Handedness, cognitive processing and intelligence in patients with epilepsy

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Summary

Introduction. The current knowledge of significance of some neurobiological and clinical variables for the development of cognitive deterioration in patients with epilepsy remains sparse and controversial.

Aim. The current study has been carried out in order to elucidate the role of handedness in terms of influence on cognitive processing and intelligence in patients with epilepsy.

Material and methods. One hundred and thirty two patients (62 males, 70 females, aged 27.8 ± 8.9 years) with epilepsy participated in the study. Patients were divided into two groups. The first group included 112 patients that were characterized by intelligence and cognitive impairment while the second group (20 patients) had no mental deterioration and was regarded as controls. The two diagnostic categories accorded with ICD-10 criteria. The diagnosis of Dementia (F-02.8) was confirmed in 54 patients, while the diagnosis of Mild Cognitive Impairment (F-06.7) was confirmed in 58 patients.

Results. Our results show that the level of left-handers among patients with cognitive Impairment achieved 14.2%, whilst in the group without cognitive deterioration there were no left-handers, and this difference was statistically significant ($p = 0.051$). An analysis of possible influence of motor lateralization on degree of cognitive deterioration, revealed that left-handedness determines the higher degrees of intelligence deterioration compared with right-handedness ($\chi^2 = 6.64$; $p < 0,05$). These data were confirmed by use of Wechsler Adult Intelligence Scale (WAIS) and the Mini Mental State Examination (MMSE) tests, and all left-handed epilepsy patients achieved lower scores on MMSE, total WAIS, as well as verbal and nonverbal WAIS scores.

Conclusion. Our data confirm a role of some neurobiological variables, with emphasis on cerebral motor lateralization, in their influence upon intelligence level and cognitive deterioration in epilepsy. These data may be used for predictive purposes of intelligence assessment in patients with epilepsy.

Key words: epilepsy • intelligence • cerebral motor lateralization • Wechsler

INTRODUCTION

Epilepsy is a disease with chronic steady course, which frequently can result in cognitive deterioration that, in turn, has negative influence on quality of life in patients with epilepsy (PWE). This seems to be quite comparable with negative effects of seizures themselves.

The factors which contribute to such cognitive deterioration and intelligence impairment in patients with epilepsy are incompletely understood and have not been completely elucidated (Lishman, 2003). Such basic characteristics as epilepsy forms, type and frequency of seizures and disease duration are believed to be the principal determinants of intelligence impairment (Stauder, 1938; Scholz, 1951; Dodrill, 1986; Aldenkamp et al., 1996; Aldenkamp, 1997; Jokeit et al., 1997; Jokeit, Ebner, 1999, 2002).

A general opinion exists, that symptomatic partial forms of epilepsy, as a rule, are characterized by more severe degree of cognitive impairment compared with

cryptogenic partial forms. Generalized tonic-clonic seizures also can cause cognitive impairment if the patient experienced not less than 100 (Stauder, 1938; Scholz, 1951; Dodrill, 1986). Moreover, basic variables such as early age of onset, seizures with high frequency and long duration of epilepsy course, predict poor cognitive functions (Dickmen et al., 1977; Dodrill, 1991; Devinsky, Tarulli, 2002).

Suggestion can be made that some other factors i.e. cerebral motor lateralization and handedness in particular *a priori* might also be important for cognitive function development, since cerebral sensorial and motor asymmetry are thought to play an important role in psychic processes not only in *Homo sapience*, but in other mammals too (Geodakian, 1993; Crow, 1998).

Moreover, numerous data obtained by different authors have shown that cerebral asymmetry takes part in pathogenesis of some mental and neuropsychiatric disorders such as depression, schizophrenia and epilepsy, although these findings are somewhat poorly understood, and remain controversial (Kalinin et al., 2010).

Data show that the rate of left-handed persons among patients with epilepsy is 1.6 fold higher than in the general population. Similarly, the rate of ambidexterity is 2.5 fold higher compared with the general population, whilst the amount of familial left-handedness among patients with epilepsy achieves 75% (Dobrochotova and Bragina, 1994; Kalinin et al., 2010). However, these data vary depending on region of the world and depend on age, gender and seasons. All these data confirm the certain relationships between epilepsy and anomalous motor lateralization and the association between epilepsy and left-handedness and ambidexterity is widely recognized (Kalinin et al., 2010). Nevertheless, much less is known about influence of motor lateralization on cognitive processing and intelligence in patients with epilepsy.

