

Frequently Asked Questions for MRI and TMS
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An important part of the chromosome 18 studies performed at the Health Science Center are Magnetic Resonance Imaging (MRI) and Transcranial Magnetic Stimulation (TMS). We have found that many people who are contemplating participating in the study have the same questions about these procedures. These questions and their answers are presented below. We hope this helps further understanding of these procedures.

Magnetic Resonance Imaging (MRI)

1. Will MRI studies acquired by local physicians at other locations be adequate for 18q-patients?

MRI studies acquired at other institutions can be read by physicians there or at the Research Imaging Center (RIC) if the film(s) is (are) sent to us. An MRI study obtained at another site can tell us whether the patient has abnormal myelin and/or other neuroradiological manifestations of the 18q- syndrome. However, for patients enrolled in the 18q- research program, special imaging procedures are required, and these can only be done at the RIC. These special studies provide high-quality research specific information that cannot be obtained from studies done at other sites.

2. Can MRI scans acquired many years ago be used for the study?

MRI scans acquired many years ago may be useful to provide some baseline information. The report from the original study may tell us whether the patient had abnormal myelin, as well as reveal structural abnormalities such as a small pituitary gland, but it will not provide most of the information that we include in research studies done at the RIC. Rather than rely on an old MRI scan, it would be more appropriate to obtain a recent MRI scan for review by a radiologist.

3. MRI studies can take a long time (~40 minutes) and children may move during the scan. What effect does this have on the study?

Movement during the MRI scan often results in poor quality images. This could result in difficulty in interpreting the MR images. In children, particularly in those who are very young or uncooperative, sedation is therefore a viable alternative.

4. What is the difference between the open-sided MRI systems and the MRI system used at UTHSCSA?

The MRI used at UTHSCSA is a conventional closed machine, and the subject is positioned in a long tube while being scanned. Open-sided versions of MRI offer a more spacious, brighter, and quieter environment and are ideal for pediatric, elderly, claustrophobic, anxious, and obese patients up to 500 pounds depending on their specific body shape. However, young children usually have to be sedated for MRI studies and claustrophobia does not affect patients who are asleep. The MRI system available at UTHSCSA (RIC) provides substantially higher quality pictures of the brain than an open-sided MRI system.

5. Do you need baseline MRI studies before beginning treatments?

The degree and nature of myelination is highly variable in subjects with the 18q-syndrome. We need pre-treatment MRI studies to obtain baseline information on each individual. This will aid significantly in monitoring response to growth hormone therapy and in determining if there is a change in the level of myelin on post-treatment MRI studies. MRI studies performed at the RIC provide additional quantitative measures of baseline and post-treatment brain status that are helping us better understand the 18q-syndrome.

6. Do all patients with chromosome 18 abnormalities need MRI scans?

The necessity to perform MRI examinations on patients with chromosome 18 disorders is dictated largely by the presence of neurological signs and symptoms arising as a consequence of the genetic disorder. Individuals with 18q- and ring-18 may be missing the gene for myelin basic protein (MBP). MBP is intimately linked to the formation and production of myelin in the white matter of the brain. An MRI scan is therefore very important for us to determine if myelin is normal or abnormal. Because MRI is a non-invasive procedure, with no exposure to ionizing radiation and with minimal risk from sedation of smaller children, your local doctor may want to obtain one.

7. Can local physicians and radiologists read MRI studies on chromosome 18 abnormality patients?

Local radiologists would certainly be able to read MRI studies obtained from subjects with abnormalities of chromosome 18. They should be able to tell you if myelin is abnormal and whether there are other abnormalities that can be seen by the MRI examination. The studies performed at the RIC provide additional unique quantitative data that are presently unavailable from MRI studies from other sites. These quantitative measures are very important and extremely valuable in furthering our knowledge and understanding of the process of dysmyelination (abnormal myelin formation), but are not presently required for clinical management.

8. What type of sedation is used?

Sedation (Chloral hydrate syrup) is required for MRI studies in very young and uncooperative children. If the time interval between sequential sedation is of reasonable length (how long??), chloral hydrate has minimal side effects. In rare cases this sedative has been associated with skin rashes (2 cases in 196,134 patients) and breathing problems (1 case in 196,134 patients). If your child is sedated, we will monitor his/her heart rate and blood oxygen levels continuously during the procedure using a light monitor that clips on his or her large toe.

