NEUROPSYCHOLOGICAL EVALUATION OF YOUNG ADULTS WITH ISCHEMIC STROKE

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JÄRVENPÄÄ SOILA: NEUROPSYCHOLOGICAL EVALUATION OF YOUNG ADULTS WITH ISCHEMIC STROKE

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Tiivistelmä

Nuorten aivoinfarktipotilaiden neuropsykologista profiilia on tutkittu suhteellisen vähän. Etiologia, riskitekijät sekä aivoinfarktin vaikeusaste eroavat nuorten ja vanhempien ikäryhmien välillä. Myös infarktiin liittyvillä neuropsykologisilla häiriöillä on mahdollisesti ikäsidonnaisia eroavuuksia.

Tässä tutkimuksessa käytimme tietoja 1008 ensimmäisen aivoinfarktinsa vuosina 1994–2007 sairastaneista 18–49 vuotiaista perättäisistä potilaista Helsinki Young Stroke Registry tutkimuksesta. Analysoimme tiedot 525 potilaasta, joille oli tehty neuropsykologinen tutkimus ensimmäisen kolmen kuukauden aikana aivoinfarktin jälkeen. Neuropsykologinen tutkimus oli luonteeltaan orientoiva keskittyen tiettyihin neuropsykologisiin häiriöihin eikä sisältänyt kattavaa tutkimusta kaikista kognitiivisista osa-alueista. Neuropsykologisen tutkimuksen tulokset luokiteltiin ryhmiin ja arvotettiin numeerisesti vaikeusasteen mukaan.

Tutkimuksessamme kielellinen (31.8%) ja visuaalinen muisti (29.4%) olivat useimmin vaurioituneet kognitiiviset osa-alueet lyhyen neuropsykologisen arvion perusteella. Orientaatiohäiriö (1.0%), amnestinen oireyhtymä (1.0%) ja agnostinen häiriö (1.9%) esiintyivät harvimmin. Vaikeusasteeltaan vaikeimpia häiriöitä havaittiin kielellisen muistin (6.7%) alueella. Demografisten tekijöiden tarkastelussa miehillä esiintyi enemmän visuaalisen muistin häiriötä (32.5% vs. 24.4%) ja naisilla enemmän depressiota (22.8% vs. 7.1%). Potilailla ikäryhmässä 40 - 49 vuotta esiintyi enemmän visuaalisen muistin häiriötiä (33.3%) kuin ikäryhmän 15 – 39 vuotta potilailla (22.1%).

Löydöksemme kielellisen muistin alttiudesta häiriöille nuorilla aivoinfarktiopotilailla on samansuuntainen aiempien tutkimustulosten kanssa. Lisäksi havaitsimme, että visuaalisen muistin häiriö on suhteellisen yleinen löydös nuorilla aivoinfartkipotilailla. Tutkimuksemme ei sisältänyt arviota toiminnanohjauksesta, ongelmanratkaisusta tai merkittävästä afasiasta, mikä on otettava huomioon tuloksia tarkastellessa.

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Key words: cognition deficit, age, cerebrovascular disorder

Abstract

Background and purpose: The neuropsychological profile of young stroke patients is a relatively underinvestigated subject. As the etiology, risk factors, stroke subtypes, and stroke severity seem to differ in the young from those of an older age group, the neuropsychological defects also may have their own age-related differences.

Methods: We used data of 1008 consecutive patients aged between 18 to 49 years with first-ever ischemic stroke enrolled into Helsinki Young Stroke Registry, 1994 to 2007. We analyzed the data of 525 patients who underwent a brief neuropsychological examination during the first 3 months post-stroke. The testing concentrated on certain neuropsychological disorders and did not include comprehensive evaluation of all cognitive fields. The neuropsychological test results were categorized and valued numerically.

Results: In our patients, verbal (31.8%) and visual memory (29.4%) and were the most commonly impaired fields according to brief neuropsychological evaluation reports, whereas orientation (1.0%), amnestic (1.0%) and agnostic (1.9%) disorders occurred most rarely. Most severe impairments were detected in the field of verbal memory (6.7%). Regarding demographic differences, men had more visual memory disorder (32.5% vs. 24.4%) and women more depression (22.8% vs. 7.1%). Patients aged 40-49 years had more visual memory disorder (33.3%) than patients aged 15-39 years (22.1%).

Conclusions: Our finding that verbal memory is susceptible to impairments is in line with previous studies around the subject. In addition, we found that visual memory is a relatively common neuropsychological field to impair in young patients after ischemic stroke. Our survey did not include evaluation of executive functions, problem solving or significant aphasia, which has to be taken account of when regarding the results.

