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Relationship between cognitive profile and neuroradiographic parameters in patients with idiopathic normal pressure hydrocephalus

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Keywords
Hydrocephalus; Normal Pressure; Cognition; Linear Model; Magnetic Resonance Imaging

Abstract

Background: Normal pressure hydrocephalus (NPH) is a reversible type of dementia, which affects 0.2 to 5.9 percent of elders. It manifests with triad of gait disturbances, urinary incontinence, and cognitive decline. In this study, association between cognitive and neuroradiographic parameters of idiopathic NPH (iNPH) was appraised to find out possible biomarkers for preventive intervention.

Methods: In a cross-sectional study, 16 patients with iNPH were evaluated for third and fourth ventricle diameter, diameter of temporal horn of lateral ventricle, Evans index (EI), callosal angle (CA), callosal bowing, and ballooning of frontal horn. The Neuropsychiatry Unit Cognitive Assessment Tool (NUCOG) was used to take cognitive profile. Relation between brain magnetic resonance imaging (MRI) indices and cognitive domains was extracted, using generalized linear model (GLM).

Results: Patients with mild callosal bowing had better function in memory (P = 0.050) and language (P = 0.001) than those with moderate to severe callosal bowing. Negative or mild ballooning of frontal horn was also associated with higher scores in memory (P = 0.010), executive function (EF) (P = 0.029), and language (P = 0.036) than moderate to severe ballooning of frontal horn. Increased 3rd ventricle diameter was associated with decline in total cognition (P = 0.008), memory (P = 0.019), EF (P = 0.012), and language (P = 0.001). Relation between other radiographic indices and cognitive function was not significant.

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Conclusion: Third ventricular diameter, rounding of frontal horn of lateral ventricle, and callosal bowing are more accurate neuroradiographic parameters to predict cognitive decline in iNPH.

Introduction

Major neurocognitive disorders (MNCD), previously known as dementia, traditionally were classified as reversible and irreversible subtypes. Normal pressure hydrocephalus (NPH) is considered as one of the reversible dementias, which affects 0.2 to 5.9 percent of elders with clear cognitive decline. According to Hakim's criteria, NPH manifests with triad of gait disturbances, urinary incontinence, and cognitive decline that would accompany with ventricular dilation and normal cerebrospinal fluid (CSF) pressure. NPH is divided to idiopathic NPH (iNPH) and secondary NPH with known etiology.[1,2]

Cognitive impairment is present even at early stages of iNPH and is described as executive dysfunction. Executive function (EF) refers to higher-order cognitive functions which consist of working memory, reasoning, task flexibility, planning, and problem-solving. Reduced speed of information processing and impairment of attention are also reported in NPH. Draining the excess CSF has been proposed as the treatment of iNPH and may prevent permanent cognitive dysfunction.[3]

The main neuroradiographic findings of NPH are marked dilatation of lateral ventricles, disproportionate to cerebral atrophy, which is usually measured based on the Evans index (EI) > 0.3 [EI is the ratio of maximum width of the frontal horns of the lateral ventricles and the maximal internal diameter of the skull at the same level employed in axial magnetic resonance imaging (MRI)], ballooning of frontal horns, bowing of corpus callosum (CC), callosal angle (CA) between 40^{o} and 90^{o}, widening of temporal horns (> 6 mm), and 3^{rd} and 4^{th} ventricular enlargement. By chronicity of NPH, periventricular hyperintensities are also present.[4]

In this study, association between cognitive and neuroradiographic parameters of iNPH was appraised to find out possible biomarkers for preventive intervention.

Materials and Methods

In a cross-sectional study from August 2020 to February 2021, brain MRIs of 676 patients, which were done at Kashani Hospital, affiliated to Isfahan University of Medical Sciences, Isfahan, Iran, were reviewed. Based on radiographic findings suggestive for hydrocephaly, 98 patients were evaluated for clinical symptoms of NPH, including gait disturbance, urinary incontinence, and cognitive decline. Patients with history of hemorrhage, mass lesion, and head trauma were excluded as secondary NPH. Finally, 16 patients with age more than 50 years and neurological and radiographic features of iNPH were recruited. Baseline characteristics, including age, gender, educational level, smoking and alcohol use, medical history, and current drugs were recorded.

Exact neuroradiographic indices were measured, including third and fourth ventricle diameter, diameter of temporal horn of lateral ventricle, EI, and CA. Callosal bowing and ballooning of frontal horn were graded by an expert neuroradiologist, based on a 3-grade Likert scale.