9. What do you do to reduce the noise associated with MRI studies?

MRI scans can be very noisy. We provide patients, and anyone staying in the scanner room, with ear plugs. Patients also have sheets placed by their ears to muffle the noise. Older subjects can have ear phones and listen to a movie. The earphones also suppress scanner noise.

10. What do iron deposits in the brain indicate?

Iron is found normally as a component of hemoglobin (the oxygen carrying compound) in red blood cells. It is required for the synthesis of neurotransmitters (chemicals that transmit information in the nerves), myelin production and energy metabolism. Fundamental differences exist between the manner in which iron is metabolized and transported in the brain and body. Iron may accumulate in the brain under both normal and abnormal conditions. However, the nature and location of iron deposition may vary. In a normal brain, non-heme iron (iron not related to hemoglobin) accumulates regionally and is highest in the basal ganglia. Pathologic abnormal brain iron accumulation is seen in common disorders, including Parkinson's disease, Alzheimer's disease and Huntington disease. It is not yet known if iron deposits in the brain indicate abnormality in individuals with 18q-.

11. What are you looking for in MRI studies?

The most common finding in 18q- subjects is abnormal myelin. We are trying to assess the degree of myelination and to determine if it is consistent with the patients chronological age and mental development. We have also seen structural abnormalities and iron deposits in some subjects.

12. What are normal values for T1 as a function of age, and how do they compare with those in 18q- patients?

The T1 of white matter (contains the myelin) changes with age. Babies (under 6 months), whether normal or with 18q- have T1s of 2000 msec or longer. The T1 of white matter decreases with age but reaches a stable value after an age of about 4 years. At age 4 years a normal child will have a T1 of about 800 msec (measured in a 2.0 Tesla imager)

and a child with 18q- will have a T1 of about 1000 msec. Children with 18q-, in the age range of 4-13 years, have a T1 value similar to that in a 2-year old normal child.

General

1. How often should studies be repeated?

We need an MRI before growth hormone treatment or upon entry into the study. We will obtain another MRI scan after 2 years and possibly after 4 years from the first scan. After a baseline MRI has been performed, it may be appropriate to do the next MRI after the subject has been on treatment with growth hormone for 18-24 months.

2. Is myelination abnormal in chromosome 18 patients other than 18q-?

Individuals with ring-18, and interstitial deletions may be lacking the gene for myelin basic protein and may therefore have abnormal myelin formation. Currently there is little information that suggests that patients with other chromosome 18 abnormalities would have abnormal myelin.

3. What does abnormal myelination mean?

Abnormal myelination means that the myelin formed is not normal in terms of content, chemical composition, or distribution. On T1-weighted MRI scans, the white matter does not look as bright as it normally should, and this probably indicates that there is not as much myelin. The quantitative measurement of T1, done at the RIC, provides a more accurate measure of myelin status. Myelin helps nerve impulses travel rapidly. If the myelin level is low, nerve impulses travel considerably slower. The relationship of abnormal myelin to behavior is currently under investigation in the 18q- study.

4. What is the normal age for maturation of white matter (i.e. where the myelin is located)?

Visually, normal white matter maturation occurs by around two years of age. However, quantitative measures of myelin indicate that changes in myelin level are mostly complete by the age of 4 years with much smaller changes occurring until the late 20's.

5. Is there any correlation between myelination and IQ?

This is one of the questions we hope to answer in our study. At this time, we do not know the relationship between IQ and myelination or its impact on individuals with 18q- syndrome. We will continue to study both children with 18q- and normal children to seek an answer to this question.

Transcranial Magnetic Stimulation (TMS)

1. Do nerve conduction studies performed using the transcranial magnetic stimulator hurt?

The TMS nerve conduction studies, in individuals with 18q-, do not hurt. The pulses produced by the stimulation coil are usually described as gentle tapping near the sites of stimulation (on the scalp and near the neck). Also, muscles in the hand and arm will twitch slightly.

2. What are normal values for nerve conduction velocity measurements?

The conduction velocity along a motor nerve in the arm is in the range of 55-60 meters/second. The conduction velocity from the hand motor area in the brain to the spine just below the neck, is in the range of 20-30 meters/second. The conduction velocity across the head for hand motor nerve fibers is approximately 10 meters/second. These velocities, measured in normal adults, vary with age, especially for children under the age of 4 years. We are now making these measurements in children with 18q-.