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THE KOHS' BLOCKS TEST AS AN IMPORTANT INSTRUMENT TO INVESTIGATE THE VISUO-SPATIAL IMPAIRMENTS IN MYOTONIC DYSTROPHY.

PART I. QUANTITATIVE AND QUALITATIVE ANALYSIS

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ABSTRACT - This study presents the performance of 39 cases of myotonic dystrophy on Kohs' blocks test (21 females and 18 males, age range from 9 to 70 years). On this test, the patients have to reproduce figures from models previously showed to them. Some of the patients had some kind of professional activity, while others had never exerted a professional occupation. The patients denoted considerable difficulty to perform the test. Some cases constructed entirely different figures in comparison to the presented drawings, translating visuo-spatial and constructional disabilities. The performance was insufficient in 71.4 % of the cases. These cases solved less than 50% of the test. The levels of analysis and synthesis were severely impaired. A total of 18 cases got less than 10 points, not reaching 20% of the test. The results showed the sensitivity of this test in detecting visuo-spatial impairment in myotonic dystrophy.

KEY WORDS: myotonic dystrophy, psychological tests, Kohs' blocks.

O teste dos cubos de Kohs como importante instrumento para investigar as alterações visuo-espaciais da distrofia miotônica: I. Análise quantitativa e qualitativa

RESUMO - Foram avaliados 39 casos de distrofia miotônica a partir do desempenho no teste dos cubos de Kohs. Havia 21 casos femininos e 18 masculinos, idade variando de 9 a 70 anos e diferentes níveis educacionais (do primário ao superior). Alguns encontravam-se ativos profissionalmente, enquanto outros nunca exerceram uma ocupação profissional. Os pacientes denotaram considerável dificuldade na execução deste teste que é instrumento que se apresenta fundamentalmente por reprodução de figuras. Houve casos que construíram figuras com formas bem diferentes dos desenhos apresentados. O desempenho foi insuficiente em 71,4 % dos casos, os quais não conseguiram resolver 50% do teste. Muitas das reproduções fugiram ao padrão correto, traduzindo comprometimento visuo-espacial pela grave distorção em comparação com a figura modelo. Os níveis de análise e síntese estavam comprometidos de forma importante. Dentre os pacientes, 18 casos não alcançaram os 10 pontos, dos 133 possíveis, não realizando sequer 20% do teste. Os resultados comprovaram a sensibilidade deste teste em detectar comprometimento visuo-espacial na distrofia miotônica.

PALAVRAS-CHAVES: distrofia miotônica, testes psicológicos, cubos de Kohs, alterações visuo-espaciais.

Myotonic dystrophy (MyD) is the most common adult muscular dystrophy. It is an autosomal dominant disorder due to an expansion of a trinucleotide CTG repeat in the 3' untranslated region of the gene 19q13.3[1-7]. This disease shows several clinical manifestations, such as skeletal muscle changes, baldness, endocrine abnormalities, cardiac and respiratory involvement[8-12]. In MyD the

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alterations of the memory, attention/concentration and of the "know-to do" are common. Such changes limit the field of the intellectual development. Some cases conclude high school, but it is very uncommon that they finish some university course, occupying functions on the work market. The majority does not exceed elementary school. This educational development failure would be caused by cerebral dysfunction since infancy.

The study of the cognitive deficiencies related to MyD is of extreme value for planning the best therapeutic. This permits actions to minimize psychosocial problems faced by the patients and their relatives. The stimulation of the patients' abilities, limited or not, has to be considered as a factor of rehabilitation and readjustment to life in a wide vision. As MyD is a potentially incapacitant illness, it must be seen according to a psychosocial approach, since it determines fall of economic productivity and social retirement, causing inexorable reduction in the quality of life[13].

Rosman et Kakulas[14] argued about the possible reasons of the social isolation. The psychosocial limitations faced by the patients, consequence of preconceptions and social barriers, would cause isolation and low productivity. These situations coupled to the cognitives and physical limitations would limit and/or raise difficulties to the patients' active social participation, involving school life, marriage, maternity, leisure and work. Such difficulties would generate depression or dissatisfaction. In conclusion, a reduction on the quality of life would be the result of physical and psychosocial factors caused by the illness and the environment[13].

