Effect of Transplantation of Human Fetal Tissues on the Development of Higher Mental Functions in Children with Down's Syndrome

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Voluntary movements and acts, attention, memory, and reasoning were examined by Luriya's neuropsychological method in 30 children with Down's syndrome aged 4 to 10 years. The intellectual development of the children was assessed using the Wechsler scale. The results indicated a reliable improvement of spontaneous and purposeful cognitive activity, mental agility, speech, and nonverbal reasoning in the Down's syndrome children who had received a human fetal tissue transplant in comparison with the control group.

Key Words: *transplantation of human fetal tissues; treatment of Down's syndrome; development of higher mental functions*

Down's syndrome is the most prevalent form of mental retardation in children. It is known to be most frequently caused by trisomy 21 or, rarely, by translocation and mosaic cytogenetic variants of karyotype abnormalities [3]. This condition occurs in approximately 1 out of 700 newborns [3], those afflicted accounting for 9 to 10% of all mentally retarded children [5,6].

During the neonatal period the reactions of an infant with Down's syndrome may be virtually the same as those of healthy newborns, except for diffuse muscle hypotonia. However, retarded development may be noted as early as during the first months of life: certain age-specific motor habits are acquired more slowly than usual. Nonetheless, since the time of acquisition of age-specific habits varies widely, the delay in the rate of development of a certain individual with Down's syndrome may be more or less marked.

At present there is no effective drug therapy for oligophrenic patients with Down's syndrome, despite the extensive use of psychostimulating agents, vitamins, and fortifying treatments. In order to improve the mental development of children with this syndrome, a method of therapy involving the transplantation, by injection, of human fetal tissues (HFT) (brain substrate) has been developed at the International Institute of Biological Medicine.

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MATERIALS AND METHODS

This paper presents the results of clinical and psychological examinations of 64 patients aged 4 to 10, 30 of whom received two HFT injections. These children were divided into two groups, group 1 consisting of 14 children aged 4-6 years and group 2 of 16 children aged 7 to 10. The rest of the children were controls. At the first examination (prior to therapy) the mean age was 5.1±0.6 years in group 1 and 7.3±0.6 years in group 2.

Thorough psychological examinations of all patients were carried out before treatment with HFT transplantation and 6 months after every transplant. The examination included neuropsychological workups after A. R. Luriya's modified method adapted for chil-

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dren and permitting not only a qualitative, but also a quantitative analysis of disorders of higher mental functions [1,4].

The method is aimed at assessing the cognition, praxis, speech, mnemic-intellectual, and higher regulatory functions responsible for the voluntary forms of mental activity. The neuropsychological symptoms were assessed using a 5-point system (0 - no symptom, 5 - its maximal expression).

In addition, the intellectual development of the children was assessed using two variants of the Wechsler scale [7] intended for children aged 3 to 7 years and adapted by A. Yu. Panasyuk in 1973 for children aged 5 to 16 years.

The reliability of changes in neuropsychological parameters was assessed using Student's t test, while for changes in intellectual development the binominal test was used.

RESULTS

Neuropsychological examination of the children before therapy showed a wide spectrum of disorders in the higher mental functions at almost all levels of mental activity organization.

Clear-cut behavioral disturbances, presenting as motor flaccidity, poor self-awareness, and a high degree of distractibility were the most salient features in the psychological picture. An expressed tendency to slip into stereotypic actions, rigidity and mental perseveration were observed at both the sensorimotor and cognitive levels. One of the outstanding features of the disturbed voluntary activity of these children with Down's syndrome was impaired task programming and control: replacement of a present task with a simplified or incidental one and an inability to compare the results with the initial purpose. Disturbances of expressive speech presenting as both reduced total verbal activity and articulation defects were frequent and rather gross. Evident inadequacy of spatial and auditory perception, marked defects in aural and oral memory and in categorical thinking were observed in virtually all the children. Disorders of impressive speech were less expressed, and there were no primary defects of praxis or visual perception. Age-specific differences manifested themselves in a more pronounced hyperactivity and more severe disorders of expressive speech in the younger group of children ($p<0.05$, Fig. 1).

