MJD FOUNDATION

MEDICAL PROTOCOLS

Eye Movement Disorders in MJD

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Action	Person	Date
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1. Background — Eye Movement Disorders and MJD

Machado Joseph Disease (MJD) (also referred to as Spinocerebellar Ataxia type 3 – SCA3) is a hereditary neurodegenerative disease that predominantly affects the cerebellar, pyramidal, extrapyramidal, motor neuron and ocular-motor neural systems. Gait ataxia is the most commonly reported first symptom, followed by diplopia, dysarthria and spastic gait (Saute, Jardim, 2015).

Humans have different classes of eye movements that can be classified by how they aid vision: 1) Visual fixation that holds the image of a stationary object. 2) The vestibulo-ocular reflex (VOR) that holds images of the seen world steady on the retina during brief head rotations. 3) Smooth pursuit that holds the image of a moving target of the fovea. 4) Saccades that are very fast eye movements that bring images of objects of interest onto the fovea. All of these types of eye movements are susceptible to disturbance in neurological conditions such as neurodegeneration. In patients with MJD, neurodegeneration within the cerebellum and brainstem, including the vestibular nuclei, commonly results in ocular disturbances such as nystagmus, vestibulo-ocular arreflexia, smooth pursuit and saccadic abnormalities and diplopia (Rub, 2004; Sequeiros and Coutinho, 1993).

Eye movement disorders frequently found in MJD include:

1.1. Nystagmus

Nystagmus, the involuntary rapid movement of one or both eyes horizontally, vertically or in a circular manner is the most frequently reported ocular disturbance in MJD patients (Vale, 2010; Jardim, 2001). Nystagmus often causes vision to be impaired. Pathological nystagmus, such as gaze-evoked nystagmus (drift of the eye) and rebound nystagmus is very common in patients with various forms of cerebellar dysfunction, particularly those with MJD, with some studies reporting nystagmus in 100% of patients examined (Buttner *et al.,* 1998). Brusse *et* al. (2011) have also found that clinical presentation of nystagmus was correlated with fatigue in MJD patients.

1.2. Vestibulo-ocular impairment

The vestibulo-ocular reflex (VOR), or 'doll's head reflex', is a physiological reflex necessary to preserve clear vision during head rotation. During head rotation, movement of fluid within the semicircular canals of the inner ear triggers the VOR to produce eye movement in the opposite direction to the head's rotation to stabilise images on the retina and preserve clear vision.

Impairment of the vestibulo-ocular reflex, as measured by the head thrust test, is a common occurrence in MJD, with one study reporting 7/7 examined patients displaying absence of horizontal VOR (Gordon, 2003). For the head thrust test (also called the head impulse test) the patient is asked to fix their gaze on the examiner nose or a target about 3 metres away and the examiner, while facing the patient and holding their head, executes sudden, rapid, unpredictable, angular head rotation to both sides. Gordon and colleagues (2003) found that whilst Control subjects could

maintain a gaze on a fixed target during the head thrust test, patients with MJD demonstrated catch-up saccades in the opposite direction to the head turn.

1.3. Smooth Pursuit and Saccades impairment

Smooth pursuit and saccades eye movements are movements that our eyes make in order to see objects of interest clearly. Saccadic or "jerky" smooth pursuit is very common in all cerebellar disorders including MJD. Whilst multiple studies have examined the degree of saccades impairment within MJD patients, discrepancies still remain within the literature on this topic. Whilst some forms of saccades impairment (e.g. square-wave jerks) do not cause visual impairment, saccadic oscillations do impair vision and can benefit from medical treatment.

1.4. Bulging Eyes (BE)

Bulging eyes, otherwise known as proptosis or exophthalmos, is a common sign of many different forms of spinocerebellar ataxia, including MJD. Bulging eyes are thought to occur in MJD because of dystonia[1] of the extrapyramidal system, causing eyelid retraction (Moro, 2013; Pedrosa, 2013).

1.5. Diplopia

Diplopia, commonly known as double vision, is the perception of two simultaneous images of a single object that may be displaced horizontally, vertically, diagonally (i.e., both vertically and horizontally), or rotationally in relation to each other. It may disrupt a person's balance, movement and/or reading abilities (Kernich, 2006).

Diplopia is often one of the first symptoms reportedly experienced by MJD patients (Saute, Jardim, 2015) and is caused by asymmetrical limitation of eye movements (limitation of eye movements is called ophthalmoplegia). Diplopia can be functionally corrected by closing on eye and anecdotally, it is common to see someone with MJD covering one eye with their hand when they are trying to focus on an object.