In our initial psychological studies, we disclosed intellectual capacity alterations and severe visuo-spatial deficiencies in patients with MyD[15-17], since the results were unsatisfactory in the majority of the cases. For this reason, we decided to magnify the sample of cases and detail the patients' performance on Kohs' blocks test[18], not only through quantitative but also qualitative studies. This qualitative evaluation rarely has been cited in the literature and we did not have knowledge of any previous publication on MyD with this kind of evaluation.

METHOD

The Kohs' blocks test is based on items related to attention, adaptation and self-criticism. This test represents an excellent instrument used for checking visuo-spatial abilities. The patient has to construct a figure after seeing a model previously organized by the examiner. The language does not act on the test. The understanding of the task requires spatial evaluation as well as analysis and synthesis ability. A good performance does not only need understanding of the task but also visual-motor coordination and constructional abilities.

The group consisted of 39 patients (21 females and 18 males), with an average age of 35±14 years (range 9 to 70). Disease transmission was maternal in 17 cases, paternal in 17, and of unknown origin in 5 cases. Most cases were localized between the ages of 20 and 45 (25 cases) (Table 1). There were several levels of education. The majority had not completed elementary school. They occupied several employments; however, the majority of them worked in low hierarchy jobs. Neurological involvement was evaluated on a quantitative scale from the Center for Myopathies Investigation and Treatment (CIM) for MyD. The punctuation varied from 0 to 15. The lesser the value, worse the disease (Table 2).

All of the cases whose motor alterations could interfere with the performance in the test were excluded. The test was applied individually and by the same examiner. No patient suffered from disease unrelated to MyD and capable of producing brain lesions or interfering with test performance. Informed consent was obtained from all subjects or their responsibles.

The test consists of cards with figure-models with an increasing level of difficulty. A set of cubes is supplied to the patient. All cubes are of equal size and each of its faces has a part of the figure-model. Initially, 4 cubes are supplied to construct the simplest figure-model of the test, like a puzzle. In order to construct the following figures, 9 and thereafter 16 cubes are supplied (the full 17-figure version was employed). Before applying the test, the examiner verifies if the patient possesses adequate visual form perception, discriminates the colors, perceives that all cubes are of equal formats and localizes the blocks in visual space. Passing this stage, the test is explained and the examiner constructs the figure-example. The maximum total of possible points is 133 and the maximum mental age, 19 years.

Table 1. Patients' relation and their results on Kohs' blocks test.