Contents

1. INTRODUCTION

Ischemic stroke is one of the leading causes of death and significant factor for long-term disability in developed countries. As stroke is considered a relatively rare event among young adults, approximately 10% of ischemic strokes occur in individuals aged less than 50 years. (1-4) As the young age is generally recognized as an advantage in recovering from stroke, the potential consequences of cerebral infarction might be more profound in the young: in their most productive age and with a long life span ahead of them, the stroke can have a very far-reaching influence on their performance, quality of life and ability to look after their possible minor offspring. When young adults seem to have a better motor recovery after stroke, there is reference that the cognitive impairment might often be long-standing. (5) In addition to the humanistic disadvantages, ischemic stroke accounts for significant financial loss on healthcare system and the society. (6,7) Only 41% of working-age ischemic stroke patients were observed to return to work after ischemic stroke in study by Kauranen et al. (2013). (8) Recent studies also suggest that stroke incidence in young adults have increased over time. (9)

The major causes of ischemic stroke in the adult population, atrial fibrillation and atherosclerosis, are in fact more common in the elderly. There is a much wider spectrum of causes among the young patients, in whom rare causes including carotid artery dissection are the most prevailing causes of stroke. (1,10-14) The different causations divide the young and the elderly adults into etiologically different patient groups and should hence be examined separately. Different subtypes of stroke also seem to divide differently between the age groups. (1)

Ischemic stroke in young adults is still a relatively underinvestigated subject. Whereas much of the research focuses on the etiology and treatment of stroke, little research has been done about the neuropsychological aspects of young stroke patients. However, there seems to be reference that the neuropsychological profiles of young and older stroke patients differ from one another. (5,15-23)

2. CHARACTERISTICS OF STROKE IN YOUNG ADULTS

2.1 Definition, incidence and risk factors of stroke in young adults

Young stroke is defined as a stroke occuring in patients between 18 - 49 years of age. (9,10) Some definitions limit the term to patients aged under 45 years. (24) 15 million people each year are affected by stroke and it has been estimated that 3.7% - 5% of all strokes occur in the young. (4,12,24) Although risk factors in the young include more rarities and are more diverse in the young, certain patterns can be observed. The most common risk factors of stroke in the young are cardiovascular disease, dyslipidemia, hypertension, migraine, pregnancy or puerperium, oral contraceptive use, exessive alchol intake, cigarette smoking and illicit drug use. (11,12,24,25)

2.2 Etiology of stroke in young adults

The etiological spectrum of stroke is much more diverse among young stroke patients than in the older age group. Although in the past most of the strokes in young adults remained of unknown etiology, nowadays a specific cause can be identified in most of the strokes with 40% of strokes categorized cryptogenic. About 20% of the strokes are caused by cardioembolism of which most common sources are atrial fibrillation, dilated cardiomyopathy, congenital cardiac disease, or patent foramen ovale. Other determined causes include cervical artery dissection, systemic vasculitis, genetic thrombophilia, and antiphospholipid syndrome. (10,13)

The same atherosclerotic risk factors that account for most of the strokes in all adults (26) also predispose young adults to stroke, but in older age groups they are more frequent (1) as younger age groups introduce more risk factors related to congenital factors, hormonal load and exposure to drugs.

2.3 Neuropsychological characteristics in young stroke patients

Neuropsychological evaluation is a method that is used to investigate the subject’s cerebral functioning through their operation and accomplishment in neuropsychological tests. It aims to define the effects on cognition and behavior that are related to disease and qualify the areas of strengths and weaknesses. The evaluation is performed by a neuropsychologist

who gathers the data about the cognitive performance, behavior and mood. The cognitive performance consists of fields of verbal memory, visual memory, executive functions, basic verbal functions, basic visual functions and voluntary motor functions. Different standardized test patterns are used to evaluate these fields. The results of the evaluation can be used to confirm a diagnosis, localize the neurological defect, to evaluate the need for individual neurological or psychological therapeutic interventions and to plan them if necessary. (25-26)

Cognitive deficits are a common finding among working-age patients with ischemic stroke even with intact National Institutes of Health Stroke Scale (NIHSS) scores. (29,30) NIHSS is a generally used score to assess clinical stroke severity. According to recent studies, the neuropsychological defects of young stroke patients seem to differ from those of the older stroke patients. As both age groups have been reported to have impairments in memory, young stroke patients seem to have more disturbances in attention, whereas older patients have their visuospatial functions more frequently impaired. (16,31) One explaining factor could be that aging itself alters the cognitive performance. Deteriorated functions reach a point at which normal compensatory mechanisms become insufficient faster in the aged which leads to the the person to fail to compensate the functions lost in the brain injury.

