CONTRIBUTION TO THE EVALUATION OF LANGUAGE DISTURBANCES IN SUBCORTICAL LESIONS

A piloty study

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ABSTRACT - Subcortical structures are in a strategic functional position within the cognitive networks and their lesion can interfere with a great number of functions. In this study, we describe fourteen subjects with exclusively subcortical vascular lesions (eight in the basal ganglia and six in the thalamus) and the interrelation between their language alterations and other cognitive abilities, as attention, memory and frontal executive functions. All patients were evaluated through the following batteries: Boston Diagnostic Aphasia Examination, Boston Naming Test, Token Test, Benton Visual Retention Test, Trail Making, Wisconsin Card Sorting Test and a frontal scripts task. All patients underwent MRI and twelve underwent SPECT. Results show that these patients present impairment in several cognitive domains, especially attention and executive functions. These alterations affect language abilities, and this fact must be considered in the rehabilitation efforts.

KEY WORDS: thalamus, basal ganglia, language, frontal dysfunction.

The study of language disturbances in subcortical lesions represents a challenge due to the diversity of symptoms that can be found. This happens not only because of the heterogeneity of the structures involved (basal ganglia, different parts of white matter and diverse thalamic nuclei), but also because of the functional complexity of whichever circuits are damaged in these lesions. Additionally, several studies have shown secondary cortical dysfunction (diaschisis or extended cortical ischemia), which contributes to this diversity.

Language alterations in striatocapsular vascular lesions are heterogeneous and can affect several aspects of voice, speech, language and other cognitive functions, in multiple combinations: hypophonia, dysarthria, speech latency, perseverations, lexical access difficulties, comprehension deficits for complex material¹⁴. Posterior lesions (putamen and posterior limb of internal capsule) can produce symptoms related to a cortical-thalamic disconnection or may sometimes compress the adjacent temporal cortex, leading to a fluent aphasia, with com-

Contribuição à avaliação dos distúrbios de linguagem em lesões subcorticais: estudo piloto

RESUMO - As estruturas subcorticais ocupam posição funcional estratégica nas redes cognitivas e sua lesão pode interferir com um grande número de funções. Neste estudo, descrevemos 14 indivíduos com lesões vasculares exclusivamente subcorticais (oito em núcleos da base e seis no tálamo) e a interrelação entre suas alterações de linguagem e de outras funções cognitivas, como atenção, memória e funções executivas. Todos os pacientes foram avaliados através dos seguintes testes: Teste de Boston para Diagnóstico da Afasia, Teste de Nomeação Boston, Teste Token, Teste Benton de Retenção Visual, Trail Making, Wisconsin Card Sorting Test e uma tarefa de scripts frontais. Todos os pacientes realizaram RM de crânio e doze realizaram SPECT. Os resultados mostram que estes pacientes apresentam prejuízo nas várias funções cognitivas, especialmente atenção e funções executivas. Estas alterações afetam as habilidades lingüísticas e devem ser levadas em consideração nos esforços de reabilitação.

PALAVRAS-CHAVE: tálamo, núcleos da base, linguagem, alteração frontal.

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prehension disturbances and phonemic paraphasias. More recently, the basal ganglia have been implicated in the lexical selection mechanisms, while another point of view stresses the concurrence of hemodynamic factors (associated cortical ischemia) as the main factor leading to aphasia in such lesions. Thalamic lesions, on the other hand, are recognized as having an effect that is related, for the most part, to the cortical activation and modulation roles exerted by the thalamus.

Frontal-subcortical circuits, which are composed from the frontal lobes, neostriatum, globus pallidus, substantia nigra, and thalamus, are effector mechanisms involved in the animal and human interactions with their environment. The dorsolateral prefrontal-subcortical circuit organizes the information in order to optimize a behavioral response; the anterior cingulate-subcortical circuit is concerned with the motivation to a certain behavior; and the orbitofrontal circuits integrate the limbic and emotional information into behavioral responses. Dysfunction in this circuit leads to apathy, impulsiveness (abnormal motivation responses) and dysexecutive symptoms. Mood disorders were also described in frontal-subcortical circuit dysfunction, especially obsessive-compulsive behavior whencribed in frontal-subcortical circuit dysfunction, executive symptoms. Mood disorders were also described in the frontal-subcortical circuit dysfunction, especially obsessive-compulsive behavior when orbitofrontal-subcortical structures are affected.

