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Original Research Article

COGNITIVE FUNCTIONING AND BEHAVIOUR IN CHILDREN WITH ACQUIRED CEREBELLAR LESIONS

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Abstract

This study describes the cognitive and behavioral disorders identified in children with cerebellar tumors removed at the University Hospital Center "Mother Teresa", Tirana (UHC), 2004-2008. **Objective**: To evaluate the speech skills and executive functions of children who underwent surgery for extirpation of cerebellar tumors. **Design:** Clinical follow up study. **Setting:** University Hospital Center, Neurology-Neurosurgery Division and community Mental Health Center. **Participants:** Children, 18 in total, who received surgery for cerebellar astrocytomas and medulloblastoma of the vermis. **Main outcome measures:** Identifying the changes in cognitive functions and behavior during a period of 24 months after surgery and/or radio or chemotherapy; the importance of differences identified in functioning of children according to the type of tumor. **Results:** The average age of the children with astrocytoma was 10.2 years (from 7- 12.6), of whom six averaging 9.8 years (6.11- 13.4) had an involvement of the right hemisphere, and four averaging 10.6 years (7.2- 13.1) saw an involvement of the left hemisphere. Average "Z" scores for left and right lesions resulted: subjects with right cerebellar lesions showed a slight, insignificant decline in their verbal performance -1.4 z- score. Children with left cerebellar lesions showed a decline in non-verbal performance -1.3 z-score. Most of the children with medulloblastomas of the cerebellar cermis (MCV) resulted in mutism without behavioral changes. **Conclusion:** The alteration of cognitive and social profiles associated with cerebellar tumors means that these lesions contribute in those deficits. These findings also support Schmahmann's hypothesis on functional topography inside the cerebellum and suggests that this topography begins to operate from an early stage.

Key Words: Children, Cognitive functioning, Behavior, Cerebellar Tumors, Vermis, Right and Left Hemispheres.

Introduction

The data presented here describe speech skills and executive functions of 18 children who underwent surgery for extirpation of cerebellar tumors. Children affected by right cerebellar hemisphere tumors had difficulty with sequential auditory memory and language processing; whereas children with left cerebellar hemisphere tumors manifested deficits in the spatial memory and sequential visual memory. Vermis lesions point to two profiles: 1. Post operative mutism amounting to speech disorders, or language disorders similar to agrammatization; and 2. Behavior disorders ranging from irritability to autism-like behaviors. These data relate closely to the cerebellum role as the modulator of social and mental functions and point to this role being active since early childhood. The role of the cerebellum is closely linked to motor control and the ability to learn complex motor sequences, but recent research has further pointed to its contribution to non-motor functions, such as language skills, thought and emotion modulation and the ability to organize symbol activities sequentially (1). The role of the cerebellum in cognitive processes is supported by anatomical demonstrations showing cerebellar hemispheres' indirect connections with the associative areas of the frontal and parietal cortex (2). Moreover, a number of research studies have found motor and cognitive deficits in adult patients suffering from degenerative vascular or cerebellar disease (3). It is known that children with congenital cerebellar hipoplasia (especially of the vermis) are often subject to a variety of disorders across the neurodevelopment spectrum. On the other hand, there are few descriptions of the cognitive disorders due to acquired cerebellar lesions (4). Schmahmann has hypothesized that an inside topography of the cerebellum wherein the vermis region represents the cerebellar limbic system, is believed to be involved in the modulation of emotions and social behavior, while lateral hemispheric regions are involved in the modulation of thought, speech and the ability to plan. Speech disorders ranging from dysarthria to mutism have been observed in children after posterior fossa tumor surgery. However, no speech disorders were noted (5, 6). In children with medulloblastoma, alterations in cognitive functions have been consistently manifested; However, these problems have not been attributed to the removal of the tumor, rather than to the effects of therapy (radio or chemotherapy) involving the whole brain. Research of posterior fossa astrocytomas have identified the presence of cognitive deficits after removal of the tumor (even greater damage was observed in cases with large amounts of residual tumor), or a selective slowdown of deliberate actions under the purview of adequate mental functioning (4). Behavioral changes observed after posterior fossa surgery are often interpreted as symptoms of reactive depression. Pallack et al have described personality changes and emotional liability (5) and more recently Levisohn et al have reported speech and visual-spatial disorders in children undergoing removal of posterior fossa tumors (7). An increasing number of clinical and experimental studies with patients suffering from etiologically different cerebellar disorders have identified involvement of the cerebellum in a variety of nonmotor language functions, including motor speech planning language dynamics and verbal fluency, phonologic and semantic word retrieval, expressive and receptive syntax processing, various aspects of reading and writing and even aphasia-like phenomena (19)

