

Patient perceived cognitive side effects of anti-epileptic drug treatment: An international perspective



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Introduction

- Cognition refers to high-order processes primarily involving the cortical structures of the brain to programme adaptive behaviour, to solve problems, memorise information and focus attention¹
- The relationship between cognition and epilepsy is complex and the exact cause of cognitive impairment is often unknown. However, three factors are clearly involved: aetiology, seizure activity and central nervous system side effects of drug treatment¹
- The relationship between epilepsy and cognitive impairment and the detrimental effect on cognitive function associated with some anti-epileptic drugs is well established;² however, the effects on individuals with epilepsy in terms of quality of life are less well understood
- A large, international survey of individuals with epilepsy was carried out to gather information about experiences relating to cognitive impairment and epilepsy, effects on areas of quality of life and perceptions on the likely contributing factors to impaired cognitive function

“ I’ve lost confidence in public speaking (I used to teach science), knowing that I will have difficulty finding the words that I want to use ”
respondent

Methods

A nine-item questionnaire comprising a combination of forced-choice and open-ended questions was distributed to 4,500 members across nine Chapters of the International Bureau for Epilepsy (IBE) – Austria, Belgium, Denmark, France, Ireland, Israel, Malta, Norway and Scotland – in July 2004. A total of 500 questionnaires were distributed in each of the nine Chapters and recipients were selected at random from the Chapter membership database. Responses were collected via return of completed questionnaires by post using pre-paid envelopes. All responses were kept strictly anonymous.

Results

Sample characteristics

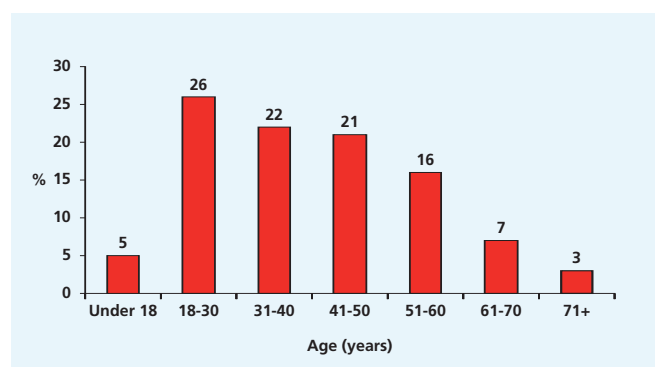
A total of 837 completed questionnaires were returned and analysed (19% return). Table 1 shows the breakdown of responses per country.

Table 1: Number of completed questionnaires included in the data analysis per country

| Country | No of completed questionnaires |
|----------|--------------------------------|
| Ireland | 171 |
| Scotland | 169 |
| Norway | 136 |
| Israel | 87 |
| Denmark | 85 |
| Belgium | 73 |
| Malta | 68 |
| Austria | 26 |
| France | 22 |

The average age of respondents was 40 years (Figure 1), with 53% of the sample female and 46% male (9 respondents did not state gender). The vast majority (95%) of respondents reported to be taking medication for their seizures and 60% of this group were taking multiple anti-epileptic drugs (AEDs) compared with 39% on monotherapy. Length of time on therapy ranged from 1 month to 74 years, with an average duration of 18.07 (±14.47) years across the sample.

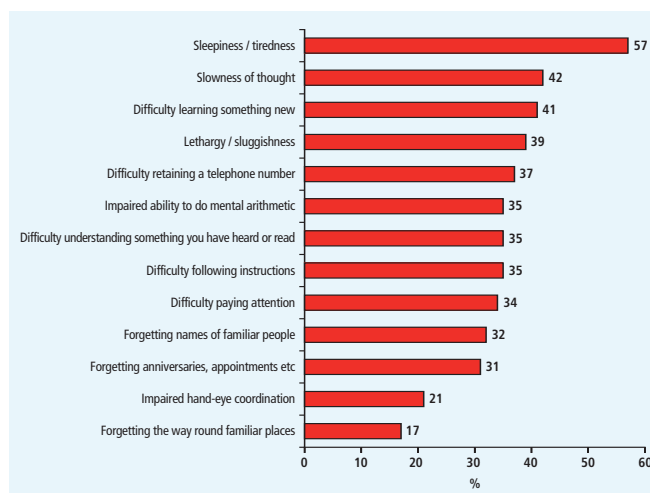
Figure 1: Age distribution across sample



Indicators of cognitive impairment

Figure 2 summarises indicators of cognitive impairment where respondents reported that they experienced difficulties ‘moderately’ or ‘very much’. Sleepiness / tiredness, slowness of thought and difficulties learning something new were the most frequently reported indicators of cognitive impairment, identified by 57%, 42% and 41% of the sample respectively.

Figure 2: Frequency of responses on indicators of cognitive impairment where respondents report difficulties ‘moderately’ or ‘very much’



Two-thirds of respondents stated that the difficulties reported in areas of cognitive function were related to their condition or AED therapy, with 41% attributing cognitive impairment to a combination of their condition and medication, 16% associating cognitive impairment with their medication alone and 9% attributing difficulties experienced to their epilepsy.

