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COGNITIVE DYSFUNCTION IN PATIENTS WITH ASYMPTOMATIC ISCHAEMIC DISTURBANCES OF THE CEREBRAL CIRCULATION AND CAROTID STENOSIS

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BACKGROUND: Impairment of cognitive function is often present in patients with carotid artery stenosis but the details of this dysfunction have rarely been reported. Our purpose was to elucidate the cognitive dysfunction in patients with Asymptomatic Ischaemic Disturbances of the Cerebral Circulation and unilateral asymptomatic severe carotid stenosis using comprehensive neuropsychological testing, and also to identify the specific underlying clinical and neuroimaging factors. METHODS: We analyzed the results of neuro-psy chological testing, the clinical history, and MR findings in 10 patients with Asymptomatic Ischaemic Disturbances of the Cerebral Circulation and severe (70-99%) stenosis of the extra cranial internal carotid artery (ICA) on Doppler sonography. Cognitive functions were examined. We excluded patients with Asymptomatic Ischaemic Disturbances of the Cerebral Circulation with contra lateral ICA occlusion or severe stenosis. RESULTS: Our neuropsychological testing revealed obvious cognitive deficits in all patients with Asymptomatic Ischaemic Disturbances of the Cerebral Circulation and unilateral asymptomatic severe ICA stenosis. The mean cognitive score on the memory test was also significantly lower in patients with asymptomatic ICA stenosis and score 3 lesions on MRI than in asymptomatic patients and lesions score 1 on MRI ($p<0.05$). CONCLUSIONS: Cognitive deficits are common in patients with Asymptomatic Ischaemic Disturbances of the Cerebral Circulation and unilateral asymptomatic severe ICA stenosis. Our findings suggest that an additional mechanism beyond the structural lesion such as chronic hypoperfusion may affect cognitive function in patients with high-grade ICA stenosis.

Key words: asymptomatic ischaemic disturbances of the cerebral circulation, ICA stenosis, neuropsychological test

Carotid stenosis is an important risk factor for stroke. The major cause of cerebral ischemia in patients with stenosis of the internal carotid artery (ICA) is intracranial arterial obstruction due to thromboembolism. Recent studies have also demonstrated the importance of hemodynamic factors to predicting the risk of ischemic stroke after ICA stenosis. Impairment of cognitive function has often been reported in patients with carotid artery stenosis.

This study analyzed the reduced neuropsychological test performance with the aim of identifying the specific clinical and neuroimaging factors that influence the effects of asymptomatic carotid stenosis on cognitive function.

MATERIALS AND METHODS

The study cohort comprised 123 patients, who were admitted to the Second Clinic of Neurology, UMHAT "St. Marina", Varna. Colour-coded duplex sonography was used to determine the extracranial blood flow velocity and the intima media thickness (IMT) of common carotid arteries (CCA), the presence of atherosclerotic plaques, their severity, echogenicity and stability. A paralell magnetic resonance imaging (MRI) was applied. From all patients with Asymptomatic Ischaemic Disturbances of the Cerebral Circulation (AIDCC) we enrolled 10, who had severe (70-99%) asymptomatic stenosis of the extra cranial ICA (tabl.1).

Neuropsychological testing

Cognition was examined. The tests administered for the examined areas of neuropsychological functioning were as follows: attention and working memory, verbal memory test, visuospatial function and visual memory test, language tests, MMSE. Cognitive scores in each patient were compared with the standard scores of normal healthy subjects.

RESULTS

The characteristics of the study participants are listed in Table 1. The severe asymptomatic ICA stenosis was on the

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left in seven patients and on the right in three patients. The mean age of the patients was 50.7± 8.4.

Tabl. 1. Baseline characteristics

characteristics		right stenosis	left stenosis	total
gender	male	2	5	7
	female	1	2	3
age	40-50	1	3	4
	51-60	4	2	6
hypertension				10
diabetes mellitus				6
hypercholesterolemia				4
heart disease				2
smoking				6

Risk factors and comorbidities included arterial hypertension (all patients), diabetes mellitus (6 patients), tobacco use (6 patients), hypercholesterolemia (4 patients), and coronary heart disease (2 patients).

The demographics and vascular affective risk factors did not differ significantly between patients with right- and left-side ICA stenosis ($p>0.05$).

