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THE BNI SCREEN FOR HIGHER CEREBRAL FUNCTIONS IN 40 MULTIPLE SCLEROSIS PATIENTS

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SUMMARY

We used the Barrow Neurological Institute Screening (BNIS) to assess higher cerebral functions in multiple sclerosis (MS) patients. The French version of the BNIS was administered to 40 remitting-relapsing multiple sclerosis (RR-MS) patients less than 5 years after onset. In order to assess the influence of depression and anxiety on cognitive performance, we administered the Spielberger Anxiety Scale and the Beck Depression Inventory. The mean BNIS score in our population (45.9) is lower than the general population (48.2). The main errors involve arithmetic problems, reverse digit span, visual sequencing tasks, number-symbol association items, and spontaneous affective expression. Attention and concentration, working memory, visuo-spatial skills and conceptualisation are altered. Moreover, an anxiety state is linked to attention performance. Our results confirm previous studies on MS cognitive impairment, as well as the sensitivity of the BNIS short screening (15 minutes to complete). This test is also valid with recent-onset MS patients.

INTRODUCTION

Multiple sclerosis (MS) is the most frequent non-traumatic neurological disease in young adults. Cognitive and emotional disturbances in advanced multiple sclerosis (MS) were clinically identified by Charcot (1875). Since 1985, cognitive impairment has been better and better assessed and documented (Rao, 1986). However, there has been no short, sensitive screening

test to detect alteration of higher cerebral functions, including affective aspects, in MS. Indeed, the Mini Mental State Examination (MMSE) is neither sensitive nor reliable for the MS population. Therefore, we intend to show the clinical value of the BNI Screen for Higher Cerebral Functions in MS, even in recent-onset patients.

Cognitive impairment in MS

In MS, neuropsychological investigations have shown that cognitive disorders are common (about 60% of MS patients) throughout the disease cycle (Rao et al., 1991). These disorders are even observed at the early stage of MS (Truelle et al., 1987), and they are a good marker of diffuse brain abnormalities in early RR-MS (Deloire et al., 2005). Moreover, even with patients having a clinically isolated syndrome suggestive of MS, such as a first episode of optic neuritis, early cognitive impairment is frequent (57%) (Lyon-Caen et al., 1988; Feuillet et al., 2007). This mainly affects attention, memory, information processing speed, inhibition and conceptualisation. Nevertheless, cognitive impairment is usually mild to moderate. Only 5% to 20% of MS patients will develop dementia (Buchanan et al., 2005).

Cognitive dysfunction is not correlated with either disability level and disease length or depression. In their study, Deloire et al. (2005) confirm that cognitive impairment, in the early stages of RR-MS, is not related to depression, assessed by the Montgomery and Asberg Depression Rating Scale (MADRS). In addition, the health-related quality of life score (assessed by SEP 59) is related to information processing speed and attention.

Patients with progressive MS, especially the secondary progressive form (SP-MS), do not perform as well on cognitive tests as RR-MS. Neuroanatomical research suggests that both gray and white cerebral matter atrophy contributes to neuropsychological deficits in MS (Sanfilipo et al., 2006).

Emotional disturbances in MS

As first reported by Charcot (1875), explosive laughing and crying, as well as euphoria, occur in about 10% of MS patients (Feinstein et al., 1997). These emotional dysfunctions are always associated with cognitive impairment. Moreover, these patients have more physical disability and have usually entered the chronic progressive stage of the disease (Feinstein et al., 1997). Emotional problems have a high prevalence throughout the course of the disease, the two major forms being depression and anxiety. The lifetime risk for a major depressive disorder, as defined in DSM IV, is around 50% in MS (Siegert et al. 2005). Cognitive impairment can occur with or without depression, and the origin of depression in MS is likely to be multifactorial (Goldman Consensus Group, 2005). The prevalence of depression is around 30% one year after the first onset (Jouvent et al., 1989). In half of the studies, depression is related to cognitive impairment, but not with disease duration or with functional impairment (Iwasaki et al., 2005). Depression is more

frequent in secondary progressive (SP-MS) than in primary chronic progressive MS (PP-MS) (Vleugels et al., 1998) and RR-MS.

