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Role of Orbital Dysostosis in the Inheritance and Pathogenesis of Strabismus

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The monohybrid inheritance of strabismus is improbable in view of the manyfold aetiology of the condition. Hypotheses concerning its origin and its hereditary transmission cannot sharply be distinguished; what is inherited are the factors responsible for the symptoms. Apart from neural involvement, some authors refer to sensorial disturbances (fusion, refraction, primary amblyopia and anomalous correspondence) in connexion with the origin and transmission of strabismus. Certain authors [4, 6] point moreover to the role played by mechanical factors. Others [16] postulate a mesodermal factor, referring to a faulty differentiation of the muscular and fascial tissues, although contraction depends to a great extent on the origin and course of the muscles in which the shape or malformation of the orbit may have a decisive part. Hyde [9] observed inherited depressions in the orbit of Siamese cats and regarded the phenomenon as a factor in the hereditary transmission of strabismus.

Imbalance of the eye muscle seems to be correlated with general skeletal malformations, e.g. with scoliosis [15]. Facial asymmetry, a frequent concomitant of strabismus, is undoubtedly of a causal nature [11]. The hereditary hypsiconchous or comaeconchous forms of the bony orbit certainly influence the development of refraction [14] which may then affect the balance of the eye muscles.

According to orbital measurements performed on submentovertical radiograms [18, 19], the angle formed by the temporal and the nasal walls of the orbit shows, in respect of the two eyes, measurable differences in cases of convergent, divergent, uni-ocular and alternating squint.

The squint occurring in certain dyscranial syndromes, is also of orbital origin [12]. For instance, Crouzon's craniofacial dysostosis, with strongly divergent and shallow orbits, is associated with divergent strabismus.

The factors responsible for the various forms of squint are obscure. Waardenburg [17] assumed the existence of a separate gene of divergent strabismus, while Jancke [10] observed no essential difference between the convergent and divergent forms in identical twins. Since strabismus still constitutes a problem from the genetic point of view, only case reports are available as to its different

aspects. In any case, it is only in 76 per cent of monozygotic twins that the point of fixation shows no deviation [5]. Our own investigations have likewise proved that in familial cases convergent, divergent and even vertical strabismus may occur in both the ascending and the descending line in an indiscriminate fashion.

The case of a father and his two children will be presented in the following, with the purpose of supplying data concerning the orbit's role in the transmission of strabismus, further the hereditary forms of squint, and, finally, the usefulness of genetic research methods.

Case Reports

Father and son have congenitally deformed skulls and congenital strabismus. The daughter started squinting at the age of 4 years without preceding illness. Pregnancy and delivery were normal. The father is mentally sound. The daughter is affected with speech defect, at the average level in her studies. The boy is a timid child, living at a detached farm, and it was not possible to establish contact with him. No other developmental irregularity or ophthalmic disorder is demonstrable in any member of the family. The mother's cranial X-rays and ophthalmological findings are normal.

J. S. (father), aged 43.

6/7 +3.0 D = + 2.5 D cyl. 90°

V.: corr Refr.

6/18 +2.0 D = + 3.5 D cyl. 90°

Asymmetric cranium, with hypoplasia of the left side (Fig. 1a). Cranial roentgenogram shows a deformed skull; the groove of both parietal bones is widened near the sagittal suture. The base of the skull is short. The left orbit and the left craniofacial bones are hypoplastic. A hazelnut-sized, sharp-edge shadow is visible in the right mandible immediately before the retromolar triangle: it pushes the roots of 8 forward, so that the tooth has a transverse sublingual position (Fig. 1b). Pupillary distance, 7.7 mm; exophthalmus, 1 mm downward dislocation, 5 mm. Intact eyeground.

Eye movements. Maddox-test (distance, 1 m): Right eye fixing at 24°; infravergence 8° divergent squint.

Left eye fixing at 24°; supravergence; 8° divergent squint. (Left eye fixes only when right eye is covered.)

Motility. Abduction to the right is inhibited by nystagmus. When looking upward, it is the left, when downward, it is the right eye which lags behind, the other being hyperactive. Bilateral fixation nystagmus, more pronounced on the left side. After-image:

Z. S. (daughter), aged 7.

6/12 + 7.0 D = + 0.5 D cyl. 80°

V.: corr. Refr.

6/12 + 7.5 D = + 2.0 D cyl. o10°

There is no conspicuous cranial or facial deformity (Fig. 2a). Cranial roentgenogram shows an asymmetrical skull; the right orbit and the right craniofacial bones are smaller (Fig. 2b). Pupillary distance, 57 mm. The eyes are normal.

Eye movements. Maddox-test (distance, 1 m): Alternating convergent squint of 25° which remains unchanged under the eyeglass. Synoptiscope, objective angle, 30° large anomaly angle. *Fixation*, bilaterally foveal.