The stroke subtypes also seem to divide unevenly between the age groups: classified by the TOAST (Trial of ORG 10172 in Acute Stroke Treatment) criteria, undetermined and other determined cause are more commonly presented in the young (1) as large artery atherosclerosis and small vessel occlusion occur more in the older age group (26).
The cognitive prognosis of stroke seems to be more favorable on young adults: in long-term follow-up approximately 28% of young adults have been reported to have cognitive impairment compared to 54% of older age group. (5,21) However, most of the current studies are restricted to small sample sizes and measure only single parameters of neuropsychological outcome and are hence lacking the comprehensive picture of the patients' neuropsychological features after stroke.(32)

3. AIMS OF THE STUDY

We aimed to study

1) The prevalence and severity of neuropsychological deficits in young patients with first-ever ischemic stroke;
2) Differences in neuropsychological deficits between demographics subgroups;
3) Connection between stroke severity and laterality of the ischemic lesion with the prevalence of neuropsychological deficits.

4. PATIENTS AND METHODS

In this study we used the detailed information collected from all patients aged 15 to 49 with first-ever ischemic stroke (n=1008) treated in Helsinki University Central Hospital (HUCS) between January 1st 1994 and May 23rd 2007 (the Helsinki Young Stroke Registry). Initial data collection into the registry has been described in detail elsewhere. (33). The data analyzed here included demographic, date of stroke, date of neuropsychological evaluation and neuropsychological evaluation reports, stroke risk factors, stroke severity, size of the ischemic lesion, and laterality of the lesion (left, right, or both). Stroke severity was graded with NIH Stroke Scale (NIHSS) and categorized as mild (NIHSS score <7), moderate (NIHSS score 7-14), and severe (NIHSS score ≥15).

Neuropsychological evaluation reports produced both in our hospital and rehabilitation centers were obtained from all stroke patients in the catchment area. Patients included in the study were evaluated by neuropsychologist in first 3 months (90 days) from the ischemic stroke. For this study we enrolled the names of neuropsychological tests applied to the patients from evaluation reports, categorized the tests by the cognitive function they predominantly assessed and registered the neuropsychological evaluation results in the database. The neuropsychological tests were categorized in fields of verbal memory, visual memory, basic language functions, basic visual functions, basic practical functions, visual scanning and mood. The data were gathered from brief neuropsychological reports considering neuropsychological disorders. Executive functions and attention could not be classified the data of brief neuropsychological examinations and hence were not used in the data analysis. The evaluation of language functions was performed only in naming, word search and academic skills (reading and calculating). Extensive study of verbal comprehension was not executed since these fields had been investigated by speech therapist in accordance with the division of labour at the clinic and the results were only referred to in the neuropsychological testing reports.

Of the included neuropsychological evaluations, 278 were comprehensive evaluations and 247 were brief orientating reports. Table 1 lists all neuropsychological tests used in the evaluation of the study population. To make the evaluation reports comparable with each other, we classified all the reports using a standard form of brief neuropsychological evaluation in which the features evaluated were orientation disorder, amnestic disorder,

verbal memory disorder, visual memory disorder, agnostic disorder, neglect, visuoconstructive or visuospatial difficulty, dyspraxia in hand control, dyslexia, dyscalculia, depression and anosognosia. These neuropsychological features were directly estimated and valued in the brief evaluations and with the professional help of an experienced neuropsychologist we were able to classify the verbal reports from the comprehensive assessments to a corresponding form. The results of the neuropsychological evaluation were graded by the degree of difficulty in the clinical symptoms as normal or mild, moderate, severe and unknown. Evaluations of certain neuropsychological disorder set in half way of severity degrees were rounded up to the higher degree.

The neuropsychological data were first gathered into Microsoft Excel file and then combined with the main study database in SPSS. Descriptive data on neuropsychological findings are reported on the entire cohort and separately for subgroups defined above. For comparison, severity of neuropsychological deficits in each domain was dichotomized as normal to mild and moderate to severe. In statistical analysis, Chi-Square Test was used. A p of <0.05 was considered statistically significant. All statistical analysis used IBM SPSS Statistics, version 22.