Two explanations have been proposed:

1) cerebral lesions are more important in SP-MS;
2) stress might be caused by the effort to find a new way of coping.

Anxiety is frequently overlooked, whereas the lifetime prevalence of some kind of anxiety disorder is recorded in 35.7% of MS patients (Korostil & Feinstein, 2007). Anxiety disorders are frequent and represent a cause of disability in MS, but their impact on intellectual performance is not well documented.

METHODS

Ethical approval

Our research received approval from the Ethics Committee at Necker Hospital, in Paris. Written informed consent was requested both after the description of the study and before the assessment.

Population

40 patients were included in the study: 25 women and 15 men suffering from RR-MS (according to Mc Donald's criteria, 2001) for less than 5 years (m=3 years; s.d.=1.54). They were recruited in the neurology department of Foch hospital by the fourth author of the present study. The inclusion criteria were as follows:

- right-handedness;
- age 20 to 55 years (mean = 37.8; s.d.=8.4);
- native French speaker or having attended a French school;
- RR-MS in clinical remission.

The exclusion criteria were as follows:

- psychiatric or somatic diseases leading to a handicap;
- severe life events (such as relative's death) over the last 6 months before assessment.

Information on the disease type, duration, treatment and disability status (Expanded Disability Status Scale, EDSS, Kurtzke) were documented by the neurologist. 14 patients were receiving continuous treatment, either Interferon or Glatiramer Acetate. 26 patients were not receiving any chronic treatment.

Procedure

Cognitive skills were assessed via a brief neuropsychological screening with the Barrow Neurological Institute Screening for Higher Cerebral Functions (BNIS). The BNIS provides both qualitative and quantitative information. The final version and validation were published by Prigatano (1995).

We used the French version, proposed and validated by Truelle, Joseph, Mazaux, Manning in 1998 and published by Truelle et al. (2004). It begins with a preliminary assessment of awareness, communication and cooperation, in order to determine whether the patient can be assessed in a reliable way. Then the BNIS itself is administered. It is composed of seven subscales:

- speech/language;
- orientation;
- attention/concentration;
- visuo-spatial;
- problem solving;
- memory;
- self evaluation of performance.

Each subscale comprises a few questions submitted by the examiner via a pocket manual. It does not require special training, as long as the examiner is skilled in neuropsychology.

The maximum BNIS score is 50 and the minimum is 3. Validation studies have shown that a score lower than 47 accounts for a deficit under the age of 55; for older people, the cut-off score is 43. Administration time depends on the patient's impairment. It takes around 15 minutes to administer.

Depression and anxiety were assessed by self-rating questionnaires:

- the Beck Depression Inventory (BDI, Beck, 1996);
- the State-Trait Anxiety Inventory (STAI, Spielberger, 1983).

Both have been validated in French.

In the BDI, 21 items (each item is assessed on a Lickert scale, 0-3) which are scored in order to determine depression intensity : 0-4 = no depression; 4-7 = mild; 8-15 = moderate; 16 or more = severe.

The French validated version of the STAI is divided into two parts. 20 items assess a state of anxiety and 20 a trait of anxiety. A low score on the global scale and on each specific subscale means a low level of anxiety.

RESULTS

The 40 RR-MS patients show a mean score of 45.9 ± 3.13 on the BNI. This score confirms that cognitive deficits may occur in the early stage of RR-MS.

The errors involved 4 areas mainly:

- arithmetic;
- attention/concentration;
- visuo-spatial praxis;
- affect.

The following items are concerned:

- Solving mental arithmetic problems: 14/40 subjects failed.
- Repeating 5 digits in the reverse order: 13/40 failed.
- Solving a visual sequencing task: 13/40 failed on this item.