“ The effect of memory loss is too incidental not to be associated with regular intake of anti-epileptic medication ”
respondent

Relationships between variables

Relationships between indicators of cognitive impairment were explored using factor analysis. Four factor structures were identified: attention and thought processes, memory, sleepiness / lethargy and hand-eye coordination (Table 2). Results of the factor analysis confirm groupings of indicators, which reflect key areas of cognitive function assessed in the survey.

Table 2: Summary of results from factor analysis highlighting the relationships between different indicators of cognitive impairment. Average intercorrelations and alpha values suggest four key groupings of variables, which can be described as: attention/thought processes, memory, sleepiness/lethargy and hand-eye coordination

| Factor | Variables | Oblique loadings | Avg inter-correlation | Alpha value |
|-------------------------------|---|--------------------------------|-----------------------|-------------|
| Attention / thought processes | • Difficulty understanding something you have heard or read | 0.82 | | |
| | • Difficulty learning something new | 0.80 | 0.72 | 0.84 |
| | • Difficulty paying attention | 0.79 | 0.69 | 0.87 |
| | • Difficulty following instructions | 0.68 | 0.66 | 0.88 |
| | • Slowness of thought | 0.68 | 0.65 | 0.90 |
| | • Impaired ability to do mental arithmetic | 0.59 | 0.61 | 0.90 |
| | Memory | • Retaining a telephone number | 0.81 | |
| | • Forgetting names of familiar people | 0.78 | 0.57 | 0.72 |
| | • Forgetting anniversaries, appointments etc | 0.71 | 0.57 | 0.80 |
| | • Forgetting way around familiar places | 0.65 | 0.53 | 0.82 |
| Sleepiness/ lethargy | • Sleepiness / tiredness | -0.85 | | |
| | • Lethargy / sluggishness | -0.77 | 0.63 | 0.77 |
| Hand-eye coordination | • Impaired hand-eye coordination | 0.87 | | |

No significant relationships were found between factors or individual indicators of cognitive impairment and sample characteristics including age, time on medication and mono / polytherapy.

The strongest correlations between variables and sample characteristics found were: increasing age and the likelihood of memory impairment (0.247) and reduced quality of life associated with polytherapy (0.204).

“ Medication helps to prevent fits, but makes me tired, confused and slow ”
respondent

Effects on quality of life

More than half (59%) of respondents reported that difficulties with cognitive function had prevented them from achieving a goal and 50% stated that their quality of life had been adversely affected (‘moderately’ or ‘very much’) including:

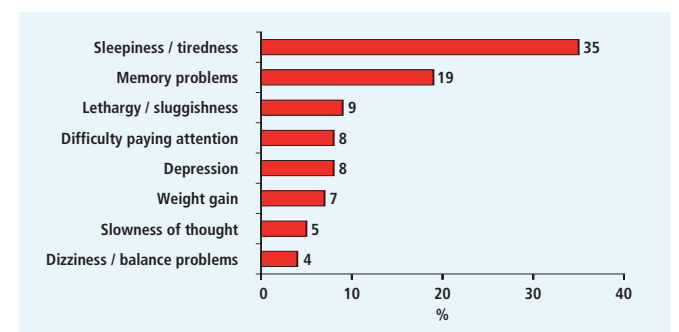
- Work (48% of respondents)
- Education (46%)
- Relationships (48%)
- Leisure pursuits (44%)

Side effects of AEDs

In an open question asking respondents to identify side effects that they would most like to avoid, indicators of cognitive impairment were reported more frequently than other commonly experienced side effects, with sleepiness / tiredness, memory problems, lethargy / sluggishness and difficulty paying attention reported most frequently. The frequency of side effects identified as those which respondents would most like to avoid are summarised in Figure 3.

“ The tiredness & lethargy seem to be related to my medication and the epilepsy seems to have scrambled my thoughts. Some days are worse than others ”
respondent

Figure 3: Frequency of side effects identified by respondents as those that they ‘would most like to avoid’



Conclusions

- Results provide an insight into the potential burden of cognitive impairment relating to epilepsy and AED therapy on individuals with epilepsy and highlight the importance ascribed to minimising cognitive impairment by a patient population
- Findings suggest that individuals with epilepsy perceive that impairment to cognitive function related to either their condition, AED therapy or a combination of both, has a detrimental effect on the ability to undertake everyday activities and areas of quality of life including education, work, family life and leisure pursuits
- Although this survey is restricted in terms of bias in sample and measurement, results provide an important basis for future research into the effects of cognitive impairment on quality of life measures and direct impact of cognitive side effects related to AED therapy, from the perspective of individuals with epilepsy
- Results from this survey provide a useful context for the interpretation of clinical and psychometric studies of AED therapy and cognition and how this is applied in clinical practice

References
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