Category	Tests
Verbal memory	WAIS* (Digit Span, Letter-Number Sequencing), WMS** (Logical memory I and II, Verbal Memory Quotient, Associative learning, Word lists, Number series, Orientation), CERAD (Word lists), RBMT (Story, Orientation), KS (Personal facts, CVLT, Orientation inqury, Mnest 1, Sentence span, AVLT, BDAE (selected subtasks)
Visual memory	WMS** (Visual reproduction, Visual learning, Visual series), CERAD (Visual reproduction), RBMT (Objects, Faces), KS (Pictures), BVRT, KIM, Benton (C,D,E), Rey-Osterrieth complex figure, Taylor complex figure
Executive functions	CANTAB (Match to Sample Search, Stop Signal Search), Brixton, Bourdon-Wiersma Double task, Benton-C Double task, Question game, D-KEFS, WCST, Fluences, Trail Making Test (Trails B), RAN, Stroop
Basic verbal functions	CERAD (Naming), Boston Naming Test (BNT), BDAE (selected subtasks), MPD, RAS, Luria's tasks for verbal interference, Calculation sample, Writing sample, Reading sample, Reading rate
Basic visual functions	CERAD (Copying task, Clock drawing), Poppelreuter, Street, Hooper, Gnost, VOSP, Rey-Osterrieth complex figure, Taylor complex figure, Thurstone, Manikin, Visuoconstructive drawings, Benton Facial recognition test, VST, Drawing of clock arms, Road map, Parallellograms, Copying, Drawing task, Line bisection, Symmetry
Basic practical functions	Luria's voluntary hand movement tasks, Tapping
Visual scanning	WAIS* (Symbol Search, Digit-Symbol Coding), CANTAB (Motor Screening Test), Trail Making Test (Trails A), Behavioral Inattention Test (BIT), Bourdon-Wiersma (BW), Vilkki's searching of parallel lines, Bells, Cancellation, Balloons, D2
Attention	WMS** (Psychic control ability), CANTAB (Simple Reaction Time), Nepsy (Visual attention), TAP
Mood	Beck Depression Inventory (BDI, different forms), Zung, DE symptom inquiry

* different forms (ie. WAIS-III, WAIS-R)

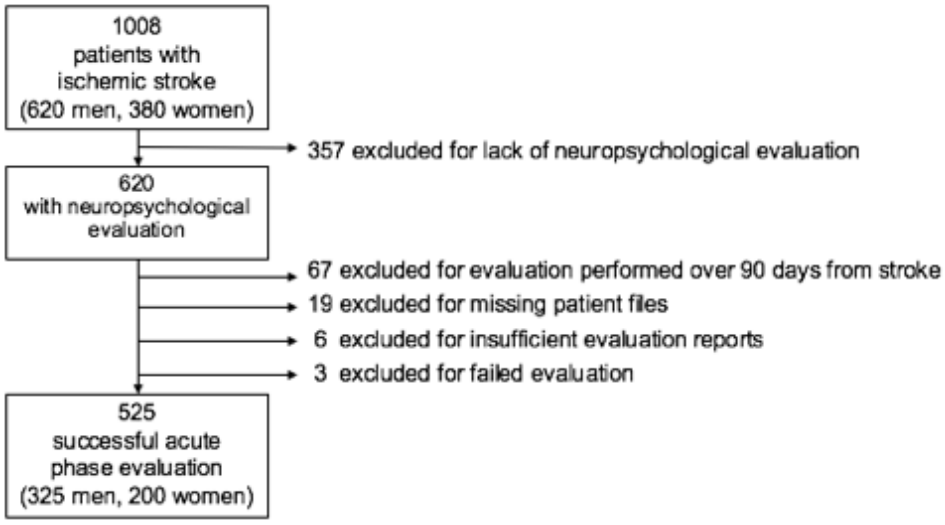
** different forms (ie. WMS I and II, WMS-R, WMS-III)

Table 1. Neuropsychological tests used on the patients and their categories.

5. RESULTS

The data consisted of 1008 patients (628 men, 380 women), of which 620 underwent neuropsychological evaluation at any time after their stroke. Of these 620 patients, successful acute-phase neuropsychological evaluation was carried out in 525 patients after a median of 10 days post-stroke (interquartile range 7-24 days). Of these, 325 were men and 200 women. Compared to included 525 patients, those who did not undergo neuropsychological evaluation (i.e. excluded, n=357) were older (median age 45 vs. 43 years, $p<0.001$), had more often small infarctions (50.1% vs. 40.3%) but less often medium-sized infarctions (18.8% vs. 33.0%, $p<0.001$), and similar NIHSS scores on admission.

Among the 95 patients who underwent neuropsychological evaluation, but were excluded from the present analysis, reasons for exclusion were missing patient files (n=19), insufficient neuropsychological evaluation reports (n=6), failed neuropsychological evaluation (n=3), and evaluation performed after the 90 days' time window from the stroke (n=67).



During the first 3 months period from the ischemic stroke 86 (16.4%) of the patients suffered from at least one severe and 293 (55.8%) of at least one moderate cognitive disorder. 223 (42.5%) patients were evaluated to have normal or mild performance in all the neuropsychological functions used and scored in this study. The most common and also most severe neuropsychological disorders among the patients were verbal memory disorder (25.1% moderate, 6.7% severe), visual memory disorder (23.6% moderate, 5.8% severe)

and visuoconstructive or visuospatial disorder (14.2% moderate, 3.3% severe). Most commonly evaluated as normal or mild were orientation disorder (99.0% normal to mild), amnestic syndrome (99.0%) and agnostic disorder (98.%).

Table 2. The neuropsychological disorders and the range of the different degrees of difficulty among the patients. Data are n (%).