- Criticism of the meaningless drawing "lemon forbidden": 14/40 failed
- Emotional expression: 12/40 failed.
- Training on number-symbol association items: 23/39 subjects received full credit; 8/39 subjects failed for one symbol; 6/39 for two symbols; 2/39 for three out of four.
- Awareness of self-performance: 8/40 underestimated and 3/40 overestimated their performance.

Gender, age and cultural level

There is no significant difference on the global BNIS score between males (mean 45.93 ± 2.6) and females (46.02 ± 3.47). In this young adult group (20 to 55 years of age) there was no difference between the younger (<38 years) and older adults (> 38 years) on the BNIS global score. Seven patients had a low education level, 12 a middle level of education and 21 a higher education. We observed that the higher the educational level, the better the BNIS total score (r=05402; p=0.0003), the visuo-spatial subscore (r=0.4435; p=0.004) and the affect subscore (r=0.4834; p=0.001).

Disease duration, disability scale and treatment

Regarding the duration of MS, we compared two groups: 12 patients under 2 years after onset and 28 patients between 2 and 5 years after onset. BNIS results did not correlate with RR-MS duration. There was no relationship between the disability score and the BNIS.

No significant difference was found between patients with (n=14) or without chronic pharmacological treatment (n=26).

Depression

Out of 40 patients, 22 had no depression (following BDI and DSMIV criteria for depression); 11, mild; 6, moderate; and 1 severe depression. No relationship appeared with the BNIS global score or subscores.

Trait anxiety

Of the 40 patients, 16 had a moderate level of trait anxiety, and 4 a severe level. 20 patients had mild or no trait anxiety. No relationship appeared with the BNIS scores.

State anxiety

The more anxious the subjects felt, the poorer their performance on the attention subscale of the BNIS.

DISCUSSION

The mean BNIS global score for the RR-MS is lower (45.9) than in the healthy French population (48.2) (Truelle and al., 2004). A validation study on

the BNIS French version has shown that a score of less than 47 under the age of 55 indicates a deficit. This corresponds to the validation data for the original English version of the BNIS (Prigatano, 1995). In our MS group, the main problems relate to attention and concentration, working memory, visuo-spatial skills and conceptualisation. These results confirm previous studies on cognitive impairment in RR-MS and the sensitivity of the BNIS short screening, even in recent-onset MS.

Frequent failures were observed on the spontaneous affect items characterized by the drawing "lemon forbidden" on the one hand, and the verbal expression of affect on the other. This result shows the originality of BNIS as compared to other classical neuropsychological tests, which do not usually include emotional assessment.

This result is consistent with our observations on alexithymia in MS. Alexithymia is characterised by an inability to express or discern feelings and emotions (Sifneos, 1973). In other studies, we described a high incidence of alexithymia in MS patients (50%) as compared to the general population (9%) by using the Toronto Alexithymia Scale and the Parallel Visual Processing Test (Montreuil, Lyon-Caen, 1993; Pelletier et al., 1998). In addition, a neuropsychological model of emotional transfer via the corpus callosum is supported, since corpus callosum lesions are frequent in MS (Pelletier et al., 1996).

In our study, state anxiety is related to a lower performance on attention tasks. In the normal population it is well known that anxiety decreases the ability to focus attention. In MS, anxiety is underestimated because it is not usually assessed. It is necessary to take it into account for all MS disabilities. However, depression and anxiety do not explain impaired performances on different cognitive skills.

Taking in account the relatively high number of failures and item concerns on BNIS, it could be foreseen that more significant correlations would occur in a larger series.

CONCLUSION

This study shows the sensitivity and specificity of the BNIS, even in MS patients with mild cognitive impairment. Our aim is to show that in daily clinical practice, dealing with MS patients at the early stage of the disease, the BNIS is useful and efficient for a short screening in order to detect both cognitive and emotional impairment. This detection could help the clinician to better understand some subjective complaints and then refer the patient for psychological support and neurorehabilitation.

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