The Persian version of Neuropsychiatry Unit Cognitive Assessment Tool (NUCOG) was used to evaluate the patients' cognitive function in the following domains: attention, visuospatial, memory, EF, and language. Each of these domains are tested by group of items as shown in table 1. The maximum score for each domain was 20, with a total score of 100. The internal consistency of the NUCOG (Cronbach's α) was 0.924.[5]

This study was approved by the Bioethics Committee of Isfahan University of Medical Sciences (registration number: IR.MUI.REC.1399.850). We discussed this study with all of the participants and obtained written informed consents. Generalized linear model (GLM) was used to find the relationship between cognitive profile and radiographic indices.

Table 1. Items of subscales in Neuropsychiatry Unit Cognitive Assessment Tool (NUCOG)

A: Attention	B: Visuoconstruction	C: Memory	D: Executive	E: Language
A1. Orientation (time/place)	B1. Drawing	C2. Verbal recall	D1. Motor sequencing	E1. Comprehension
A2. Digit span	B2. Praxis	C3. Spatial recall	D2. Categorical fluency	E2. Repetition
A3. Overlearned sequence	B3. Left/right orientation	C4. Long-term recall	D3. Abstract thinking	E3. Naming
	B4. Neglect		D4. Interferences	E4. Writing
	B5. Calculation			E5. Reading
				E6. Word finding

Results

16 patients with iNPH were included in this study. Baseline demographic, cognitive, and radiographic variables are demonstrated in table 2. Relation between brain MRI indices and cognitive domains was extracted, using GLM, while gender, age, and years of education were controlled. The results are shown in table 3.

Patients with mild callosal bowing had better function in memory (P = 0.050) and language (P = 0.001) than those with moderate to severe callosal bowing. Negative or mild ballooning of frontal horn also was associated with higher scores in memory (P = 0.010), EF (P = 0.029), and language (P = 0.036) than moderate to severe ballooning of frontal horn.

Increased 3rd ventricle diameter was associated with decline in total cognition (P = 0.008), memory (P = 0.019), EF (P = 0.012), and language (P = 0.001). Relation between other radiographic indices and cognitive function was not significant.

Discussion

There was a negative relationship between severity of radiographic changes and cognitive function. Patients with mild callosal bowing had better performance in memory and language. CC is the major fiber bundle in the brain which connects two hemispheres and also cortical and subcortical regions and plays an important role in cognitive functions. CC is involved in the neural organization of memory and language.[6] Diffusion tensor imaging (DTI) studies have shown damages to interhemispheric fibers passing through CC in patients with iNPH.[7] Morphological changes of CC in iNPH due to lateral ventricular dilation and impingement of the CC against the falx cerebri and consequent axonal loss may lead to callosal damage.[8] This might explain our findings regarding language and memory impairment associated with callosal bowing in iNPH.

Patients with moderate to severe ballooning of frontal horn had lower scores in memory, EF, and language. Participants with ventriculomegaly performed worse in the domains of global, attention, delayed recall memory, and EF on the neuropsychological assessments compared to those without ventriculomegaly.[9] Frontal horn of lateral ventricle has close anatomical relation with CC and also is laterally limited by caudate nucleus. Caudate nucleus is an important part of frontal-thalamic-striatal circuit. This frontal-subcortical circuit plays an important role both in movement and cognitive performance, especially learning and EF.[10]

Table 2. Patients' demographic characteristics, radiographic features, and cognitive profile

Variable		Value	Median (minimum-maximum)
Gender [n (%)]	Men	12 (75.0)	
	Women	4 (25.0)	
Age (year) [n (%)]	50-59	4 (25.0)	
	60-69	8 (50.0)	
	70-79	3 (18.8)	
	80-89	1 (6.2)	
Education [n (%)]	≤ college	10 (62.5)	
	> college	6 (37.5)	
Handedness [n (%)]	Right	15 (93.8)	
	Left	1 (6.2)	
Callosal bowing [n (%)]	Mild	8 (50.0)	
	Moderate/severe	8 (50.0)	
Ballooning of frontal horn [n (%)]	Negative/mild	6 (37.5)	
	Moderate/severe	10 (62.5)	
4th ventricle diameter (mean ± SD)		13.12 ± 3.80	13.50 (6.60-22.00)
3rd ventricle diameter (mean ± SD)		13.10 ± 3.40	13.40 (8.20-21.20)
Temporal horn diameter (mean ± SD)		13.80 ± 4.20	14.20 (6.00-20.50)
Callosal angle (mean ± SD)		118.00 ± 19.10	126.70 (71.00-146.70)
Evans index (mean ± SD)		0.32 ± 0.05	0.31 (0.27-0.48)
Attention (mean ± SD)	Score (0-20)	7.80 ± 5.10	6.25 (0-18.00)
Visuoconstruction (mean ± SD)	Score (0-20)	12.50 ± 4.20	12.20 (7.00-10.00)
Memory (mean ± SD)	Score (0-20)	8.80 ± 3.80	7.80 (2.00-15.00)
Executive function (mean ± SD)	Score (0-20)	7.70 ± 4.90	6.80 (0-18.00)
Language (mean ± SD)	Score (0-20)	15.70 ± 3.70	
Total score of NUCOG (mean ± SD)	Score (0-100)	52.80 ± 19.10	

