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MTHFR, HYPOTONIA & VISION

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INTRODUCTION

The methylenetetrahydrofolate reductase gene mutation, known as MTHFR is a relatively new discovery. Approximately 35% of the U.S. population have a form of the MTHFR gene mutation (Rady et al, 1999).

Table 1
MTHFR MUTATION FREQUENCY

TABLE IV. Allele Frequencies of MTHFR C677T Mutation in Different Ethnic Populations

Population	Allele frequency	References
Colombian	0.487	Camacho-Vanegas et al., 1998
Northern Italy	0.45	Sacchi et al., 1997
South Europe	0.41	Gudnason et al., 1998
Italian	0.40	de Franchis et al., 1996
Asian	0.4	Franco et al., 1998
French–Canadian	0.38	Frosst et al., 1995
Australian	0.37	Wilcken et al., 1996
Brazil–Caucasian	0.373	Arruda et al., 1998
European–White	0.362	Franco et al., 1998
French	0.36	Mornet et al., 1997
British	0.36	Papapetrou et al., 1996
United Kingdom	0.353	Gudnason et al., 1998
White Americans (U.S.)	0.35	Stevenson et al., 1997
South Wales (U.K.)	0.32	Clark et al., 1998
Middle Europe	0.312	Gudnason et al., 1998
German	0.31	Koch et al., 1998
Irish	0.27	Whitehead et al., 1995
Utah Mormons (U.S.)	0.27	Papapetrou et al., 1996
Japanese	0.27	Papapetrou et al., 1996
Dutch	0.26	van de Put et al., 1996
Amerindian	0.24	Franco et al., 1998
Baltic	0.233	Gudnason et al., 1998
U.S. Population II	0.22	Ou et al., 1996
U.S. Population I	0.21	Ou et al., 1996
Brazil Black	0.2	Arruda et al., 1998
Brazilian–Black	0.12	Franco et al., 1998
Brazil Indian	0.114	Arruda et al., 1998
African–Americans (U.S.)	0.11	Stevenson et al., 1997
African Black	0.052	Franco et al., 1998
	Present study	
Ashkenazi Population	0.477	
Texas Population	0.287	

The two most common forms of the mutation are: C677T, and A1298C. As a result of the genetic mutation there is no MTHFR, an enzyme, to convert folic acid to the metabolizable methylfolate, an essential component of the cell's methylation cycle. An associated high level of homocysteine is a consequence of the MTHFR gene mutation (Rozen, 1997, 2002; and Spotila et al., 2003).

Diagram 1
CELL METHYLATION CYCLE

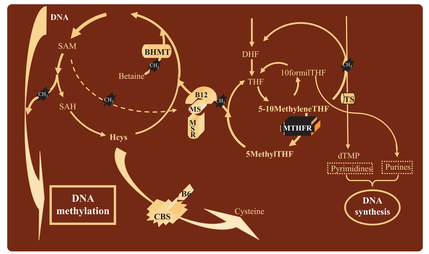


Fig. 1. Simplified scheme of DNA methylation/synthesis cycle. Dihydrofolate (DHF), tetrahydrofolate (THF), methionine (MET), S-adenosylmethionine (SAM),S-adenosylhomocysteine (SAH), homocysteine (Hcy), 5,10-methylenetetrahydrofolate reductase (MTHFR), thymidylate synthase (TS) methionine synthase(MS), methionine synthase reductase (MSR), betaine:homocysteine methyltransferase (BHMT), cystathionine-synthase (CBS), B6 vitamin (B6), and B12 vitamins (B12).

OVERVIEW

Only two articles in the optometric literature discuss the ocular effects from the MTHFR gene mutation. The purpose of this presentation is to introduce these topics to those in optometric community unaware of MTHFR , its related ocular effects, and treatment.

In particular, one of the sequela of MTHFR is hypotonia. Vision related manifestations of hypotonia include binocular eccentric fixation, eye movements disorders, convergence and accommodation insufficiencies, latent hyperopia, suppression, and poor binocular vision (Al-Essa, et al., 1999; Berman, 2013; Black, 2008; Bodenstgeiner, 1994; Boustany et al, 1983, Brooke, Carroll and Ringel, 1979; Cohen et al., 1973; Fattal-Valevski, et al. 2000; and Kondo, Nagataki, and Miyagi, 1990). While optometrists are familiar with treating the vision disorders, they may not be familiar with the underlying MTHFR.