Materials and Method

Clinical Investigation: The target group was comprised of 18 children, who received surgery for cerebellar astrocytomas (10) and

the rest (8) for medulloblastoma of the vermis in the University Hospital Center in Tirana during a four year period 2004-2008. Only the children fulfilling the criteria below were included in the study group: a. normal social and emotional behavior before the onset of illness; b. normal academic performance; c. radiological confirmation of tumor removal; d. three or less points following the appearance of major neurological cerebellar signs: [1. ocular disorders (nystagmus); 2. movement disorders (dysmethria and intentional tremor); 3. ataxia. Scores ranged from 0 (absence) to 3 (severe)]; e. willingness to cooperate during the assessment; f. granted parental consent; g. lack of psychiatric pathologies in immediate relatives. Each of the patients underwent neurological examination; Nuclear Magnetic Resonance (NMR) was used in accordance with standard protocol guidelines.

Patient Characteristics: Ten children received surgery for astrocytoma in the left or right cerebellar hemisphere and 8 for medulloblastoma of the cerebellar vermis. The average age of children in the astrocytoma group was 10.2 years (from 7-12.6), of whom six averaging 9.8 years (6.11- 13.4) had an involvement of the right hemisphere, and four averaging 10.6 years (7.2- 13.1) saw an involvement of the left hemisphere. The average age of patients with medulloblastoma was 10.7 years (6-12.1). This group was divided into 2 subgroups: 5 children manifesting speech disorders after surgery averaging 7.2 years (between 6 and 8 years old); 3 children exhibit post-operative behavioral disorders average 8.7 years (between 6.8 and 12.1). None of the children received 3 points for any of the 3 cerebellar signs in the selection criteria; nor was the amount of points greater than 3 in any case. NMR examination did not reveal brain lesions, except for cerebellar tumors.

Psychiatric and psychological assessment: Each child was examined on battery tests, including: **I.** Speech based on: **a**. word production (Boston Naming Test) and comprehension (Peabody's Picture Vocabulary Test); **b.** syntax (Token Test) and **c.** speech production based on the average length of expressive language (MLU), involving the description of a story based on visual stimuli. **II**. Executive skills, as reflected in: **a**. sequential visual and auditory memory using the Illinois Test of Psycholinguistic Abilities (ITPA); **b**. abstract reasoning and the ability to adopt reactive cognitive strategies (in response to a controlled change in the environmental setup) using the Wisconsin Card Sorting Test (WCST)); **c.** creative fluency in the production of words on the basis of semantic-category stimuli; non-verbal drawings and attention-span using the Cancellation Test designed to overcome a series of simple stimuli as soon as possible.

The protocol used in this study has been designed to study behavior and high functions in children with cerebellar lesions; it is part of a broader protocol to assess the subsequent neuropsychological effects of various medical treatments on children with brain tumors. All the tests were used in the Italian version. Standard scores have been published for some of them: BNT, Token Test and ITPA. As concerns the Design Fluency Test, the Peabody Picture Vocabulary Test, and the Cancellation Test, normative data was gathered by our group. Due to their neurological status and/or failure to realize the severity of their illness, the children's general pre-operative condition did not allow for reliable assessments; therefore they were all assessed post operatively. In all the cases, assessments took place at least 5-6 weeks after surgery. Patients with malignant tumors needing further radio and chemotherapy were assessed before the

initiation of therapy. The entire group was re-evaluated according to a designed schedule every 3 to 6 months for a period of 24 months.