NUCOG: Neuropsychiatry Unit Cognitive Assessment Tool; SD: Standard deviation

Table 3. Results of generalized linear model (GLM) with function gamma of effect of radiographic indices on cognitive profile

Variables		Attention		Visuoconstruction		Memory		Execution		Language		Total score	
		β	P	β	P	β	P	β	P	β	P	β	P
Callosal bowing	Mild*	0.134	0.676	0.129	0.623	0.696	0.050	0.225	0.414	0.596	0.001	0.513	0.061
	Moderate/severe	0		0		0		0		0		0	
Ballooning of frontal horn	Negative/mild*	0.066	0.897	0.295	0.190	0.746	0.110	0.926	0.029	0.364	0.036	0.517	0.079
	Moderate/severe	0		0		0		0		0		0	
4th ventricle diameter		0.078	0.169	0.045	0.209	0.097	0.034	0.121	0.007	0.072	0.003	0.093	0.120
3rd ventricle diameter		-0.031	0.390	0.030	0.281	-0.083	0.019	-0.077	0.012	-0.058	0.001	-0.071	0.008
Temporal horn diameter		0.082	0.059	0.043	0.011	0.065	0.032	0.088	0.010	0.070	< 0.001	0.080	0.003
Callosal angle		0.028	< 0.001	0.010	0.311	0.013	0.153	-0.006	0.527	0.014	< 0.001	0.013	0.077
Evans index		8.178	0.085	5.349	0.167	9.882	0.021	5.609	0.132	8.446	< 0.001	8.940	0.005

*B: Mean difference NUCOG score between mild, moderate, severe

It is assumed that cognitive decline in iNPH may relate to reduced caudate volume. Brain MRI volumetric studies showed diminished caudate volumes in iNPH. Although the cause of volume loss is not clear, tissue compression may lead to reduced blood flow and following cell loss.[11] In addition, MRI investigations with DTI techniques revealed that ventriculomegaly was accompanied with increased fractional anisotropy in caudate nucleus. It may be due to tissue compression.[12] This may describe the picture of impaired language and memory accompanied with frontal horn ballooning.

Increased 3rd ventricle diameter was accompanied with lower scores in memory, EF, language, and total cognitive performance. Third ventricle is a narrow space between two hemispheres. It is laterally limited by right and left thalamus. Thalamus is the main relay station of brain and has a key role in frontal-thalamic-striatal circuit. It has an important role in higher-order cognitive processes including EF and memory. Anterior thalamic nucleus, as one part of the Papez circuit, involves in learning memory.[13] Based on cortico-thalamic language network, thalamus also plays an important role in production and comprehension of language.[14] DTI studies have shown that mediodorsal nucleus of thalamus is connected to dorsolateral prefrontal cortex and integrity of prefrontal cortex-thalamic connectivity is important in optimal EF.[15] Therefore, thalamus function could be affected by 3rd ventricular dilation and this may lead to decline in memory, language, EF, and eventually total cognitive function.

Our study did not find any relation between increased diameter of 4th ventricle and temporal horn of lateral ventricle with cognitive decline. Association of EI and CA with change in cognition was not determined. In morphological studies, also, no significant relationships between cognitive decline and EI were reported.[16] Therefore, these parameters, in comparison with third ventricular diameter, rounding of frontal horn of lateral ventricle, and callosal bowing are less helpful in predicting cognitive decline in iNPH. It may also be due to small number of patients.

The limitations of the present study were the cross-sectional design, the limited sample size, and using less specific cognitive assessment tool.

Conclusion

Third ventricular diameter, rounding of frontal horn of lateral ventricle, and callosal bowing are more accurate neuroradiographic parameters to predict cognitive decline in iNPH.

Conflict of Interests

The authors declare no conflict of interest in this study.

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