NU	NM	Sx	REC	T	AG	AO	TD	NI	NI %	ST	ST %	WS	IQ	MA
1	AF	M	068589	m	50	05	45	5	64	003	002	08	098	06
2	AGB	F	036311	m	62	47	15	7	50	003	002	08	098	06
3	AMG	F	074904	f	44	18	26	4	71	076	057	12	102	14
4	CF	M	027894	m	56	35	21	5	64	077	058	13	103	14
5	CFS	M	101114	?	15	00	15	8	43	131	098	16	106	19
6	DSR	M	094797	f	23	10	13	5	64	032	024	10	100	10
7	EDG	F	068587	f	35	00	35	7	50	000	000	07	097	05
8	FRM	M	039194	f	07	00	7	5	64	000	000	07	097	05
9	GAM	M	036530	?	42	16	26	6	57	028	021	09	099	10
10	IMN	F	040904	f	29	00	29	5	64	003	002	08	098	06
11	IRM	F	044441	f	09	00	9	8	43	000	000	07	097	05
12	JAM	M	088488	f	38	07	31	5	64	074	056	12	102	13
13	JCS	M	069657	?	31	14	17	5	64	021	016	09	099	09
14	JSM	M	056262	m	23	00	23	2	86	001	001	08	098	05
15	JLS	M	089792	f	31	16	15	5	64	031	023	10	100	10
16	LCN	F	038284	f	28	05	23	5	64	080	060	13	103	14
17	MCS	F	073615	f	56	40	16	2	86	000	000	07	097	05
18	MGR	F	088487	m	27	00	27	5	64	028	021	09	099	10
19	MHN	F	040903	f	34	00	34	5	64	003	002	08	098	06
20	MIM	F	091412	m	38	37	1	8	43	124	093	16	106	18
21	MSM	F	057109	m	28	00	28	8	43	000	000	07	097	05
22	MLM	F	057109	m	26	00	26	5	64	003	002	08	098	06
23	MLS	F	073616	m	27	24	3	5	64	021	016	09	099	09
24	MPC	F	095881	m	70	10	60	5	64	009	007	08	098	07
25	MSF	F	063156	f	25	23	2	8	43	070	053	12	102	13
26	MSS	M	020243	f	40	27	13	3	79	000	000	07	097	05
27	MVS	M	073615	?	23	20	3	8	43	133	100	16	106	19
28	OSR	F	063292	m	47	22	25	5	64	003	002	08	098	06
29	RSR	F	054135	m	42	12	30	5	64	003	002	08	098	06
30	SGG	F	046465	f	42	31	11	8	43	008	006	08	098	07
31	SJB	M	070883	?	29	11	18	7	50	037	028	10	100	11
32	TRA	F	074902	f	18	00	18	8	43	102	077	14	104	16
33	WFS	M	102750	m	30	10	20	5	64	000	000	07	097	05
34	VSG	M	088492	m	37	22	15	5	64	024	018	09	099	09
35	WML	M	057719	m	44	00	44	4	71	021	016	09	099	09
36	VLT	M	107758	m	29	24	05	5	64	133	100	16	106	19
37	CMA	F	108149	f	44	26	18	7	50	081	061	13	103	14
38	JPB	F	056879	m	19	00	19	5	64	005	004	08	098	06
39	RCP	M	090948	f	52	17	35	3	79	133	100	16	106	19
			Mean		35	14	21	6	44	038	029	10	100	10
			SD		14	13	13	2	17	046	035	03	003	05

NU, case number; NM, patient's name (initials); Sx, sex; REC, patient's record at INDC; T, transmitter; AG, patient's age; AO, age of onset; TD, time of disease; NI, degree of neurological impairment; NI%, the percentual loss of the neurological performance; ST, scores obtained on test; ST%, percentual of performance according to ST; WS, weighed score; IQ, intellectual quotient; MA, mental age; SD, standard deviation; M, male; F, female; m, mother; f, father; ?, unknown transmitter.

Table 2. Scale performance from CIM to score the patient with myotonic dystrophy.

Item	Points	Description
1	14	Normal
2	13	The diagnostic only can be made by electromyography, slit lamp examination or DNA analysis, cause there is no clinical muscular impairment
3	12	The patient presents only myotonia and/or nasal voice
4	11	Item 3 plus facial weakness and/or ptosis
5	10	Item 4 plus sternomastoid weakness with no distal weakness
6	9	Item 5 plus distal weakness
7	8	Item 6 plus proximal triceps weakness
8	7	Item 7 plus other proximal muscles with weakness. The patient can walk and climb stairs without assistance
9	6	The patient climbs stairs with aid of railing
10	5	The patient cannot rise from chair without aid
11	4	The patient cannot rise from chair without aid and walking on irregular pavement only with assistance
12	3	The patient cannot rise from chair without aid and walking on smooth pavement only with assistance
13	2	The patient is limited to wheelchair, but the patient can move it
14	1	The patient is limited to wheelchair and requires aid to move it.
15	0	The patient is limited to bed.

During the test, the patient's movements are counted when manipulating the cubes in order to construct the figure. There is a time scale for each figure, with a maximum limit. Exceeding the maximum limit, the examiner will have to construct the figure. The patient must see all examiner's movements during this construction. The examiner does not have to give any verbal explanation at this moment of the test. Soon after, the examiner presents the following figure-model, with the same procedure. The performance has to be stopped after 5 consecutive failures. The score is the sum of the points obtained with each figure.

The examiner verified that the patients were very slow to do the test. If the time were determined in a rigid form, the great majority would not passe the first group of figures-model (with only 4 cubes). The authors had concluded that the test would be realized without taking into consideration the time factor and the frequency of movements. The priority of the investigation was to verify if the patient had the ability to construct the figure-model correctly. Of course, this allowed a better performance. It was only considered if the reproduction was correct or not, attributing maximum punctuation to the item when the reproduction was correct. The intellectual quotient (IQ) deviation was calculated on basis of the sample (normative group, GN), in order to verify the performance in the group of the patients.