AIM

The current study was undertaken in order to determine the possible relationships between handedness, gender, and seizure types, on the one hand, and intelligence including cognitive processing on the other hand, in patients with partial epilepsies.

MATERIAL AND METHODS

One hundred and thirty two patients with partial epilepsy (PWE) were investigated of which 62 were males and 70 females. Their mean age was 27.8 ± 8.9 years. Thirty patients had a diagnosis of symptomatic partial epilepsy and 102 patients had a diagnosis of cryptogenic partial epilepsy.

All patients had provided written informed consent to participation in the study. Patients were divided into two groups. The first group of 112 patients were characterized by intelligence and cognitive impairment while the second group (20 patients) had no mental deterioration and was the control group.

The two diagnostic categories accorded with ICD-10 criteria. The diagnosis of Dementia (F-02.8) was confirmed in 54 patients, while the diagnosis of Mild Cognitive Impairment (F-06.7) was confirmed in 58 patients. The patients with diagnosis of Dementia were further subdivided into two subgroups according to the grade of Dementia. The first group of 37 patients were categorized to have mild grade Dementia whilst the second group of 17 patients had a diagnosis of medium grade.

The mean rate of intelligence in mild grade dementia achieved 70–89 points in WAIS and 20–23 points in MMSE. In the subgroup of medium grade dementia these values achieved less than 69 and 19 points respectively. In the group of mild cognitive impairment, the values achieved were 90–109 points in WAIS and 24–27 points in MMSE.

All patients were tested for handedness, and for this purpose the Annette scale was used (Annett, 1970).

The level of intelligence was measured by use of Wechsler Adult Intelligence Scale (WAIS III) (Wechsler, 1991) and Mini Mental State Examination (MMSE) scale (Folstein et al., 1975).

All data have been processed on personal computer (program "Statistica", 6th version). Student t-test has been used for comparison of independent quantitative variables, whilst chi-square test (χ^2 test) has been used for the assessment of linkage between nominal data, i.e. between dementia grades and handedness.

RESULTS

Handedness and intelligence

The main results are listed in Tables 1–5. In the Table 1 the data on distribution of handedness are highlighted. As can be seen, the comparison of group with cognitive deterioration and group without such deterioration revealed the higher presence of left-handed patients among the persons in the first group. Thus, among the first group were 16 patients with left-hand-

Table 1. Distribution of PWE in relation to handedness

Group	Left-handers	Right-handers	Total
PWE with cognitive impairment	16 (14.2%)	96 (85.8%)	112 (100%)
PWE without cognitive impairment	0 (0%)	20 (100%)	20 (100%)

Notes: a prominent trend to discrepancy between proportion of left-handers and right-handers with cognitive impairment was observed ($p = 0.051$). PWE – patients with epilepsy

Table 2. Cognitive deterioration grade in relation to handedness

Handedness	Mild cognitive impairment	Dementia of moderate grade	Dementia of medium grade	Total
Left-handers	5	6	5	16
Right-handers	53	31	12	96
Total	58	37	17	112

Note: $\chi^2 = 6.64$; $p < 0.05$

edness (14.28%), while in the second (control) group none left-handers occurred. Although the stochastically significant discrepancy between the groups was absent, nonetheless there was an essential trend to discrepancy between the groups ($p = 0.051$). This suggests a role of left-handedness in the origin of cognitive and intelligence deterioration in PWE.

Since a trend to relationship between left-handedness and intelligence deficiency in PWE has been observed, a presumption has been made that intelligence and cognitive impairment with more prominent degree should occur in left-handed patients. These findings are noted listed in Table 2.

As can be seen from Table 2 there was a statistically significant preponderance of higher dementia grades in left-handers compared with right-handers ($\chi^2 = 6.64$; $p < 0.05$) i.e. left-handedness determines the higher degrees of intelligence deterioration compared with right-handedness.

In order to confirm these findings on the next stage the comparison of mean values of MMSE and WAIS between left- and right-handed patients was performed, and these data are highlighted in Table 3. As can be seen left-handed patients had mean values of MMSE and WAIS that were significantly lower than in the right-hander patients. Principally, these discrepancies concerned all variables of WAIS, including General intelligence, as also verbal and nonverbal intelligence, although the maximal deficiency in left-handed patients has been observed for nonverbal intelligence.