MRI findings: localized hyperintensive lesions in the periventricular or subcortical white matter (but not the cortex) on MRI was devided in three groups dependend of different type of white matter lesions [*European Task Force on Age-R elated White Matter Changes (ARWMC) rating scale [Baert A.L., Sartol K., 2005; Barkhof F., Scheltens P., 2002*]: punctate hyperintensities type 1, early confluent type 2, and confluent lesions type 3.

Tabl. 2. Cognitive performances in patients with AIDCC and severe stenosis of ICA

	Score (mean ±SD)	p
attention	6.75 ±3.37	0.44
language and related function	16.38 ±5.87	0.93
visuospatial function	21.80 ±6.11	0.48
memory	53.8 ±8.22	0.014*
MMSE	23.12 ±4.09	0.42

Neuropsychological testing

Neuropsychological assessments revealed that 8 of the 10 patients had cognitive deficits in more than one domain of attention, visual and verbal memory impairments, or visuospatial dysfunction. Memory dysfunction was found in 7 of the patients (63%); of which 4 showed working memory impairment and 3 had verbal memory impairment. Six patients had visual memory impairment, of which 3 patients showed the pattern of retrieval deficit and 2 showed the pattern of an encoding deficit. Four of the 7 patients with memory problems had both verbal and visual memory problems.

Attention problems were found in 5 of the 10 patients (50%), and visuospatial dysfunction was present in 4 of the 10 patients (43%). The score in the memory domain of the neuropsychological test was significantly worse in patients with type 3 lesions on MRI (Table 3). The mean cognitive score in the memory test was also significantly lower in patients with type 2 and 3 lesions than in asymptomatic patients with type 1 lesions on MRI ($p<0.05$) (Table 3).

Tabl. 3. Cognitive performances in patients with ICA stenosis and different type of the lesions on MRI

	lesion type 1	lesion type 2	lesion type 3	p
attention	8.12±2.75	8.05±1.67	6.82±2.64	0.35
language and related function	15.40±6.32	15.34±5.10	17.10±5.12	0.64
visuospatial function	24.83±4.12	23.29±3.82	20.64±4.30	0.19
memory	53.90±16.42	51.62±14.40	42.18±13.72	0.22
MMSE	24.00±4.18	23.15±4.02	21.82±3.16	0.39

DISCUSSION

Patients with AIDCC and severe stenosis of ICA are at risk of cognitive loss and vascular dementia, and this may also be a modifiable risk factor for cognitive decline. There have been many reports of a relationship between ICA stenosis and cognitive function, concluded that cognitive deficits are present in patients with either symptomatic or asymptomatic carotid obstruction, with a mild and diffuse detrimental effect of carotid stenosis on cognitive function.

Our neuropsychological testing revealed obvious cognitive deficits in all patients, with the severity varying from very mild to severe. The most common cognitive dysfunction was mild-to moderate. Visuospatial dysfunction, and the performances of the verbal and visual memory did not differ significantly between the left and right sides. The type of lesions on MRI were associated with significant differences in MMSE score.

Our study appears to show that neuropsychological tests are more sensitive than MRI to early changes in cerebral functioning due to atherosclerosis. We therefore recommend the routine inclusion of cognitive testing in patients with more than two risk factors for cerebrovascular disease and asymptomatic stenosis. We ascertained that the MMSE