	Normal to mild	***Moderate***	***Severe***	**Sampling *(percentage tested)***
Orientation disorder	506 *(99.0)*	5 *(1.0)*	0 *(0)*	511 *(97.3)*
Amnestic syndrome	511 *(99.0)*	4 *(0.8)*	1 *(0.2)*	516 *(98.3)*
Verbal memory disorder	347 *(68,2)*	128 *(25.1)*	34 *(6.7)*	509 *(97.0)*
Visual memory disorder	365 *(70.6)*	122 *(23.6)*	30 *(5.8)*	517 *(98.5)*
Agnostic disorder	509 *(98.1)*	10 *(1.9)*	0 *(0)*	519 *(98.9)*
Neglect	465 *(89.3)*	41 *(7.9)*	15 *(2.9)*	521 *(99.2)*
Visuoconstructive or spatial disorder	431 *(82.6)*	74 *(14.2)*	17 *(3.3)*	522 *(99.4)*
Dyspraxia	481 *(94.7)*	23 *(4.5)*	4 *(0.8)*	508 *(96.8)*
Dyslexia	468 *(91.6)*	27 *(5.3)*	16 *(3.1)*	511 *(97.3)*
Dyscalculia	420 *(81.7)*	77 *(15.0)*	17 *(3.3)*	514 *(97.9)*
Depression	382 *(86.8)*	49 *(11.1)*	9 *(2.0)*	440 *(83.8)*
Anosognosia	439 *(94.0)*	52 *(11.1)*	5 *(1.1)*	467 *(89.0)*

In analysis of dichotomized values between men and women, statistical significance was reached in fields of visual memory and depression. Men were affected with moderate to severe visual memory disorder more often (32.5% vs. 24.4%, p=0.049) whereas women suffered more from depression (22.8% vs. 7.1%, p<0.001). Comparing age groups of 15-39 years and 40-49 years, the latter was observed to have visual memory disorder more often (33.3% vs. 22.1 %, p=0.007). The correspondence of NIHSS scale score with the neuropsychological testing results reached the point of statistical significance in most of the fields: orientation disorder, visual memory disorder, neglect, visuoconstructive or spatial disorder, dyspraxia, dyslexia, dyscalculia and anosognosia. Lateralization of the infarct on the right side of the brain produced more neglect (17.4%) on patients versus the infarctation

lateralized on the left (6.2%) or both sides (1.9%, p<0.001). More visuoconstructive or spatial disorder was also observed on the right (21.6%) or both sides (24.5%) than when the infarct was localized on the left side (11.9%, p=0.009). Left sided and bilateral lateralization produced more verbal memory disorders (46.8% on the left side and 36.5% on both sides 36.5% versus 17.1% on right side, p<0.001). Dyslexia was also more frequently observed on infarcts on the left side (14.8%) versus right (3.8%) or both sides (3.8%, p<0.001). In addition, dyscalculia appeared more on left side infarcts (24.5%) than on the right (12.8%) or both sides (17.0%, p=0.005).