Proceedings: Tests were administered by 1 Child and Adolescent Psychiatrist and 2 Clinical Psychologists at the Community Mental Health Center No. 1, Tirana (CMHC).

Statistics: All the test results were given in "Z" score (average score = 0 and standard deviation = 1). The "Z" results yield a standard from which all other results can be derived. They also reflect the range of 1 point deviation from the average population score. The average of individual "Z" points was then determined in order to allow for quick comparisons among tests and groups.

Results

Astrocytomas of the cerebellar hemispheres

Speech and executive performance (Z scores) in children who underwent surgery for cerebellar tumors of the right or left hemispheres are given in Table 1. Subjects with right cerebellar lesions showed a slight, insignificant decline in their verbal performance (-1.4). All speech tests results revealed an impairment which was less detectable by lexical tests such as naming tests (-1.5) and comprehensive tests (-1.3). Rather, the impairment was subject to detection by tools of a more complex linguistic nature such as syntax (Token Test, -1.6) and wording as reflected in the MLU (-2.3). Executive functions measured by verbal fluency tests and the WCST revealed deficits (-2.9 and 2.5 respectively for each test), although sequential memory impairment was only evident in the verbal component (-1.8). Children with left cerebellar lesions showed a decline in non-verbal performance (-1.3). As regards speech, impairments were noted only in the lexical components (naming objects: -1.4; comprehension: -1.9); However, the more complex aspects such as syntax, comprehension and MLU were preserved.

Table 1: Average "Z" scores for left and right lesions

	Right cerebellar tumor (Z score)	Left cerebellar tumor (Z score)
Naming objects	-1.5	-1.4
Expressive language	-1.3	-1.9
Token Test	-1.6	+1.4
Sequential visual memory	+0.8	-1.7
Sequential hearing memory	-1.8	+1.2
Graphic fluency	Missing	-2.4
Verbal Fluency	-2.8	-1.7
Attention span	-3.1	-3.2

Medulloblastomas of the Cerebellar Vermis (MCV)

As regards the 8 children who underwent surgery for MCV their clinical post

operative condition can be classed into 2 groups: the first is characterized by mutism without behavioral changes (5 children) and the second by marked behavioral changes with some neurological dysfunction (3 children).

Post operative mutism

Problems in speech production were caused by post-operative mutism which evolved in such a way that two different types of disorders surfaced: 2 children exhibited serious speech anarthria and 3 other children suffered from severe speech disorders. Postoperative cerebellar mutism syndrome (CMS) is characterized by severely diminished or absent speech output as well as other neurological, cognitive, and behavioral impairments (18).

Three to four weeks after the intervention, the children regained the ability to produce sounds and subsequently whole words; in 5-6 weeks children were trained to utter grammatically correct sentences, albeit quite dysarthric. Clinical findings were confirmed by the subjects' performance in tasks carried out in laboratory conditions (with the exception of the verbal fluency task where scores were lower than 2SD due to the dysarthria slowness). Three to six months after the surgery, children fully regained the ability to use expressive language but speech continued to be dysarthric and monotonous. Over the next 6-24 months, all children returned to completely normal speech.

However, the mutism of the other 3 subjects deteriorated to genuine speech disorders. Following an improvement in the production of words, their speech did not appear dysarthric, but was slow, monotonous and lacked the previous prosodic intonations. Notwithstanding a tendency for normal communication and a lack of dysarthria, children got used to utilizing telegraphic speech, often in the form of simple sentences of the noun/verb pattern. Their speech was similar to the agrammatical speech of aphasic patients with left frontal lesions.