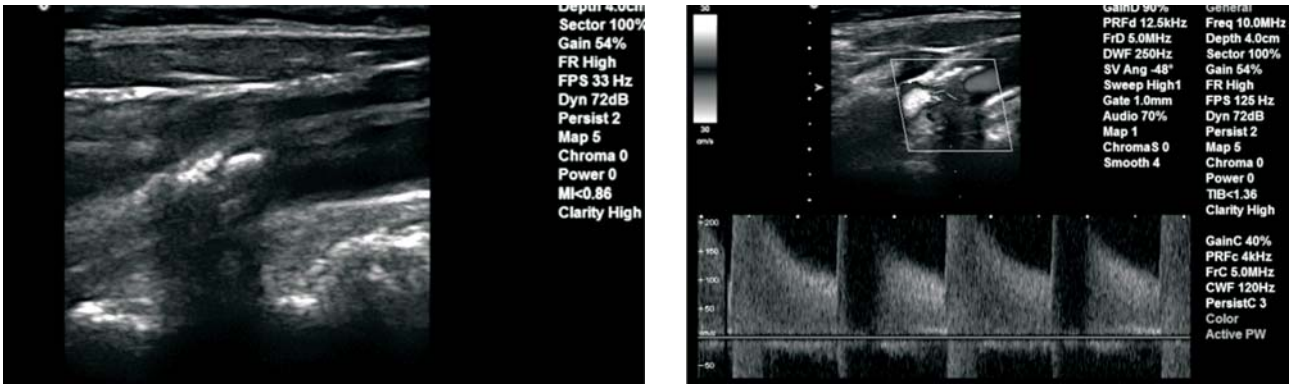

Fig. 1. High grade stenosis of left internal carotid arthery

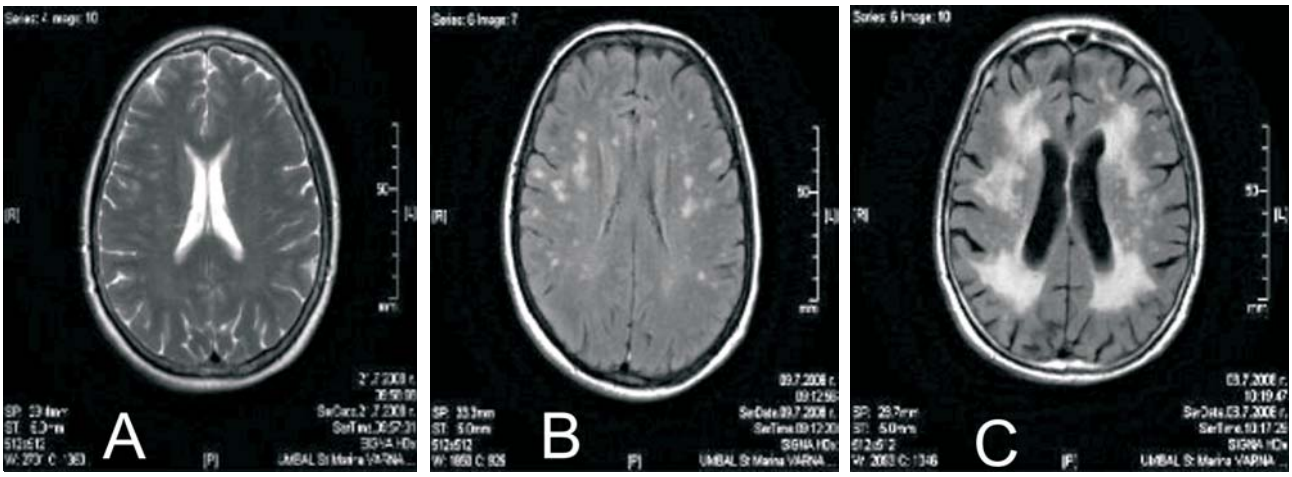

Fig 2.Different type of white matter lesions: punctate hyperintensities type1 (A), early confl uent type2 (B), and confl uent lesions type3 (C) Classificatoin by European Task Force on Age-Related White Matter Changes (ARWMC) rating scale [Baert A.L., Sartol K., 2005; Barkhof F., Scheltens P., 2002].

was also sensitive to detect modest improvements in cognitive performance in the patients with carotid stenosis, and would be useful in predicting occurrence of stroke or TIA in patients with asymptomatic carotid artery stenosis.

Carotid stenosis may be a marker of intracerebral or generalized atherosclerosis, perhaps resulting from microcirculatory disturbances due to microangiopathy and a reduction in cerebral perfusion due to impaired vasoreactivity with increased small-vessel resistance. The carotid lesions could affect the development of lacunar infarction in dependent areas of the perforating arteries via a homodynamic or micro embolic mechanism. The limitations of our study are that it did not include a control group, and the sample was very small. We found that the presence of asymptomatic ICA stenosis by patients with AIDCC has an important effect on cognitive function, because structural lesion (e.g., chronic hypoperfusion) affects the cognition in patients with high-grade ICA stenosis. We suggest that detailed neuropsychological testing should be used to detect vascular cognitive impairment in patients with carotid stenosis, and that chronic hypoperfusion ischemia is the cause of vascular cognitive impairment.

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