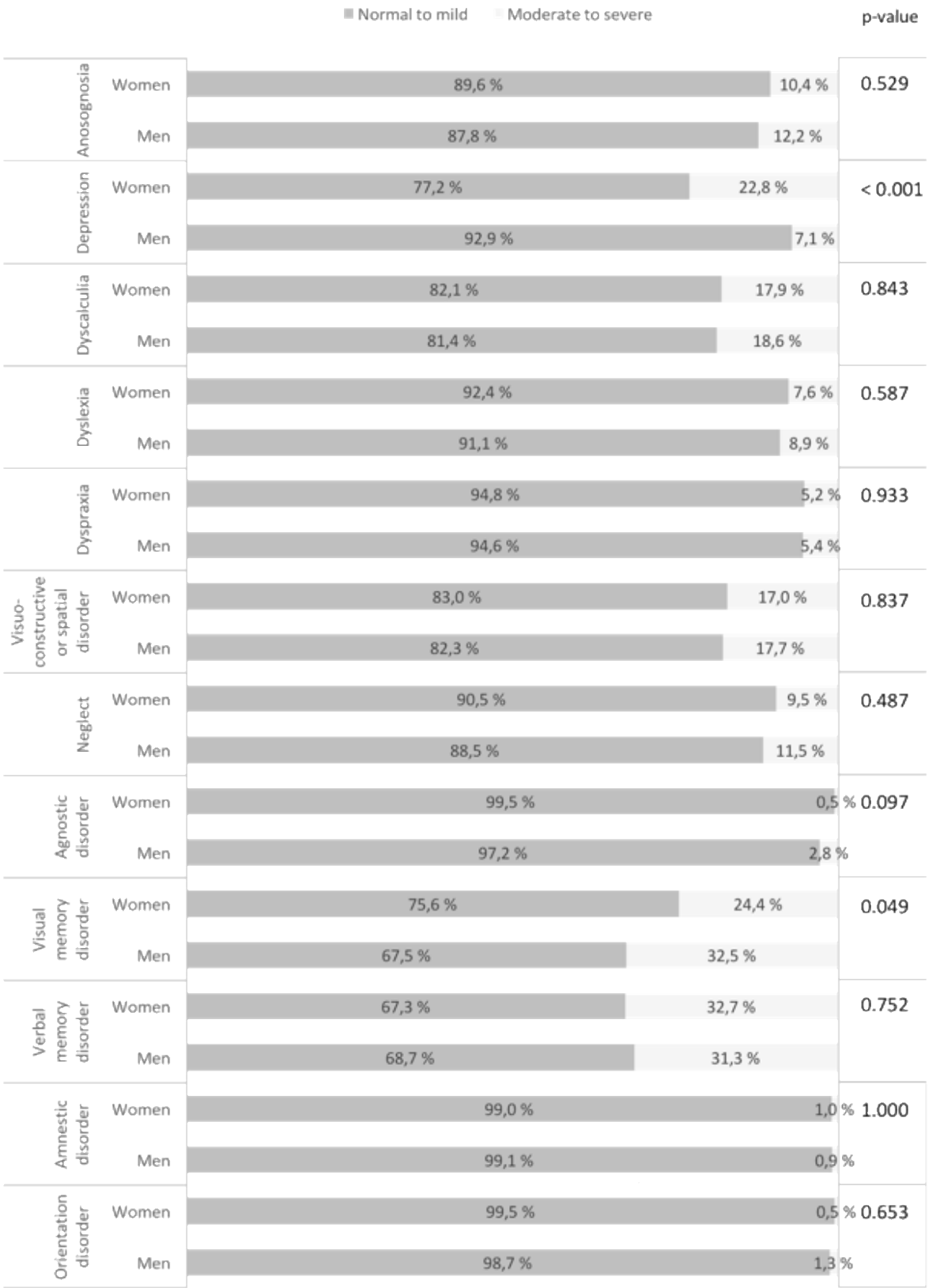


Figure 1. Comparison of neuropsychological profiles of men and women. Chi-Square Test was used in the analysis.