[1] Dystonia - involuntary muscle spasms that produce peculiar postures of different body parts.

2. Ocular symptoms as clinical indications of MJD

2.1. Nystagmus

In a study of Azorean families with MJD, nystagmus was found to be present in 88% of the symptomatic MJD patients (96% of late stage MJD patients), 17% of the presymptomatic MJD patients, and 0% of the MJD negative group (Raposo, 2014). Burk et al (1999) similarly reported significant rates of nystagmus within MJD patients (specifically gaze-evoked nystagmus in 75% of patients and rebound nystagmus in 55% of patients). These rates were much higher than the rates of nystagmus found in patients with other SCAs. The frequency of nystagmus identified in presymptomatic MJD positive patients within the Raposo study (2014) suggests that nystagmus may appear before gait disturbance, and therefore, if detected, could be an early sign of MJD.

2.2. Vestibulo-ocular arrefexia

Multiple studies have found that the Vestibulo-ocular reflex (VOR) is impaired in MJD patients (Buttner *et al.* 1998; Gordon, 2003, 2014, 2016). Buttner *et al.* (1998) found that 4/7 studied MJD patients had impaired VOR whilst an additional 2/7 had low VOR within normal range. Another small study reported the absence of VOR in all 7 patients examined (Gordon, 2003). In a recent study, VOR deficit detected on bedside examination was found in 90% of the 53 tested patients (Gordon, 2016).

2.3. Saccades impairment and Saccadic (jerky) smooth pursuit

Saccades eye movements are the voluntary movements that our eyes make in order to see objects of interest clearly. There are discrepancies within the literature regarding the condition of saccades eye movements in MJD patients. (Burk et al, 1999; Rivuad-Pechoux 1998; Buttner et al 1998; Caspi et al, 2013). The most frequent and clinically easily detected abnormalities in MJD are: saccadic smooth pursuit, slow saccades, hypo or hypermetric saccades.

2.4. Bulging Eyes

In a study of 369 patients from Brazilian families with SCAs, bulging eyes (characterised by the presence of eyelid contraction) was identified in 65.3% of MJD patients examined, compared to 33.3% of all SCAs patients examined (Moro 2013). The authors concluded that observation for bulging eyes could be used as a tool for the differential diagnosis of MJD from other SCAs.

3. Recommended Guidelines for addressing Eye Movement Disorders in MJD Patients

No trial or systematic study has evaluated the efficacy of therapies for eye movement disorders in SCA3/MJD or other SCAs (Saute 2015).

Patients with MJD should be reviewed bi-annually by a neurologist and by an ophthalmologist and annually by an optometrist. As symptoms are progressive, a faster pace of degeneration may be experienced at different stages of the disease e.g. prismatic lens prescriptions may need to be renewed more often than someone without MJD.

Appendix A provides a proposed table for scoring eye movement abnormalities. (Gordon, 2016)

It is a requirement of the Northern Territory Government Disability Equipment Program, that any patient being prescribed a powered wheeled mobility aid must first undergo an optometry assessment in order to ensure they are able to use the aid safely.

4. Pharmaceutical Treatments Options

4.1. Botox

Botox injections into the extraocular muscles or the retrobulbar space have been reported to be effective for the treatment of nystagmus in ataxia patients (Saute, 2015; Stahl, 2002). Botox injections into the orgibularis oculi muscle have also been reported to treat eyelid contraction, the cause of bulging eyes (Cardosa, 2000).

Limitations of botox treatment are the short period of action (2-3 months) and adverse side effects such as ptosis (drooping eyelid), and diplopia, which may be more bothersome to the patient than visual symptoms that the botox is treating (Leigh et al, 1992; Stahl, 2002). Other limitations of botox include the cost and availability of a neurologist with the skills to administer the injections – especially in more remote parts of Australia.

4.2. Baclofen

Baclofen has been reported to be effective for the treatment of nystagmus (Tegetmeyer, 2015). However, baclofen can produce side effects such as drowsiness, dizziness, weakness, nausea and fatigue and these effects are enhanced by alcohol and other CNS depressants. Patients should be warned of the potential for baclofen usage to cause drowsiness that can be dangerous if the patient has an automobile or boat licence.