It was found that, under laboratory conditions, the children were extremely capable of understanding and fluently repeating even very complicated words (proof of absence of dysarthria); however, they showed a clear lack of spontaneity in active speech and tended to speak very little. Also, these findings were later confirmed by the poor syntax understanding in the Token Test (-2.7) and the poor score in the sequential hearing memory (-2) and MLU (-2.5). Furthermore, they went down by 2SD below the standard score in the sequential memory test of the graphic fluency. Although their situation improved over time, it did so at a much slower rate than that of the 2 patients mentioned above.

Post operative behavioral disorders

The Cerebellar cognitive affective syndrome (CCAS) is a concept introduced for the first time in late 1990s by Schmahmann and Sherman to identify a range of cognitive and affective disturbances in patients with isolated cerebellar lesions (20). The core features of this syndrome consists of (1) executive dysfunctions such as disturbances in planning, abstract reasoning and working memory, (2) visuo-spatial deficit, such as impaired visuo-spatial organization and memory, (3) mild language symptoms including agrammatism and anomia and (4) behavioral-affective disturbances, consisting of blunting of affect or disinhibited and inappropriate behavior (20). Three children with an average age of 8.7 years showed behavioral disorders after surgery. All patients showed behavioral disorders of various degrees and forms. In addition to psychological assessment, these children were also examined for autism against DSM-IV diagnostic criteria. The average "Z" scores are presented in Table 2.

Table 2: Speech and executive performance in children with behavioral alterations after vermis surgical intervention

	Minor behavioral disorders (Z score)	**Autistic behavior (Z score)**
Naming objects	-1.2	-3.4
Expressive language	-0.9	Missing
Token Test	-0.9	-2.1
Sequential visual memory	Missing	Missing
Sequential hearing memory	-0.9	-2.9
Graphic fluency	Missing	-2.6
Verbal Fluency	-1.1	-3.6
Attention span	Missing	Missing

Two of the subjects presented irritability, decreased ability to stay in a group with others (including family members) and a general tendency of avoiding physical and eye contact. They displayed no dysathria; however, their speech was quite monotonous with a lack of emotional colors and was rarely used as a communication tool. Briefly, their behavior showed reluctance to establish contact. Their performance fell below normal limits in all the tests. Behavior changes gradually began to reverse and return to normal within 3-4 weeks.

One subject showed a complete lack of eye contact and lack of tolerance for nearness with others (including his mother). A number of complex rhythmic and stereotyped movements of the trunk, body and hands were noted, as well as a series of indecipherable speech intricacies which completely undermined communication. There was a total lack of spontaneous speech by way of communication in the first days following surgery. There was only restricted repetition which was bizarre and stereotypical. This subject's behavior met the DSM-IV diagnostic criteria of autism characterized by disinhibition, including the production of a series of strange and dirty words not previously used. These behavioral disorders made it impossible to continue with the post operative neurological assessment. A week following formal assessment, a deficit was noted in the ability to name objects (-3.4) and understanding syntax (-2.1) coupled with reduced verbal fluency, both spontaneous (MLU -2.3) and stimulated (-3.6). Semantic problems fueled confabulatory mechanisms. The tests indicated damage to the frontal regions: -2.9 sequential hearing memory; -2.6 projecting fluency; perseverance in the WSCT 2.4. One month after the surgery, the subject's behavior settled down and she became more tolerant of physical nearness with others and even allowed eye to eye contact. However, she remained introvert; her speech started to relate to context and was no longer telegraphic, but she displayed a lack of empathy toward the others, including her peers.

Discussion

Tumors of the right cerebellar hemisphere correlate with changes in processing complex linguistic tasks; tumors in the left cerebellar hemisphere correlate with elimination of the ability to process non-verbal tasks and, in some cases, even with damage to prosodic intonation. Whatever the lesion's location, there was a slight deterioration of the ability to name objects and understand speech, as well as difficulty in processing executive tests and timed tests requiring attention.