METHODS

Two queries made to:http://www.ncbi.nlm.nih.gov/sites/gquery were for MTHFR and VISION, which showed 155 articles, and HOMOCYSTEINE and VISION, which showed 582 articles. Another two queries to the database were: MTHFR and OPTOMETRY, and HOMOCYSTEINE and OPTOMETRY, which revealed zero, and two articles respectively.

In regard to hypotonia, the query HYPOTONIA AND VISION found 77 articles and HYPOTONIA AND MTHFR showed four publications.

RESULTS

The most frequent articles were on the following topics: (1) MTHFR: Behcet's disease, primary open angle glaucoma, primary closed angle, glaucoma, age related macular degeneration, and Leber Hereditary Optic Neuropathy, and (2) HOMOCYSTEINE: glaucoma, central retinal vein occlusion, macular degeneration, death of retinal ganglion cells, migraine, proliferative diabetic retinopathy, rhegmatogenous retinal detachment, and non-arteritic ischaemic optic neuropathy.

CONCLUSION

Many common ocular defects are related to the MTHFR gene defect, and high homocysteine. In the diagnosis and treatment of the diseases that have been listed as a result of the literature search, it is most important that the presence or absence of either the gene defect and/or homocysteine determined. Both can be measured with blood tests.

After reading the above description of the relationship of hypotonia to vision problems, the signs and symptoms are very similiar as those described by Streff's non-malingering syndrome.

Before vision training commences, it is therefore recommended to have patients with hypotonia also tested for MTHFR and homocysteine. If the homocysteine is high, i.e. above 12, the following regime is suggested: methylfolate, B12, B2, B6, and betaine HCl. The dosages can be coordinated with the patient's eare provider. It is important to note here that gluten interferers with folate absorption. Accordingly, patients found having MTHFR are put on gluten-free diets.

In addition to hypotonia, MTHFR and homocysteine are also related to primary open angle glaucoma, primary closed angle glaucoma, age-elated macular degeneration, central retinal vein occlusion, death of retinal ganglion cells, migraine, proliferative diabetic neuropathy, retinal detachment, and non-arteritic ischaemic optic neuropathy.

HYPOTONIA EVALUATION & TREATMENT

Table 2
HYPOTONIA TRAINING

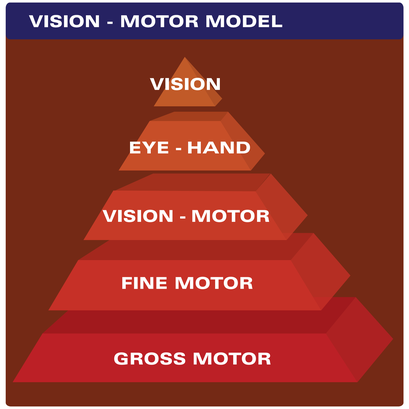
HYPOTONIA TRAINING	PAGE
SUPINE: RIGHT, LEFT, CENTER	
TNR	31, 32
FACES	
DANGLING RING	14, 49
LIGHTS: BLINKING COLORS	
MOBILE	
DANGLE BELL	
SEATED AT TALBLE / FLOOR: RIGHT LEFT CENTER	
HAND: Prehensory integration	35, 66
BOTTLE	75
LARGE OBJECTS: Vary texture, shape, color	
SMALL OBJECTS	59, 62, 66
DANGLE RING	11
DANGLE BELL	31
SPOON	63
FACES	
MIRROR	70
BALL	72
BUILDING BLOCKS	77, 80
LARGE OBJECT PUZZLES	77
HOLDING SPOON	
HOLDING CRAYON, PENCIL	86

SOURCE: Gesell, Arnold, Ilg, Frances L andBullis, Glenna E (1998) VISION: IT'S DEVELOPMENT IN INFANT AND CHILD Santa Ana, CA: Optometric Extension Program Foundation ISBN 0-943599-92-X

Table 3
SIGNS & SYMPTOMS

SIGNS & SYMPTOMS	
CLINICAL OBSERVATIONS: CHILDREN WITH HYPOTONIA	
POOR EYE MOVEMENTS	Typically the head leads the eyes in following objects and in tracking
POOR EYE FOCUSING	Cannot sustain reading or other near vision tasks
REFRACTIVE STATES	Children are usually farsighted
BINOCULAR VISION	The child may see double and /or have an eye that tums in or out
EYE - HAND COORDINATION	Usually slow in developing due to the lack of accurate eye movements and eye focusing
SKILLS:	With the lack of these vision skills, the child will typically use other senses to obtain information about his space world, i.e. touch.

Diagram 2
VISION - MOTOR MODEL



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