielded responsiveness indices comparable to those of the epilepsy targeted (specific) measures (Birbeck et al., 2000).

In a randomized controlled study May and Pfäfflin emphasized the efficacy of an educational treatment program for PWE. Modular service package epilepsy (MOSES) which was developed to improve patients' knowledge and understanding about their epilepsy, its treatment and psychosocial consequences, was used in the study. The study clearly indicated the need for patient education. Even patients with a long history of epilepsy and with additional handicaps or diseases benefitted from the MOSES program (May & Pfäfflin 2002).

Psychologically, persons with epilepsy may have feelings of worthlessness, fear, stigma, anger, and hopelessness, and may exhibit passive behavior (Chen et al., 2010). Stigmatization leads to discrimination, and people with epilepsy have been the target of prejudicial behavior in many aspects of life, over many centuries and in many cultures (De Boer et al., 2008; Pahl & De Boer, 2005). These factors decrease their psychosocial function, self efficacy, and quality of life (Chen & Tsai, 2003; Pramuka et al., 2007) and even increase the suicide rate (Bell et al., 2009).

Evidence shows that there is a spectrum of cognitive, behavioural and psychiatric disorders that accompany many forms of epilepsy. New discoveries may contribute to the development of therapies and management techniques that will better enable physicians to treat the full spectrum of disorders that epilepsy and tails (Berg, 2011).

ILAE recently recommended that the term "benign" no longer be used to describe epilepsy, precisely because of the large number of disorders often seen in association with even relatively uncomplicated epilepsy (Berg et al., 2010). Berg suggested that any patient with epilepsy should be viewed as someone who is at risk of encountering a variety of consequences including cognitive problems, behavioural disorders, depression, suicide and also sudden death (Berg, 2011).

### 3. Conclusion

Epilepsy, with its rich clinical features, is particularly important for HRQOL research. Despite a substantial increase in the number of published articles in recent years, research in the literature regarding the quality of lives of epileptic patients is relatively limited (Aydemir et al., 2008; Birbeck et al., 2002). Most of the current reports in this field share a common message emphasizing the negative effects of epilepsy on patients' HRQOL. Epileptic patients may experience various problems which will result in a lower quality of life. Seizure frequency, side effects of the antiepileptic drugs, psychological comorbidity and stigma are important factors associated with the severity of the disease and these factors may cause an important impact on life quality of epileptic patients. Stemming from a thorough review of the current literature, we can conclude that there is still a need for further scientific research with further validated instruments to find out more clear relation between epilepsy and HRQOL.

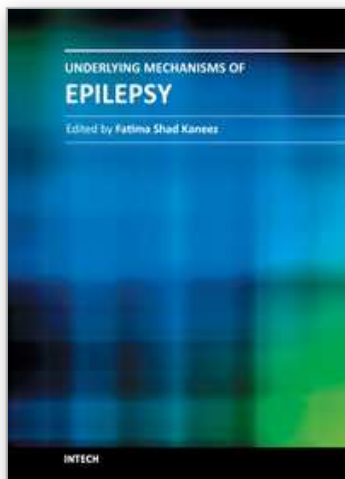
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## **Underlying Mechanisms of Epilepsy**

Edited by Prof. Fatima Shad Kaneez

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This book is a very provocative and interesting addition to the literature on Epilepsy. It offers a lot of appealing and stimulating work to offer food of thought to the readers from different disciplines. Around 5% of the total world population have seizures but only 0.9% is diagnosed with epilepsy, so it is very important to understand the differences between seizures and epilepsy, and also to identify the factors responsible for its etiology so as to have more effective therapeutic regime. In this book we have twenty chapters ranging from causes and underlying mechanisms to the treatment and side effects of epilepsy. This book contains a variety of chapters which will stimulate the readers to think about the complex interplay of epigenetics and epilepsy.

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