Analysis of the time course of neuropsychological symptoms during therapy shows a reliable regression of such symptoms as hyperactivity, poor attention, mental inertness ($p<0.01$), verbal inactivity, and faulty articulation ($p<0.05$) after two courses of treatment in group 1. In group 2, besides amelioration of the above symptoms, an improvement of aural and oral memory and of visual and constructive activity ($p<0.05$) were observed after the second HFT transplant.

The control group of children with Down's syndrome was examined by the neuropsychological method in order to differentiate between the effects of HFT transplantation on the development of higher mental functions and the "natural" course of their development. The control and the main group were age-matched at the time of examination after the second HFT transplant. The mean age of group 1 children was 6.3±0.5 years (6.5±0.6 in controls), and 8.2±0.7 years in group 2 (8.4±0.5 in controls).

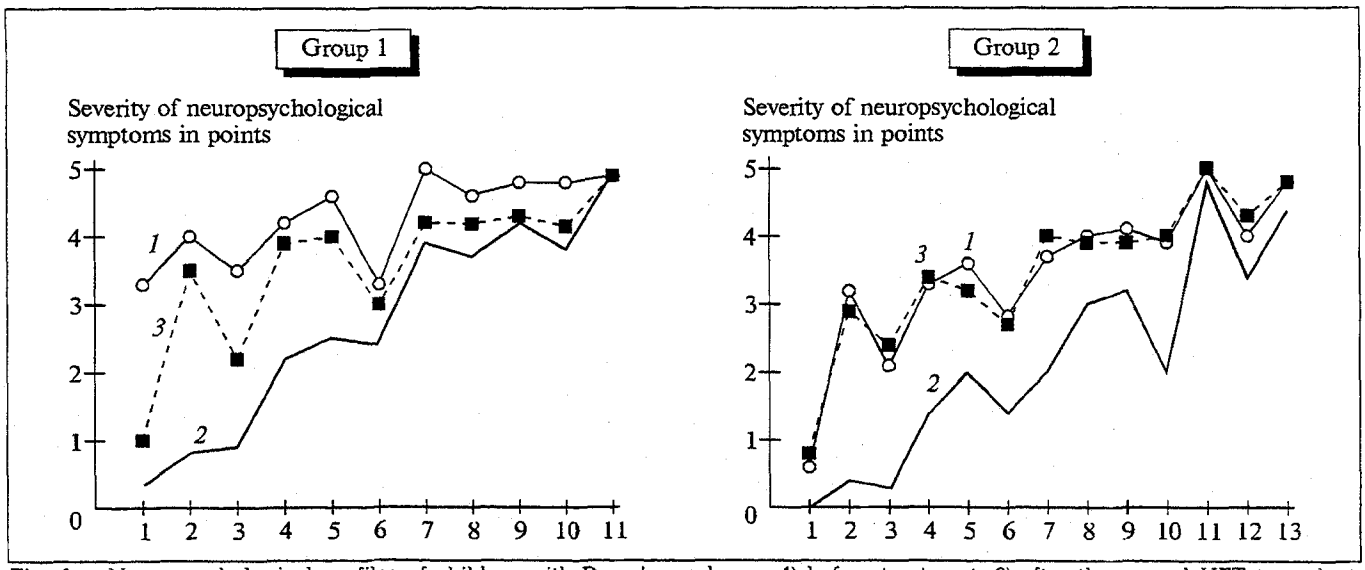

Fig. 1. Neuropsychological profiles of children with Down's syndrome. *1*) before treatment; *2*) after the second HFT transplant; *3*) control group. Abscissa: *1*) hyperactivity; *2*) attention deficit; *3*) mental inertness; *4*) verbal inactivity; *5*) defective articulation; *6*) disordered impressive speech; *7*) disordered aural and oral memory; *8*) impaired categorical thinking; *9*) problems with counting; *10*) disordered visual and constructive activity; *11*) disordered auditory perception; *12*) poor reading; *13*) poor writing.