In the large-scale cognitive networks proposed by Mesulam, Broca’s and Wernicke’s areas are the epicenters of the language circuit, being interconnected with the striatum, the thalamus and some frontal, temporal and parietal regions. The basal ganglia and the thalamus participate in all cognitive networks described in Mesulam’s model, in the so-called “state” functions (attention, working / short term memory) and in the executive functions; their lesion has a multifactorial effect in the mental processing.

Clinical data obtained from patients with subcortical lesions rarely disclose a classic aphasia syndrome when performing standardized linguistic tests some time after injury (usually months), but the patients may still complain that their language skills are not the same when compared to a premorbid situation, frequently impairing their professional and social lives. Thus, the additional evaluation of the performance of these patients with complementary language tests and the simultaneous evaluation of executive functions and attention may be helpful to a better understanding of the language deficit and its possible reciprocal interference with the other cognitive impairments. The aim of this study is to contribute to the evaluation of language dysfunction in subcortical lesions considering its interrelation with attention and executive impairments.

METHOD

Participants - The study included 14 subjects with exclusively subcortical lesion: eight predominantly in basal ganglia (seven left-sided and one right-sided, numbered from 1 to 8 and denominated BG group) and six predominantly in the thalamus (three left-sided and three right-sided, numbered from 9 to 14 and denominated T group). All were native Portuguese speakers and right-handed, except for subject 7 whose native tongue was Japanese but spoke Portuguese fluently. There were not antecedents of neurological or psychiatric diseases, hearing deficiency, use of CNS acting drugs or difficulties in language acquisition. All the participants were informed about the procedures and purpose of the study and signed an agreement form. The study was approved by the Commission of Ethics for Analysis of Research Projects - Hospital das Clínicas – University of São Paulo School of Medicine. The demographic, clinical and neuroimaging data of these patients can be seen in Table 1.

Procedure - The language evaluation was performed through the Boston Diagnostic Aphasia Examination (BDAE), the Boston Naming Test and the Token Test. A frontal scripts test, translated to Portuguese from the original publication of Allain was applied in 10 patients. This evaluation aims to investigate the ability of recovering information about familiar action sequences presumed to be sensitive to frontal lobe dysfunction. The subjects were asked to arrange six scripts (“Going to the supermarket”, “Making a cake”, “Going to the movies”, “Going to a wedding”, “Going to the restaurant” and “Taking the subway”). Each script is composed from 10 to 17 actions written on cards that must be placed in order. The title of each script is presented on a separated card that can be assessed by the subject during the performance of the task. Distractors (irrelevant actions) are introduced in three scripts, and must be recognized and excluded. The number of ordination (subversion of the correct sequence of actions), intrusions errors (addition of actions that do not belong to the script) and omission (subtraction of actions belonging to the script) are, then, counted. Patients 2 and 13 did not perform this test because they were illiterate and patients 3 and 11 had comprehension and reading disturbances that interfered with its execution. Thirteen patients were submitted to attention, memory and executive function evaluation through Benton Visual Retention Test (BVRT), Trail Making and Wisconsin Card Sorting Test (WCST) (patient 2 was excluded because she could not comprehend the commands). MRI was performed in all patients and 12 underwent SPECT exams (exception: cases 6 and 10), after at least two months from symptom onset.
Intra and inter-groups (BG and T) comparison in both linguistic and neuropsychological tests was performed through one-way ANOVA. In the frontal scripts task, statistical analysis was not carried out due to the small number of patients in the T group; the patients were compared to a group of eight normal subjects using unpaired t-test, Welch corrected; in the Token Test, they were compared to a group of 17 normal subjects using the Mann Whitney test. Brazilian reference scores were used for the BDAE results22. Scoring and interpretation of the results obtained in the Trail Making, WCST and BVRT were performed according to the respective reference guide. We used the GraphPad InStat® software version 3.05 to execute statistical analysis; a p value of less than 0.05 was considered significant. Patient 2 was excluded from inter-group statistical analysis because she had very poor scores in all tests and her clinical picture resembled that of global aphasia.