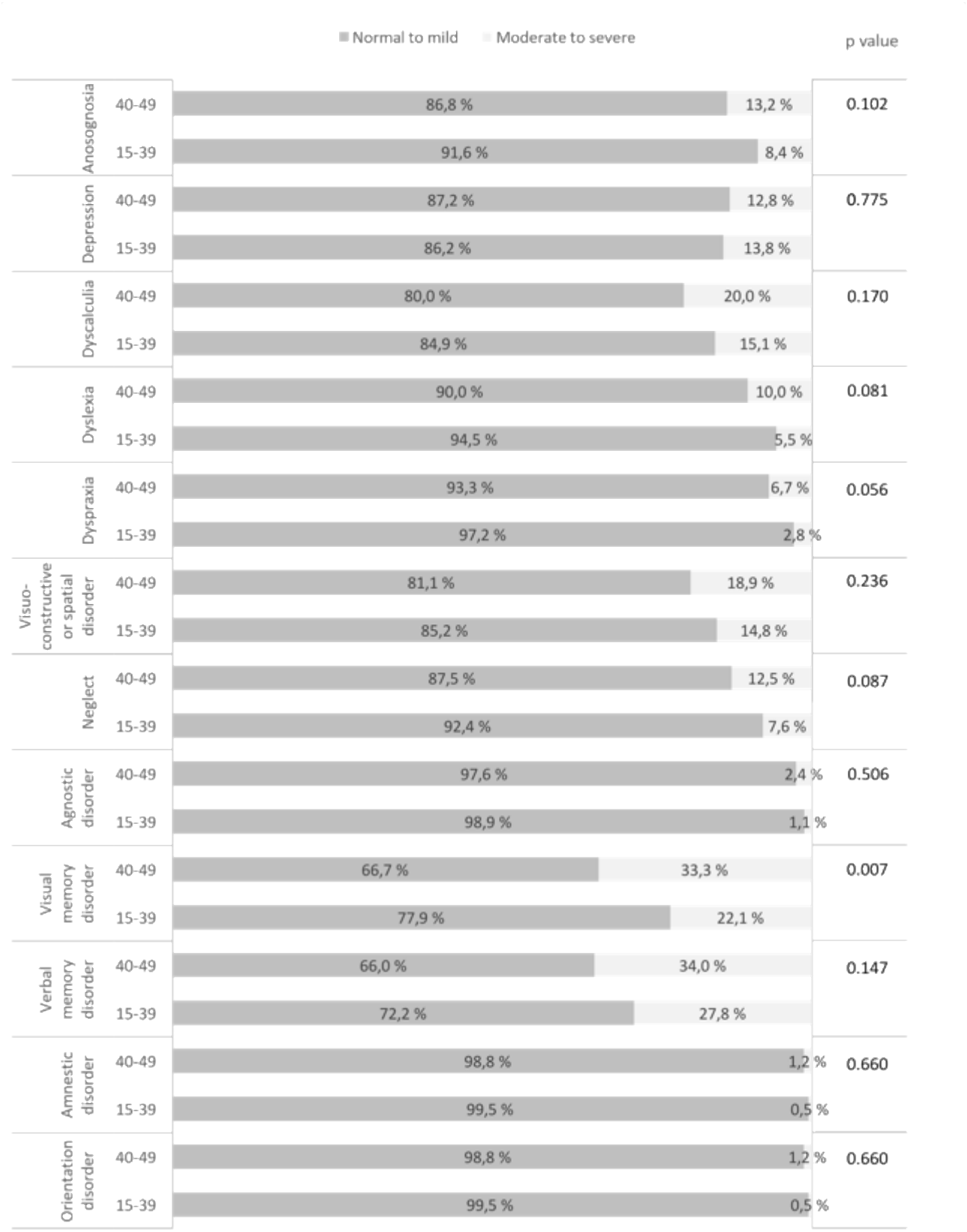


Figure 2. Differences in neuropsychological disorders in younger (15-39 yrs) and older (40-49 yrs) age groups. Chi-Square Test was used in the analysis.

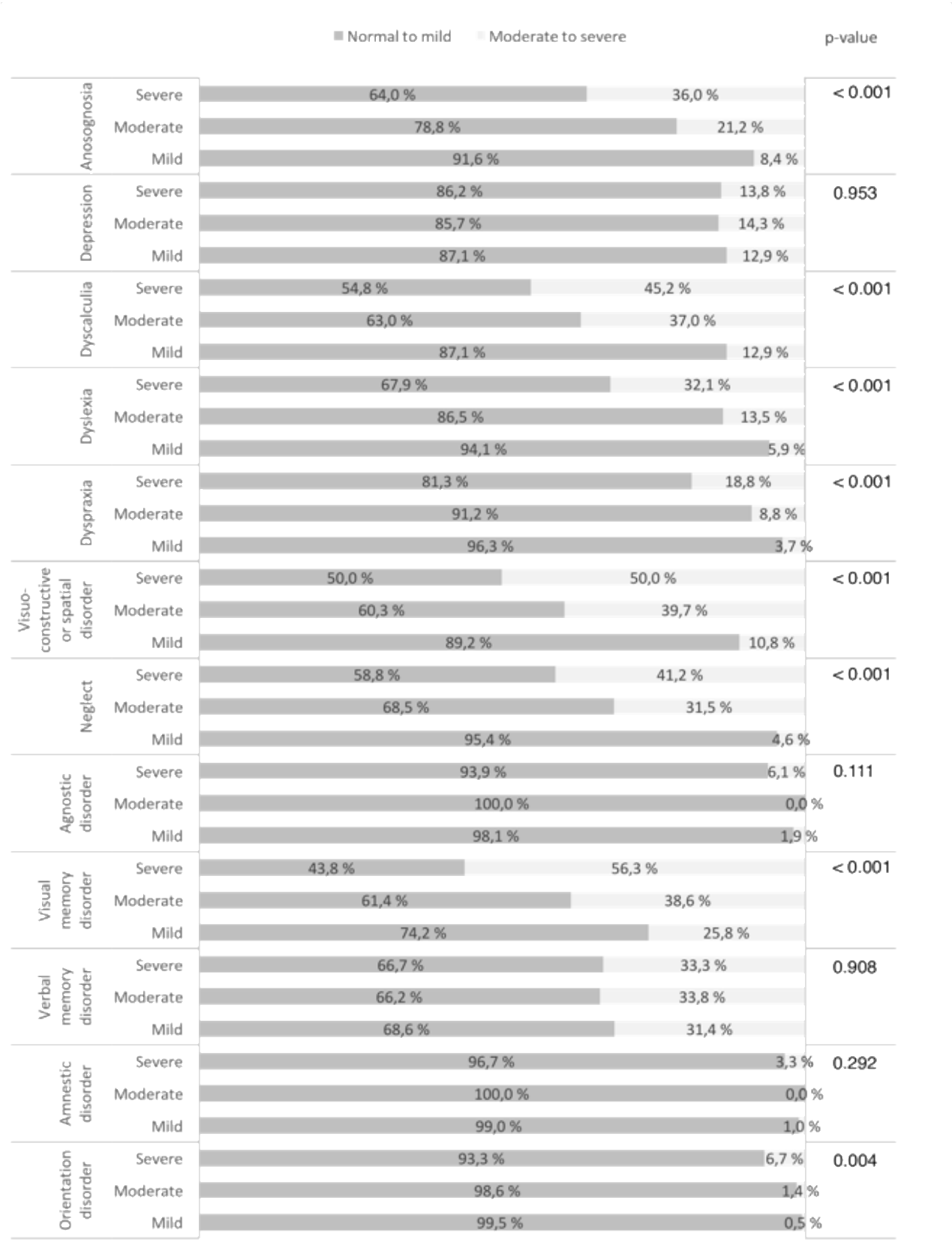


Figure 3. NIHSS scale score related to neuropsychological performance. On y-axis the NIHSS scale score and on x-axis the severity of neuropsychological disorders. Chi-Square Test was used in the analysis.