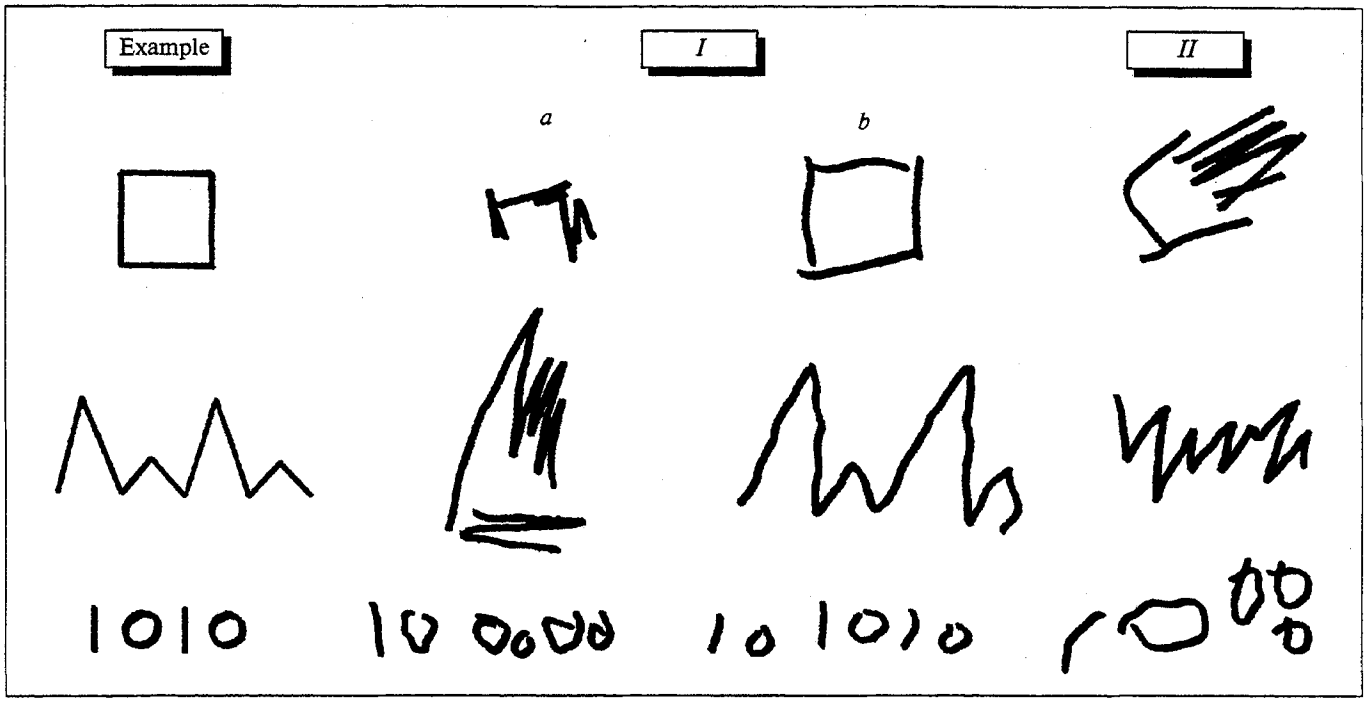

Fig. 2. Copying of geometrical figures by children with Down's syndrome. *I*) drawings by N. G., aged 5.5 years (*a*: before treatment, *b*: after the second HFT transplant); *II*) drawing by L. R., aged 6.5 years (control).

The results of data processing are presented in Fig. 1. Attention deficit, mental inertness, and disorders of expressive speech were far less pronounced after two courses of treatment in both age groups in comparison with the controls ($p<0.05$). The visual and constructive activity of the older children was also developing much better than that of the controls.

Analysis of published data shows that the main factors underlying oligophrenia are mental inertness and poor verbal control [3]. The results of the neuropsychological workups of the children prior to treatment with HFT indicate that difficulties in the performance of tasks involving integral activity (graphic tests, constructive activity, copying of a given sequence of geometrical figures, etc.) were the most typical. Gross perseverations were as a rule observed in the children aged 4-5 years attempting to draw a simple geometrical figure.

The inertness and stereotypy were particularly evident when the children were performing complex tasks involving a series of voluntary actions. For example, if a child was asked to draw a series of simple geometrical figures, this task was very soon replaced by multiple repetitions of one and the same element. Figure 2 shows examples of graphic tests performed by the children of the main and control groups. It demonstrates the improvement of the voluntary activity, primarily of its planning component, during the course of treatment.