RESULTS

The chronological age varied from 9 (this patient got zero point in the test) to 70 years (this patient got 9 points in the test). The group presented a loss of 60% on neurological performance (average of AN% in Table 1). The average performance on the test was only 29% (average of ST% in Table 1).

A total of 26 cases (66.66%) presented very unsatisfactory performance (mental age up to 10 years). From these 26 cases, 18 scored less than 10 points (less than 20% of the test; their ages varied from 7 to 70 years, with an average of 36.0 years). These 18 cases got the following punctuation: 0 point, 7 patients; 1 point, 1 patient; 3 points, 7 patients; 5 points, 1 patient; 8 points, 1 patient; 9 points, 1 patient.

Table 3. Qualitative analysis.

NU	A1	A2	A3	A4	A5	A6	A7
1	+	-	-	+	+1	-	+
2	+	-	+	-	+1	-	+
3	+	-	+	-	-	-	-
4	+	-	+	-	-	+	+
5	+	+	-	-	-	-	-
6	+	-	+	-	+6	-	+
7	+	-	-	+	+n	+	+
8	+	-	-	+	+n	-	-
9	+	-	+	-	+5	-	-
10	+	-	-	+	+1	-	+
11	+	-	-	+	+n	-	-
12	+	-	-	+	-	+	+
13	+	-	+	-	+4	+	+
14	-	-	-	+	+n	-	-
15	+	-	-	+	+9	+	+
16	+	-	+	-	-	-	-
17	+	-	-	+	+n	-	+
18	+	-	-	+	+6	-	+
19	+	-	-	+	+1	-	+
20	+	+	-	-	-	+	+
21	+	-	-	+	+n	-	-
22	+	-	-	+	+1	-	+
23	+	-	+	-	+4	-	-
24	+	-	-	+	+3	-	+
25	+	-	+	-	-	-	-
26	+	-	-	+	+n	-	+
27	+	+	-	-	-	-	-
28	+	-	-	+	+1	-	+
29	+	-	-	+	+1	-	+
30	+	-	+	-	+2	-	+
31	+	-	+	-	+10	-	-
32	+	-	+	-	-	-	-
33	+	-	-	+	+n	-	-
34	+	-	-	+	+8	-	-
35	+	-	+	-	+4	+	+
36	+	+	-	-	-	-	-
37	+	-	-	+	-	+	+
38	+	-	-	+	+2	-	+
39	+	+	-	-	-	-	-

The digit +, present; the digit - , absent; A1, the patient recognized perfectly the colors and the shapes; A2, after making a mistake, the patient perceived where was this mistake and corrected it; A3, the patient perceived that his reproduction was incorrect, but did not have the ability to locate and/or correct the mistake; A4, the patient did not have the ability to recognize that his construction was wrong; A5, the patient did not conclude the test (the number beside of the digit + means the last figure that the patient had reproduced; the letter n correspond to the cases with no figure constructed); A6, the patient constructed figures with inversions and disclosed difficulties to construct figures in lozenge shape; A7, the patient constructed figures with severe distortions and disclosed difficulties to construct figures in lozenge shape.

Thirteen cases were at a mental age between 11 and 19 years (33.33% of the sample). From these 13 cases, 6 scored more than 100 points (CFS, 15 years, 131 points; MIN, 38 years, 124 points; MVS, 133 points, TRA, 18 years, 102 points, VLT, 133 points, RCP, 133 points). The chronological age of these 13 cases varied from 15 (131 points) to 56 years (77 points).

Three cases (7.7% of the sample) scored the maximum punctuation (MVS, 23 years; VLT, 29 years; and RCP, 52 years). Just the case CFS (15 years, 131 points) demonstrated mental age superior to the chronological one (IM=19 years). More than 50% of the sample had analysis and synthesis levels severely affected. The group showed great difficulty to perform the test, despite the easiness allowed, as above explained. Some deformed reproductions were constructed, very different from the figure-model.