RESULTS
The patients’ performance in the language and neuropsychological tests is shown in Tables 2 to 4.
We verified mild anomia in 10 patients (six in the BG group and four in the T group), repetition alterations in 5 cases (three in the BG group and two in the T group) and reduced animal fluency in 12 patients (seven in the BG group and five in the T group). The statistical analysis did not show any significant inter or intra-group differences in the BDAE. In the Token Test, there were also no differences in inter and intra-group analysis; the comparison of the two groups with controls disclosed a worse performance of the former in the fourth and fifth parts \( (p = 0.01 \text{ and } 0.002) \) (Table 3).

The analysis of groups in the frontal scripts task presented some difficulties, as there are no standardized reference values in Portuguese. In a sample of eight normal individuals, we observed an average of 2.6 errors of ordination and 0 of intrusion. Our results showed a tendency of both subcortical groups in presenting more ordination mistakes than normal subjects, with relatively fewer intrusion errors (Table 3). There were no omission errors.

The evaluation of attentional deficits disclosed a low performance in the BVRT (5 moderate and 8 severe); in the subtest of visual discrimination, the average performance was better (being 3 normal, 8 moderate and 2 severe). Dysexecutiveness was found in the performance of the Trail Making test: only two patients had normal scores in part A and 1 in part B; the remaining had a severe delay in the execution time. The executive dysfunction was verified in the WCST results. Again, we did not find any statistically significant differences between performances inter or intra – groups (Table 4).
DISCUSSION

In our series, both groups (BG and T) behaved similarly in most of the tests, and it was not possible to discriminate the groups based on their performance (Table 4). The neuropsychological evaluation shows attention, memory, planning, strategy, ordination and execution disabilities. We can speculate that the alteration of these cognitive domains contribute significantly to the observed language disorders in these patients. The similarity between BG and T groups reinforces the idea that several anatomical lesions can produce congruent symptoms, as long as they are inserted in the same “cognitive network”. Lesions in the dorsolateral frontal-caudate circuit can affect the generative aspects of language (executive function); lesions in the caudate-MSA-cingulate circuit affect speech initiation (the bilateral lesion causing akinetic mutism); the putamenal circuit damage will cause speech latency23. In our series, hypophonia, speech apraxia, speech latency and dysarthria was found only in the BG group, probably due to the caudate nucleus and putamen damage24.

The lexical-semantic access is made of multiple processing that requires caudate integrity, with its multiple afferents pathways from cortical association areas25. Lesions of the anterior limb of internal capsule can interrupt thalamic-frontal connections and frontostriatal-thalamic-frontal loops12. Phonological disturbances are less frequent in these cases due to temporal cortex preservation. Our patients had lexical-semantic difficulties which could be seen in tasks such as verbal fluency and naming; eleven patients were below the percentile 10 for Brazilians in the verbal fluency subtest, despite being above the cut-off score for aphasics22; ten patients were below the percentile 10 in the naming subtests. Lexical access difficulties were more evident as there were a greater number of errors in the visual confrontation than in the responsive naming task (which always has a semantic clue).

In the Token Test, the whole BG-T group differentiated statistically from the control group in the fourth and fifth parts (performing worse), and this alteration had correlation with the extension of stimuli, when there is a need for a greater verbal short-memory memory span26. However, other primary deficits in the understanding of the grammatical features of a sentence might as well contribute to comprehension deficits, these ones related to frontal dysfunction27.