None of the children showed pure behavioral disorders. In the group of children with tumors, the manifested deficits depended on the hemisphere and were similar to those observed in children with acquired unilateral lesions of the cerebellar hemispheres. Slight deficits in understanding and speech production were noted in children with right or left unilateral cerebellar lesions. The difference between right and left lesions was also noticed in the scores the subjects made in frontal executive tests: patients with right cerebellar lesions presented deficits in sequential hearing memory and children with left cerebellar lesions presented deficits in the sequential visual memory. The limited data, though, point to the need for further research; however, all subjects erred in the WCST test compared with their healthy peers.

Children with vermis lesions presented two different profiles readily distinguishable in clinical terms: a profile of mutism and another profile of affective and behavioral alterations, the severity of which varied as per the display of clinical signs. The mutism profile was distinct and well differentiated. Once mutism was overcome, children with speech disorders showed dysarthric speech, which lasted several months after the surgery; however, language structure remained intact in both the lexical and syntactic components. Spontaneous speech was creative and natural and no executive deficits were displayed. Van Dongen et al 1994 characterized this profile as mutism with subsequent dysarthric syndrome (MSD), a speech disorder the dysarthric features of which can deteriorate to the point of anarthria, albeit reversible.

The other profile featured agrammatization (4) with obvious deficits in complex linguistic tests despite the children's excellent skills in the repetition of even very complex sentences. The right cerebellar hemisphere participates in language processing as a result of the connections with the associative frontal areas of the left cerebellar hemisphere passing through the thalamus.

Vermis lesions, more particularly posterior-inferior lobules, cause social and communication skills to be disturbed to various degrees. Alterations of the cerebellar vermis were previously noted even in psychiatric and schizophrenic patients. Animal experiments have shown that damage to the cerebellar vermis generated primitive protection and insulation behavior as well as changes in sexual behavior. A number of radiological and autopsy studies show that lobules VI and VII of the vermis participate in the pathogenesis of infantile autism. These studies suggest that vermis plays a role in the processing of complex social and emotional behaviors. Such processing occurs in a complex network that includes other associative areas of importance in mediating social and cognitive behavior (such as the frontal lobes and the limbic system) (9; 10; 11).

All children displayed sluggish performance in the timed tests. Such performance is best measured by the Cancellation Test (the only test that leads to reduced performance levels of more than 3 standard deviations). Such sluggishness was noted by earlier studies in children who had sustained cerebellar astrocytoma. It has been described as the result of the proximity of surgical paths with the reticular system of truncus cerebri. However, it can be hypothesized that the slowdown of the executive functions is also the result of the poor functioning of the internal structure of the cerebellum, a micromodular unit of crystalline shape that works parallel with it. Each of these modules can be considered as some kind of microprocessors, a large number of parallel paths leading to an extraordinarily powerful center which processes information speedily to ultimately enable learning.

The presence of cerebellar symptoms such as dysmethrias and tumors may worsen performance on timed tests. However, this was not the case with the current target group, as all the children with major motor impairments were excluded from the study. It should also be noted that neurological signs in children with posterior fossa tumors are always very slight due to the plasticity of a child's brain and the early diagnosis of lesions.

Cognitive-behavioral alterations noted here support those encountered in adult patients (12) and the group of patients with different cerebellar pathologies (8). Although the patients in these studies are very heterogeneous and do not allow for the distinction of symptom constellations stemming from the lesion's location, the results made it possible to conclude that lesions of the vermis cause major behavioral changes, whereas those of the cerebellar hemisphere (in particular the posterior lobes) play a crucial role in cognitive behavior alterations (8). Cognitive and behavioral alterations of varying severity are also encountered in children with congenital cerebellar hipoplasia, both when isolated, and when forming part of complex cerebral malformations. However, due to severe intellectual deficits and the difficulty to establish the kind of trusting relationship necessary for thorough assessment, it has not been possible to further detail the picture. Literature offers very few descriptions of cases of children with normal intelligence who acquires cerebellar pathologies. Pallak et al and Levisohn et al describe children with lesions caused by surgical intervention. These children sustain cognitive and affective deficits whenever the vermis was involved. (4) However, these cases, too, highlight the fact that the cerebellum plays a fundamental role in the creation and organization of high cognitive and social behavior. Moreover, recent research allows us to discern patterns that correspond to the side of the lesion and the differentiation of the models support Schmahmann's hypothesis on functional cerebellum topography (2).