In the analysis of the patients as a normative group (GN), we verified, by the IQs analysis, that the cases had demonstrated mean performance (IQ from 98 to 107, with average of 100) with results very near each other (standard desviation=3), demonstrating a homogeneous performance. The weighed notes were situated between 8 and 17. There was no inferior result to the average in the comparison between the participants of the sample.

In a qualitative analysis of the results (Table 3), we verified that: a) 97.44% demonstrated recognizing the colors and shapes perfectly (this denoted a good occipital organization); b) 46.15% perceived that their reproductions were incorrect; 12.82% located the failure, but 33.33% did not recognize where the failure was; c) 53.85% did not recognize the failure, affirming that the reproduction was correct.

With regard to the analysis and critic abilities, 30.77% obtained some understanding of the tasks associated with the conclusion of items and 69.23%, not. There were inversions and difficulties with figures in lozenge shape in 20.51% of the sample; 56.41% of this group had significant distortions in constructing the figures. None of the cases of this last group exceeded the figure 10 and 20.51% did not construct any figure.

DISCUSSION

As above defined, to performe the test, the patient will have to see the model presented by the examiner and reproduce it. Moreover, the examiner explains the test and, continuing, asks the patient to reproduce the presented figure. At this moment of the test, a successful performance requires a correct appreciation of the spatial relations among the constituents of the figure. The patient will have to program the appropriate practic motor action for reproducing the figure, with adequate visuo-spatial orientation and topographical ability. The patient's cortical pathways and the areas of visual and auditory integration will have to be normal

The results of this test proved that abilities of analysis, combination, figure completion, judgement and critic were impaired. The group showed spatial conceptualization and ability of construction severely affected.

In cases of visuo-spatial disability, the patient has difficulty to assemble the blocks with the purpose of reproducing the figure-model. Benton[19] defined as constructional apraxia an impairment in the elaboration of the movement that enables the patient to reproduce the figure from a model. Kleist (1918, apud Benton[19]) considered that the disability would be neither visuoperceptual nor visuo-motor in nature, but rather an impairment in the process of translating intact visual perceptions into appropriate motor action, or a kind of rupture between visual and kinesthetic processes.

Benton divided the constructional apraxia into visuo-spatial (due to lesions of the right hemisphere) and executional apraxia (due to lesions of the left hemisphere).

In Benton's analysis from patients with impairment in the visuo-spatial orientation (they were not cases of myotonic dystrophy), there were cases with full rotation of the figure or some

parts. This was interpreted as an expression of loss of directional sense (which we observed in our patients). Some cases showed failure in executing one half of construction (the patient constructed only the right or the left side). This figure was defined as unilateral spatial neglect.

He disclosed the "closing-in" phenomenon. In this case, the patient mixed the model presented with his proper construction, assembling everything in only one construction, or either, the patient actually utilized part of the model in his final construction. This occurrence was defined as serious derangement in spatial apprehension.

Disturbances in spatial orientation have been observed more frequently in lesions due to diseases of the occipital and posterior parietal areas, specifically of the extrastriate regions and the supra-marginal and angular gyri. Some cases showed disturbances in the temporal lobe and, occasionally, in the frontal one.

Hécaen et Angelergues (1963, apud Benton[19]) studied patients with spatial alterations from several etiologies. The majority of them disclosed impairment of the right hemisphere (67 cases with right hemisphere lesions, 14 with left hemisphere lesions and 35 with bilateral lesions). Of these, 31 denoted defective topographical concepts (21 with right hemisphere impairment and only 4 with left ones; the others subjects had bilateral lesions). Other authors have also shown visuo-constructive disabilities with significantly higher frequency in patients with impairment of the right hemisphere[20,21].

Malloy et al.[22] and Censori et al.[23] have also described impairment of the visuo-spatial functions and constructive abilities. Tests of language, verbal memory and the prefrontal executive functions were intact, while spatial and nonverbal memory abilities were considered significantly impaired[22].