Figure 4. Impact of infarct lateralization on frequency of neuropsychological disorder. Chi-Square Test was used in the analysis.

6. DISCUSSION

In this retrospective descriptive study, we found that verbal and visual memory as well as visuoconstructive or visuospatial functions seem to be the most commonly impaired neuropsychological features within the first 3 months post-stroke in young adults. The severe embodiments of orientation, amnestic and agnostic functions seem to occur more rarely. Altough visuoconstruction seems to be one the domains that impaired relatively often in our study, visuospatial functions are generally considered to deteoriate with increasing age and older patients are seen to be more susceptible to its impairments. (31) The selection of cognitive domains assessed in brief neuropsychological examination might overly emphasize the significance of this finding in our study since attention and executive functions, domains often impaired in young stroke patients (16), are not part of the analyzed test pattern.

Schaapsmeerders et al. (2013) reached a similar finding considering impairments in verbal memory and visuoconstruction in their study. (5) Röding et al. (2009) suggested that cognitive functions would impair more in women after stroke, but this finding was not evident in our study. (15) We found, however, that women seem to suffer more from depression as men seem to have more visual memory disorders after stroke.

The strengths of this study are that the sampling of patients is relatively vast and the used neuropsychological test battery covers cognitive functions relevant to estimate at the first weeks after stoke. Despite being hospital-based, the sampling is likely to include all the first-ever stroke patients aged 18 to 49 years in the catchment area. However, as a single-center setting it may not represent the whole Finnish population. Other limitation of this study was that the neuropsychological testing was executed within 3 months post-stroke, a period of time during which the most powerful symptom alleviation is usually observed. In this regard, some of the patients have been evaluated in the hyperacute phase of stroke and some patients later when the symptoms have spontaneously begun to decrease.

Our study did not include follow-up of the patients. However, Cao et al. (2007) suggested that stroke-associated cognitive impairment in young adults may emerge even 6-12 months after the stroke. (16) Stroke subtypes have not been classified in age groups in our study, although there is reference that stroke subtypes seem to differ among young and older

stroke patients. (1,26) In addition, etiological subgroups have not been distinguished in our study. Hao Z et al. (2013) suggested that etiological subgroup would predict outcome in mild stroke patients. (34) In this study we focused on stroke patients and lacked comparison of a control population. There is no representation of the neuropsychological profiles of the 65 young ischemic stroke patients that were excluded from the study for not having a neuropsychological evaluation in 3 months timelimit. These patients were most likely to have no suspicion of any cognitive defect or alternatively had such massive neurological impairments that did not permit neuropsychological testing reliably this soon after the stroke, or died soon after the stroke.

The basis of this study is a brief neuropsychological evaluation that primary aims to assess the aspects considering the ability to function at home and immediate requirements for neuropsychological rehabilitation. In addition to these brief reports, the study also consists of significant amount of comprehensive neuropsychological reports that represent a larger and more consistent view of the patients neuropsychological condition but only categories available in the brief examination were used. Concentrating on certain specific disorders may produce a biased picture of the patients' overall performance. Attention and executive functions were evaluated but the results could not be put to account due to the qualitative representation of the data that could not be categorized in the classifications of this study. Disturbances in these fields may however constitute significant cognitive disorders that may not come up in this study. Another shortcoming of the study is the lack of scoring in aphasia symptoms in the neuropsychological reports. The reliable picture of the patients' aphasia symptoms cannot be portrayed because the patients with severe aphasia symptoms were evaluated in a general manner and hence their most significantly defected cognitive sections could not be scored.

7. CONCLUSIONS

We found that verbal memory is susceptibe to impairments, a finding that is in line with previous studies. In addition, we observed that visual memory is likely to impair nearly as often as verbal memory in young stroke patients. In our study men contracted more visual memory disorder as women more depression and patients aged 40-49 years had more visual memory disorder than patients aged 15-39 years. As demographic factors in young stroke patients have not been studied extensively, these findings might be valuable regarding future studies around the subject. In addition, NIH Stroke Scale proved to be reliable tool for assessing the stroke severity. More research of comprehensive neuropsychological features of young stroke patients with a long term follow-up and standardized test patterns are required on the subject.

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