Frontal scripts: Frontal lesions impair the subject’s ability to integrate sequential information and to organize them temporally; moreover, they interfere with the capacity of recognizing and eliminating distractors and elements that are irrelevant to the main action18,28. Hypotheses to explain this fact vary: frontal lesions might weaken the asso-

Table 4. Neuropsychological evaluation results.

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<tr>
<th>Patient</th>
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<td>102</td>
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<td>247</td>
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† patient 2 was excluded from statistical analysis; NP, not performed; ns, not significant.
citations between elements within the working memory (the task of maintaining these associations is a pre-frontal attribution)\textsuperscript{29}. Another possibility is that the frontal lesion may provoke sensitivity reduction in perceiving the relations between the actions of scripts\textsuperscript{30} noticeable finding is that the number of ordination errors greatly surpasses those of intrusion (110 versus 5), suggesting selective sequencing impairment, with relative preservation of the control mechanisms over distractors. Ordination errors in our patients (M = 11; SD = 10.5) were much more frequent than those found in Allain’s group of 23 patients with frontal cortical lesions (M = 2.4; SD = 3.4). The number of intrusion errors, however, was lower in our group (M = 0.5; SD = 1) when compared to the same Allain’s frontal patients (M = 3.3; SD = 2.7)\textsuperscript{18}. Lesions in different parts of the frontal lobe produce different combinations of neuropsychological symptoms, especially when comparing the orbitofrontal and dorsolateral portions\textsuperscript{31}, which is compatible with the existence of multiple functional executive systems\textsuperscript{32}. For Allain\textsuperscript{18}, the ability of performing a sequential ordination and that of eliminating irrelevant elements can represent two distinct executive processes accomplished by the frontal region.

Neuroimaging findings: The cortical hypoperfusion patterns found in these cases give a dimension of the functional repercussion of subcortical lesions, showing that a cortical involvement is present, even when the MRI scans do not show any alterations in the cortex. The idea that the underlying mechanism in the aphasias caused by basal ganglia lesions might be secondary cortical ischemia due to the occlusion of the internal carotid and its bifurcation (junction T) or the M1 portion of the middle cerebral artery\textsuperscript{7,35} is highly provocative, and finds some support not only in the vascular anatomy, but also in the positive correlations between clinical improvement and involution of these hypoperfusion areas. Another important finding is the cortical atrophy encountered in MRI exams performed in later phases\textsuperscript{34}. A question that emerged in our study, however, is related to the similar patterns of hypoperfusion found in the thalamic patients, that can not be primarily justified by ischemia, since thalamic lesions are frequently the result of injury in terminal arteries of the posterior or circulation (vertebral-basilar system). A possible explanation for the occurrence of cortical ischemia in some of our thalamic cases might be the small vessel compression by the hematoma, similar to what happens in some putamenal hemorrhages\textsuperscript{35}. In our series, we had one patient (case 2) that could be considered an example of this mechanism, as she showed fronto-temporal cortical atrophy in an MRI performed 18 months after her stroke.

In conclusion, we believe that the language alterations in subcortical lesions must be considered in the context of a dysexecutive syndrome (of planning, working memory and attention). The mechanisms by which this dysfunction occurs are multiple, and may include a disconnection at any point of frontosstriatothalamocortical loops, vascular alterations leading to secondary ischemia in the language cortex, or white matter and adjacent cortex compression, especially in hemorrhagic injuries. Although it has been a frequent practice to classify the subcortical aphasias in “thalamic” and “nonthalamic”, we were not able to find such a clear differentiation in our patients if only the clinical picture was taken into account, and a great overlapping of symptoms could be found\textsuperscript{36}. Our view is that the difficulty in making such a distinction is due to the fact that the lesions themselves are not “pure”, and that the pathways involved belong to the same frontal-subcortical circuits, although each particular lesion may lead to specific symptoms. It is our belief that a more widespread evaluation of other cognitive domains, as described in this study, might contribute to the understanding of the complaints presented by these patients, and that the characterization of these associated deficits can help in the rehabilitation efforts.

REFERENCES