The skull computerized tomography and magnetic resonance images did not disclose characteristic alterations[24]. Beyond alterations from cortical origin, some authors have described cytoplasmic eosinophilic bodies inclusion within neurons of the thalamus[25-29]. Ono et al.[28] found neuronal arrangement considerably altered within the cortex, with disordered orientation of neurons, more marked in the frontal and temporal lobes. The intracytoplasmic inclusion bodies were present in cerebral cortex (3rd layer of the frontal and temporal lobes), thalamus, caudate nucleus and putamen. These bodies were oval and elongated with sharply defined contours, usually located at the periphery of the cell[28,29]. They were more abundant in the dorso-medial and anterior nuclei of the thalamus[28]. The controls had bodies only in the thalamus, significantly lower compared with the patients (the proportion of the bodies of the total celular population in the thalamus in patients was 15.7%-20.3% and in controls, 0-1.6%)[28]. Culebras et al.[26] concluded that the loss of thalamic neurons could explain the inattention, apathy and memory defect found in patients with MyD. Ono et al. did not agree with this point of view and affirmed that it would be unlikely that the thalamic lesion only causes mental impairment.

Friedlander et Bittenbender[30] correlated the electroencephalographic alterations (slow alpha rhythms) to diencephalic dysfunction (of which the thalamus is one of the structures). Considering the inclusions within neurons of the thalamus added to the electroencephalographic alterations from patients of Friedlander et Bittenbender, Culebras et al.[26] believed in the possibility of abnormalities in the activator circuit of the cortical neuronal activity from the thalamus. This impairment, associated with the frontal dysfunction, would be responsible for difficulties in the perception of laws and series of increasing complexity. According to Culebras et al. pachygyria and neuronal heterotopias would underlie congenital varieties of stable mental retardation, whereas cytoplasmic bodies within thalamic neurons would explain progressive forms of acquired behavioral changes and dementia.

Penez (apud Granier[32]) and Walker et al. (apud Censori et al.[23]) asseverated that the visuo-spatial and visuo-motor alterations would be frequent in cases of MyD.

Censori et al.[23] found severe intellectual deficit in 50% of the cases. They showed several cases with visuo-spatial impairment and disability to make constructions from models. These authors chose the Kohs' blocks test as suitable for the evaluation of visuo-spatial and constructional functions.

Abe et al.[31] evaluated 14 patients by means of neuropsychological tests and magnetic resonance images. All of them had ventricular enlargement and white matter abnormalities. However, the severity of the abnormalities was variable. There was no difference in neuropsychological testing between patients with mild ventricular dilatation and those with severe dilatation, but they found significant differences between patients with mild white matter lesions and those with severe white matter abnormalities in regard to verbal fluency and attention. One brain was autopsied. The interfascicular space of the white matter was increased and this alteration was responsible for the pallor on myelin staining. They concluded that this white matter alteration would be the cause of the cognitive impairments.

Several authors found a lot of impairment on neurophysiological studies[33,34,35,36]. Nowadays, the P300 wave has been studied in several diseases. The component of auditory and visual event-related potentials have been considered an electrophysiological marker in patients with disorders of cognition and may provide an objective index of impaired mental functioning[37-40]. This wave is generated when the patient discriminate different auditory or visual stimulations. The demonstration of prolonged latency has confirmed the presence of cognitive dysfunctions and impairment in the information processing[41].

Perini et Colombo[37] found P300 wave with normal latency and amplitude significantly lower than that of the control subjects. Their patients showed an accentuation of the pattern characteristic of psychiatric disorders (schizophrenia, alcoholism and depression). These results indicated the possibility of a widespread central nervous dysfunction in MyD.

Kazis et al.[42] have studied the wave P300 in 14 patients (early components N1;P2 and later components N2;P3). Components N2;P3, which are thought to reflect cognitive processes, were abnormal in 8 patients who were the oldest subjects. Magnetic resonance imaging was performed in 12 patients. Multiple focal white matter lesions were found in 5 of them, but were not correlated with the neurophysiological abnormalities.

The results of the performance of our patients demonstrated subnormal mental age and incapacity to reproduce pre-organized figures from a model. We conclude that the evaluation through the Kohs' blocks test is an important way to investigate visuo-spatial alterations, so frequently cited in MyD.

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