As an illustration we will describe the time course of higher mental functions in a girl with Down's syndrome. Natasha G. was admitted for the first course of HFT transplantation at the age of 5.5 years. Before treatment the most manifest symptoms in the psychological picture were marked hyperactivity and uninhibited behavior; the girl could hardly concentrate on the tasks to be performed, was easily distracted by incidental stimuli, and exhibited stereotypic actions. Gross perseverations and task simplification were observed during the performance of motor and graphic tests. Spontaneous speech consisted mainly of isolated syllables and single words easy to articulate; manifest perseverations and echolalias were observed. Voluntary repetition of words or even of separate syllables was virtually impossible. There was no phrased speech. The object correspondence of words and understanding of addressed speech were relatively preserved. An appreciable deficit of aural and oral memory was observed. With a little assistance the girl could classify objects, but had difficulty understanding the figurative meaning of stories and topical pictures. After the first HFT transplant a clear-cut positive dynamics of higher mental functions was observed. The girl became much more appropriately behaved, her hyperactivity was noticeably reduced, her concentration improved, and her interest in her surroundings appreciably increased. The regression of mental disorders was particularly evident in her speech processes, manifested by complete cessation of echolalias and perseverations, a marked improvement of total verbal activity, and the development of phrased speech. The girl could repeat

TABLE 1. IQ Values of Children with Down's Syndrome for Various Age Groups ($M \pm m$)

Stage of HFT treatment	Total IQ		Verbal IQ		Nonverbal IQ	
	group 1	group 2	group 1	group 2	group 1	group 2
0	43±5.1	42±7.1	49±7.5	51±6.8	48±5.1	47±9.1
I	49±5.3	50±10.4	53c5.1	55±7.3	53±5.7	54±10.5
II	57±8.1*	67±6.6*	57±9.0	60±4.6	63±9.0*	76±10.4*

Note. *$p<0.05$ in comparison with the pretreatment examination; group 1, $n=14$, group 2, $n=16$.

simple words at will. Difficulties arose when she attempted to pronounce words with a complex syllable structure: articulation was somewhat slurred and parts of words were chopped off. Similarly as before therapy, when classifying objects, the girl would resort to a concrete situational-type solution in some tasks. Difficulties in performing graphic tests were still observed at this stage. Psychological examination of the child after the second course of treatment showed further improvement of verbal activity: at this point difficulties were observed as a rule with a detailed utterance; grammatical errors and mild defects of articulation occurred in spontaneous speech. The girl performed a number of graphic tests successfully. Examination of the intellectual sphere showed primarily a reduced level of generalization. On the Wechsler scale the total intelligence quotient (IQ) was 60, this corresponding to moderate mental retardation. The verbal IQ was 63, nonverbal IQ 55.

Hence, the time course of the development of higher mental functions under the effect of HFT in this child indicates a clear tendency toward normalization of voluntary purposeful cognitive activity. This manifests itself in improvement of voluntary attention and control, gradual reduction of mental inertness, and improvement of expressive speech.

The level of development and structure of the intellect were assessed using The Wechsler scale (Table 1).

Analysis of the data shows that an increase of the total and nonverbal IQ ($p<0.05$) was observed in both age groups after the second course of HFT treatment, whereas the verbal IQ values did not appreciably change during the course of treatment. Qualitative analysis of the structure of the intellect showed that the above changes of the total IQ were mainly due to improvement of the parameters of nonverbal intelligence, that is, due to such abilities as logical thinking at the level of objects, the ability to perceive spatial relationships and identify the most significant characteristics of objects, and the capacity for analysis and synthesis at the level of objects. On the other hand, operations with numbers, the solving of arithmetic problems, and abilities with regard to analogies and generalization were virtually unchanged.

Along with the amelioration in the mental sphere, a positive time course of motoricity was observed in all the children, presenting as a more accurate performance of finely coordinated actions and improvement of everyday living skills.

Electroencephalographic examination following the first course of HFT treatment documented a better tolerance of functional tests and the disappearance of nonspecific paroxysmal activity in all but 6 patients.

Hence, the study permits us to draw the following conclusions. The addition of the first two stages of HFT transplantation to the treatment regimen of children with Down's syndrome aged 4 to 10 years results in a reduction of the severity of mental disorders. The most significant shift is regression of disorders in the total neurodynamics, presenting as a reduction of disturbances in the tempo and agility of mental processes. Moreover, a tendency toward normalization of voluntary purposeful cognitive activity and improvement of voluntary attention and control are clearly seen. The HFT transplants evidently had an influence on the development of nonverbal intellectual functions in these children with Down's syndrome.

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