T. S. (son), aged 5.

V. cannot be ascertained (the boy refusing to speak). Refraction: +1.5 D = = + 2.0 D cyl. 90°, bilaterally.

Asymmetrical skull with dextrolateral hypoplasia. Cranial and facial anomaly heterolaterally similar to that of father (mirror-image symmetry). No marked exophthal-

mus or dislocation (Fig. 3a). Cranial X-rays show short base of skull and high, projecting forehead. There is a strikingly deep impression on the calvaria. The right

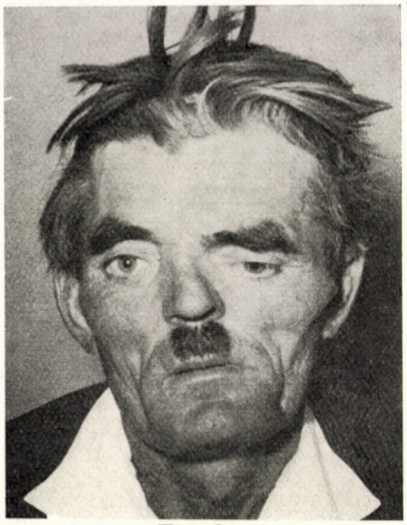

FIG. 1a

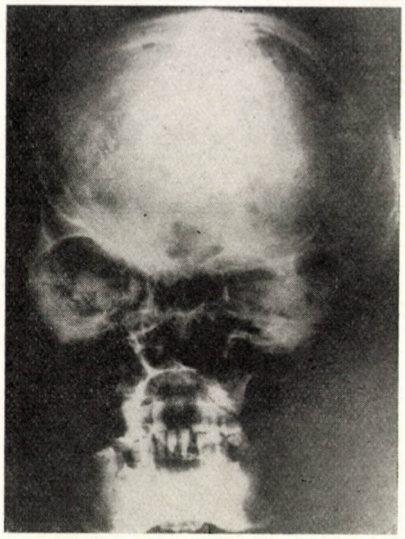

FIG. 1b

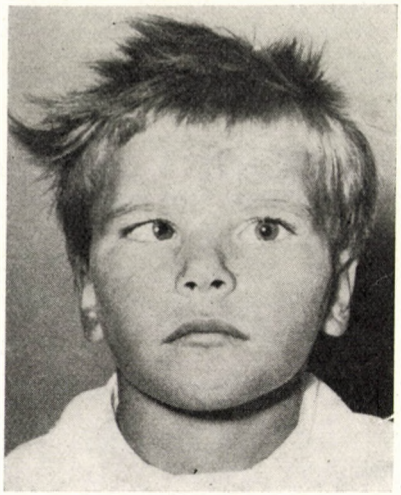

FIG. 2a

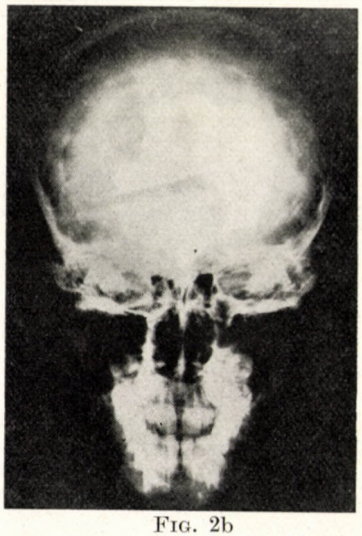

FIG. 2b

craniofacial bones are moderately hyperplastic (Fig. 3b). Pupillary distance, 62 mm. Normal eyegrounds.

Eye movements. Maddox-test (distance, 1 m): With the right eye fixing, the left eye shows from time to time a supravergence of 10° to 12° and turns into a slightly convergent squinting position. With the left eye fixing, there is no deviation even if the right eye is covered. Occasional disappearance of strabismus. Subjective examinations cannot be performed.