Subsequently a comparison of concrete subtests in WAIS was carried out between left- and right-handed patients. This analysis could reveal stochastically significant discrepancies between compared groups only on four subtests, and mean values on all four subtests were less in left-handers than in right-handed patients. These subtests included arithmetical calculation (6.3 ± 3.4 vs. 8.3 ± 2.9, $p < 0.01$); visual-motor coordination (26.8 ± 14.3 vs. 34.5 ± 13.8, $p < 0.04$); attention (10.6 ± 4.6 vs. 13.0 ± 4.0, $p < 0.03$) and constructive praxis (12.8 ± 5.7 vs. 16.8 ± 7.0, $p < 0.03$). Since arithmetical calculation seems to be the single test that is determined by the left hemisphere, while the other three tests belong to right-hemisphere functions, it can be concluded that in the left-handed patients intelligence deficiency relates mostly to the right hemisphere compared with right-handed patients, although the left hemisphere functions are also disordered.

Table 3. Comparison of mean values of MMSE and WAIS in left-handers and right-handers

Test	Left-handers	Right-handers	Significance
MMSE	22.68 ± 4.89	24.76 ± 3.55	$p = 0.04$
WAIS total	80.68 ± 16.79	90.95 ± 13.60	$p = 0.01$
WAIS verbal	84.75 ± 15.80	92.62 ± 14.90	$p = 0.04$
WAIS nonverbal	77.31 ± 17.56	87.80 ± 13.50	$p = 0.005$

MMSE – Mini Mental State Examination; WAIS – Wechsler Adult Intelligence Scale

Table 4. Influence of some basic characteristics of epilepsy on WAIS values in left- and right-handers

Item	WAIS in Left-handers	WAIS in Right-handers	Significance
Symptomatic partial epilepsy	69.28 ± 17.19	85.33 ± 13.16	p = 0.009
SGS	60.0 ± 5.29	90.28 ± 13.53	p = 0.001
Left-sided focus	96.40 ± 12.40	84.20 ± 13.27	p = 0.01
Right-sided focus	79.45 ± 14.62	89.86 ± 13.31	p = 0.024

WAIS – Wechsler Adult Intelligence Scale; SGS – secondary generalized seizures

Table 5. Joint influence of lateralization and gender on WAIS and remission duration in PWE

Item	Left-handed PWE	Right-handed PWE	Significance
WAIS males	77.25 ± 14.92	91.34 ± 12.51	p = 0.006
WAIS females	84.12 ± 18.83	88.78 ± 14.47	n.s.
RD males	2.37 ± 3.62 years	0.92 ± 1.88 years	n.s.
RD females	3.93 ± 5.15 years	0.66 ± 1.24 years	p = 0.0001

WAIS – Wechsler Adult Intelligence Scale; PWE – patients with epilepsy; RD – remission duration

Handedness and some basic variables of epilepsy

Our final analysis of concerned the influence of basic variables of epilepsy on intelligence rate separately for left-handed and right-handed patients. The principal findings of this analysis are shown in Table 4.

From this table is can be seen that the diagnosis of symptomatic partial epilepsy and occurrence of secondary generalized seizures both reduced WAIS level in left-handers compared with right-handers. Principally, the other epilepsy forms and seizure types have no influence on WAIS level. It implies that symptomatic partial epilepsy with secondary generalized seizures represents the risk factors for intelligence decrease in left-handed but not in right-handed patients with epilepsy.

The side of epileptic focus seems to be important for general WAIS rate, but to exert different influence on intelligence in relation to handedness. Thus, the left-sided foci result in decrease of WAIS level in the group of right-handers, but not in left-handed patients. Quite the contrary, the right-sided foci usually result in decline of WAIS level in left-handers, but not in right-handed patients. In other words, so-called mirror image relationships exist between focus lateralization and handedness in terms of their influence on intelligence.

Handedness and gender

The main stochastically significant data on their joint influence on WAIS rate and remission duration in PWE are shown in Table 5. From this table is seen that in left-handed males had lower mean WAIS values compared with right-handed males with epilepsy. Such discrepancy was not observed in females. In other words, left-handed males with epilepsy are more vulnerable to intelligence damage due epilepsy course than the right-handed males, whilst females seem to be protected from such deterioration. In addition, in left-handed females the remission duration (absence of seizures) was longer than in the right-handed females; however, such a discrepancy was not seen in males.