The role of the vermis as a cerebellar limbic system is also supported by the harm caused by vermis lesions on behavioral disorders, ranging from irritability to a general avoidance tendency that can amount to transient autisms. The fact that cerebellar hemisphere lesions lead to deficits in the complex mental activities support the role of these hemispheres in the modulation of thinking, speech and executive skills. Although these conclusions should be considered carefully, both cerebellar hemispheres may have a left-right specialization similar to that of cerebral hemispheres.

The results described above support the hypothesis that, given the young age of some of the children involved in the study, this intercerebellar specialization happens rather early, as shown by the fact that congenital abnormalities of the vermis or its hypoplasia are accompanied by a range of developmental disorders, including autism (13). The early specialization of the cerebellar fields has also been observed in animals and in children with specific deficits following the emergence of focal cerebral lesions acquired at a very early age and affecting different parts of the brain 4); however the rate at which this specialization matures varies from region to region. Moreover, these psychological abnormalities noted in children with cerebellar lesions are similar to those in children with cortical supratentorial lesions, including the deficits in executive functions of children with lesions in the prefrontal right or left dissociative regions (16) and alterations in the social and communicative relations of children with lesions in the limbic structures (14).

Reciprocal relations between the cerebellum and the cortical areas (here are considered only the frontal and pre-frontal areas, and the limbic regions) have been shown to reach the frontal cortex and the cerebellum through the pons (14) and vice versa through the thalamus, (14) and mutual anatomical links have been discovered among the pre-hippocampal structures, cingular girus and the hypothalamus. (14) That fact that the cerebellum forms part of the cerebral-cerebellar network and of the cerebellar-cerebral connections that process and enable complex socio-cognitive behaviors are confirmed by studies of normal subjects during the execution of various tasks, shows that disorders subsequent to cerebellar pathologies are due to malfunction of the network connections. (15)

Long-term deficits caused by cerebellar injuries are revealed by PET studies which have shown areas of hypoperfusion in the associative cortical areas and in the cerebellar areas in the cases of cerebral lesions.

Conclusions

Our results confirm cognitive-behavioral deficits subsequent to cerebellar lesions reported by previous studies, but the more accurate localization and homogeneity of the pathology has enabled the identification of different neuro-behavioral models related to the vermis or hemispheric origin of the lesions themselves. These findings also support Schmahmann's hypothesis on functional topography inside the cerebellum and suggests that this topography begins to operate from an early stage. The alteration of cognitive and social profiles associated with cerebellar tumors means that these lesions cause deficits.

However, we cannot conclude by saying that the lesions themselves are a direct cause of these cognitive-behavioral deficits since their primary effect is deprivation of complicated connections between the cerebellum and the associative cortical field as a result of which the cerebellum is able to modulate itself.

Moreover, it should be noted that many children have undergone the same intervention for the same pathology without showing any post-operative cognitive-behavioral alteration, or the alterations were so insignificant that they were hardly noticed. This shows that the question put forth should be even more complex, so that responses to cerebellar lesions, both major and minor may also depend on the genetically variable neural composition of the subject itself.

Properly designed multicenter trials are needed to provide stronger evidence regarding effective prevention of cerebellar mutism and the best therapeutic approaches for such patients with a combination of pharmacological agents and multidisciplinary speech and behavior augmentation.

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