4.3. Other pharmaceutical options

Other drugs that have been trailed for the treatment of various forms of nystagmus (not reported specifically for MJD) include Clonazepam, memantine and Gabapentin (Currie and Matsuo, 1986; Shaikh et al, 2013; Thurtell el al, 2010). Like Baclofen, these drugs have side effects such as drowsiness, dizziness, lethargy, headache and incoordination. Two studies have shown that some forms of nystagmus can be treated by the potassium channel blockers 3, 4-diaminopyridine and 4-aminopyridine and that these drugs are relatively well tolerated by patients (Strupp et al, 2003; Kalla et al. 2004). The potential of these drugs specifically for the nystagmus experienced by MJD patients has not been investigated.

5. Therapeutic Treatment Options

5.1. Prismatic lenses

Many patients report diplopia improvement with prismatic lenses (Saute, 2015; Matilla-Duenas, 2012). Prismatic lens prescriptions may need to be renewed more often than someone without MJD, due to the progressive neurodegeneration affecting the degree of diplopia present.

5.2. Orthoptic exercises

Orthoptic exercises, such as prism therapy (adding optical prisms to a patients glasses to train the eye) may be beneficial for patients experiencing diplopia (Saute, 2015).

6. Other Treatment Options

6.1. Surgery

Surgery is not recommended for the treatment of ocular disorders in SCA patients due to the progressive nature of the disturbance, causing squint angles to vary with time (Matilla-Duenas, 2012).

Appendix A – Proposed table for scoring eye movement abnormalities

Eye movements disturbances in MJD				
	Normal or Absent	Slight Abnormal	Moderate Abnormal	Severe Abnormal
Visual fixation				
Diplopia/Ophthalmoplegia				
Smooth Pursuit				
Saccades				
VOR – Head Impulse Test				
Gaze Evoked Nystagmus				
Bulging Eyes				

Source: Prof Carlos Gordon (2016)

Appendix B – Contributors and Reviewers

Contributors

Ms Nadia Lindop
BSc(Hons), Cert IV Finance, Cert IV WHS
MJD Foundation

Dr. Angela Laird
BSc (Hons), PhD

Prof Carlos R Gordon, MD; DSc
Department of Neurology,
Meir Medical Center,
Kfar-Saba and Sackler Faculty of Medicine,
Tel Aviv University,
Israel

Ms Libby Massey
B.Ap.Sc(OT), MPH(Dtn)
MJD Foundation

Desireé LaGrappe
B.Sc.Nurs. (RN)
MJD Foundation

Associate Professor John MacMillan
B.Med.Biol(HonsPath), MB.ChB, MD,
MRCP(UK), FRACP, FRCP, GradCert Health
Management, GradCert Nutrition Medicine.
Genetic Health Queensland

Reviewers

Dr. Angela Laird
BSc (Hons), PhD

Prof Carlos R Gordon, MD; DSc
Department of Neurology,
Meir Medical Center,
Kfar-Saba and Sackler Faculty of Medicine,
Tel Aviv University,
Israel

Appendix C – Definitions

Baclofen – is a derivative of gamma-aminobutyric acid (GABA). It is primarily used to treat spasticity and also acts as a muscle relaxant.

Botox – Botulinum toxin (BTX) is a neurotoxic protein produced by the bacterium *Clostridium botulinum*.

Diplopia – double vision

Dysarthria – is a group of motor speech disorders resulting from disturbed muscular control of the speech mechanism due to the damage of the peripheral or central nervous system causing weakness, incoordination, or paralysis of speech musculature (See Communication Difficulty medical protocol).

Dystonia – involuntary muscle spasms that produce peculiar postures of different body parts.

Extrapyramidal neural system – part of the motor system that causes involuntary reflexes and movement, and modulation of movement (i.e. coordination).

Fovea - is a small, central pit composed of closely packed cones in the eye. It is located in the centre of the macula lutea of the retina. The fovea is responsible for sharp central vision.

Nystagmus – is a condition of involuntary eye movement, acquired in infancy or later in life, that may result in reduced or limited vision. Due to the involuntary movement of the eye, it is sometimes called "dancing eyes".

Ophthalmoplegia – is the limitation of eye movements.

Ptosis – drooping eyelid

Pyramidal neural system – includes both the corticospinal and corticobulbar tracts. These are aggregations of upper motor neuron nerve fibres that travel from the cerebral cortex and terminate either in the brainstem (*corticobulbar*) or spinal cord (*corticospinal*) and are involved in control of motor functions of the body.

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