DISCUSSION

This study is believed by the authors to be the first in which the influence of motor lateralization on intelligence level and cognitive processing in epilepsy has been investigated. However, this study could be criticized on the basis that the authors exclusively investigated handedness, while other possible risk factors for intelligence decline was not properly investigated; but it was beyond the scope of the study. Nonetheless, the choice of topic for investigation was determined by the lack of data on the role of motor lateralization (handedness) in intelligence deterioration in patients with epilepsy.

Moreover, the cerebral organization and handedness, in particular, depicts the evolutionary way of *Homo sapiens* among other species. It should be stressed that left (dominant in right-handers) hemisphere are connected with evolutionary novel signs (variables), while subdominant right hemisphere contents the old and even archaic characteristics and functions which

have appeared at early stages of evolution (Dobrochotova and Bragina, 1994). Besides, the different roles of male and female gender should also be taken into consideration, since the female gender is believed to link with old characteristics and signs, while the male gender is connected with characteristics which are novel in evolutionary terms.

The main findings of the current trial have shown the discrepancies in intelligence rate in PWE with the different motor lateralization. The principal finding is the unfavorable role of left-handedness in intelligence decline development in PWE that was seen after comparison left-handers and right-handers. Noteworthy, left-handedness resulted mainly in a decrease of nonverbal intelligence.

Left-handedness can be divided at least into two subtypes (hereditary and organic) due the factors that cause them. Here should be stressed that, unlike the right-handed persons the left hemisphere in left-handed population is characterized by lack of maturity and function differentiation that a priori could lead to certain deficiency in verbal and analytical functions. Nonetheless, most left-handers seem to cope successfully with verbal and analytical tasks in everyday life. The possible explanation for this contradiction may be such that the right hemisphere takes on the functions of left hemisphere for compensation purpose. Moreover, a notion exists that the brain of left-handers consists as if of two right hemispheres that again implies the less functional differentiation of left hemisphere in left-handers.

If one takes into account such suggestion the results observed in the current study may be reasonably explained. Thus, in left-handed patients, except for arithmetical calculation, the most deteriorated were the functions linked with the right hemisphere (visual-motor coordination, attention and constructive praxis). Moreover, the fact, that right-sided foci in left-handed patients caused more serious intelligence reduction, than left-sided foci confirms that the right hemisphere in left-handers is not less important (and perhaps more?), than the left hemisphere.

On the contrary, in right-handed patients the left-sided foci were more important for the intelligence decline because the left hemisphere (dominant for right-handers) was damaged.

Obtained results have also shown that symptomatic partial epilepsy and secondary generalized seizures can more reduce intelligence level in the left-handed, than in the right-handed PWE. In other words, the diagnosis of symptomatic partial epilepsy that has been confirmed in MRT scanning is a risk factor for intelligence deterioration more for left-handers than for right-handed PWE.

Data on interaction between gender and motor lateralization have revealed an interesting relationship between them in terms of their joint damage effect on intelligence strictly in men, but not in women. The question has arisen, how these findings may be explained?

The female brain is believed to be less differentiated in terms of functional states than the male brain and in this context is similar to brain of ambidextrous persons, and more resistant to damage, since cerebral functions are less lateralized than in the brain of right-handers and males (Geodakian, 1993; Crow, 1998). That is why the right hemisphere in females can take on itself a part of left hemisphere functions, i.e. functions responsible for intelligence. On the contrary, the male brain is much more differentiated with dominant role of left hemisphere, which is more susceptible to organic damage in PWE, especially in males with symptomatic partial epilepsy. This finally can result in severe deterioration of intelligence in men compared with women with epilepsy.

From the evolutionary point of view, the female brain seems to be older than male brain (Geodakian, 1993; Crow, 1998). It implies that less differentiated cerebral functions occurred more frequently in ancient times, whilst more differentiated functions like in the male brain are thought to evolve at the later stages of evolution of *Homo sapiens*. In this context the left-handedness in males with epilepsy with concomitant intelligence decline should be regarded as regress to older structural and functional cerebral organization.

Clearly more detailed investigations are needed in the future in order to answer the many unresolved questions.

CONCLUSION

The data obtained in this study have confirmed the role of some neurobiological variables with emphasis on handedness in its influence upon intelligence level and cognitive deterioration in epilepsy. Moreover, the different role of male and female gender on the influence of intelligence level has also been observed. It stresses the significance of evolutionary influence upon intelligence level in patients with epilepsy. These data may be used for predictive purposes of intelligence assessment in patients with epilepsy.

CONFLICT OF INTEREST DISCLOSURE

The authors have no conflict of interest to declare.

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