Motility. The right eye lags behind when looking upward, the left when look-

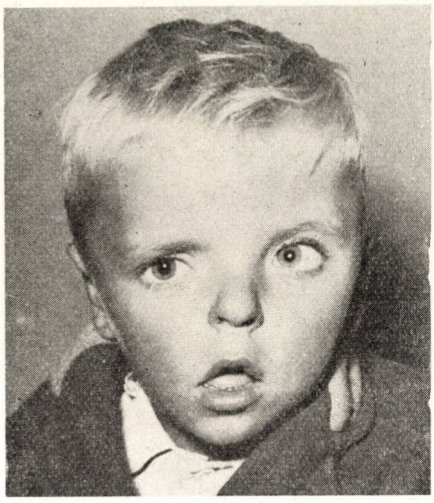

FIG. 3a

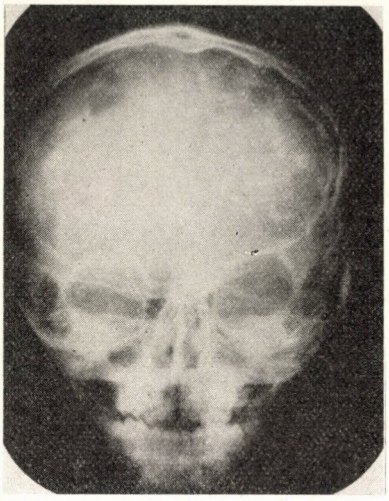

FIG. 3b

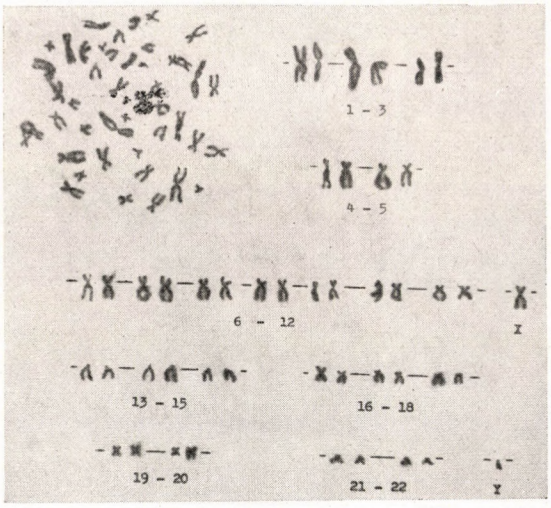

FIG. 4. J. S. (father): normal (46 XY) chromosomal set. Micromethod cultivation. Unna-blue staining

ing downward; hyperactivity of the contralateral organ. There is no irregularity in horizontal motility.

Fixation: bilaterally foveal.

Chromosomal examination

Chromosomes of the father and son were examined in lymphocytes cultured from peripheral blood. Using the technique of MOORHEAD et al. [13] as also our special version of HUNGERFORDS [8] micromethod, we observed 20 mitoses each. Both the father's and the son's chromosomal set was normal. They comprised 46 chromosomes, and no numerical or morpho-

logical abnormalities were registered (Fig. 4). The third pair of chromosomes was examined with particular care since it was here that GERLÓCZY et al. [7] observed deviations in a case of hemihypertrophy. No such anomaly was found in our cases.

Dermatoglyphic examinations

J. S. (father) Total number of ridges. 196; 9 whorls, 1 loop. ATD angle: right, 48°; left, 45°. Hypothenar triradiation on both palms.

Mrs. J. S. (mother). Total number of ridges, 196; 1 whorl, 8 loops, 1 arc. ATD angle: right, 47°; left, 48°. Hypothenar triradiation on both palms.

Z. S. (daughter). Total number of ridges, 110; 6 whorls, 4 loops. ATD angle: right, 48°; left, 47°.

T. S. (son). Total number of ridges, 99; 6 whorls, 2 loops, 1 arc. ATD angle: right, 49°; left, 51°. Hypothenar triradiation on both palms.

In themselves, these data are not particularly valuable, but may become useful as parts of a later larger material.

DISCUSSION

The vertical squint of father and son is evidently correlated with orbital deformity. CAPALBI and GUZZINATI [3] pointed out the hereditary nature of the vertical component.

In the son, the strabismus on the side opposite to the orbital deformity must have developed in the course of adaptation to the vertical paresis, which was followed by a weakening of the contralateral antagonist. It was in this way that the downward squint turned into a contralateral upward squint.

In the daughter, only X-rays revealed the cranial asymmetry. Her strabismus was horizontal. With the right side pathologic, strabismus was decidedly alternating; incomitance turned into concomitance. It follows that imbalance of the eye muscles may be due to hidden and not only to manifest cranial or orbital asymmetry.

Deviation was different in the three examined persons: downward in the father, upward in the son and convergent in the daughter. It was vertical (and, at the onset, probably identical) in the phenotypes (father and son), but had a different character in the daughter. Therefore, as regards the direction of deviation, inheritance of orbital dysostosis and strabismus does not seem to play a decisive role.

Hypermetropia combined with astigmatism — a familial feature in the examined persons and marked in the daughter — may likewise have contributed to the observed phenomena.

The so-called mirror image symmetry, referred to above and described also in squinting identical twins [2, 14, etc.], is noteworthy from a genetical point of view. In the examined family, it was observed on the skull and on the orbital deformity.

According to the chromosomal examinations, asymmetry in the brother and sister was restricted to certain

bones of the skull; within normal limits, the third, large mediocentral chromosomes were equal in size. Thus, in the present case the anomaly was inherited at a subchromosomal level, with the transmission of comparatively few genes. At least one of these genes was dominant against the normal allele, but the appearance of a developmental anomaly in two successive generations is, of course, far from being a conclusive proof.

Summary

Examination of three squinting members of a family (father, son, daughter) who had orbital dysostosis combined with mirror-image symmetry has led to the following conclusions.

Hidden orbital irregularity may constitute a significant factor in the development and hereditary transmission of strabismus. The direction of the deviation is not decisive from the point of view of heredity; readjustment of the muscles changes the form of squint even in cases displaying an orbital anomaly. Anomalies with significant dysostosis are also inherited at a subchromosomal level, with the transmission of but a few genes. Dermatoglyphic examinations have been carried out in order to create a basis for comparison.

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