Robot Assisted Transcranial Magnetic Stimulation for Subjective Visual Vertical Assessment

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May 10, 2018

Abstract

The subjective visual vertical (SVV) is a measure of upright perception attributed to vestibular feedback. Differences in the SVV and the true earth-vertical could potentially be linked to activity of the posterior aspect of the supramarginal gyrus (SMGp), a region in the right hemisphere of the brain. To investigate the link between the SMGp and the SVV, transcranial magnetic stimulation (TMS) can be used to inhibit activity in localized regions of the brain. By studying the impact of this inhibition, an activity map can be generated to help identify specific areas within the SMGp that lead to the greatest impact on the SVV. However, there is a need for a tool that can automatically conduct TMS during SVV assessment in a grid-like fashion. For this reason, we developed a robotic tool that will apply TMS in precise positions specified by researchers following MRI scans. Our progress included building a custom tool that can fit over a UR5 robot and translate between specified points linearly with some limited force feedback. Eventually, we hope this tool will be used to help assess brain activity in other regions once grid location can be customized and TMS can be reliably adjusted in between measurement points.

1 Background

Upright perception relies on numerous external and internal factors but is primarily related to vestibular feedback.[1] Vestibular feedback contributes to the maintaining of balance and spatial orientation such that the head remains in line with the body, perpendicular to the ground. Spatial orientation can be measured using a test called the subjective visual vertical (SVV).[2] Vestibular input integration appears to be linked to regions in the right hemisphere of the brain, including the superior temporal gyrus and the inferior parietal lobule. One specific area of the latter, the supramarginal gyrus (SMGp) has been studied to observe its effects on vestibular feedback. It has been established through functional neuroimaging studies and behavior analysis following cortical lesions in the area that there is a potential relationship with balance and the SVV [2]. However, not all functional roles in the SMGp are known nor how information is processed in and between these areas. To assess the impact of changes in these regions, the SVV is employed. [1] One method of SVV assessment is to display a line in front of the person and tilt it to various angles to measure the extent to which tilting the line produces the same response as a vertical line. Subjects identify what they consider to be perpendicular to the ground ("earth vertical"). This vertical is normally stable, which is referred to as orientation constancy, but can be affected by the vestibular system, proprioception (determining relative head and body positions), and vision. [3]. Acknowledging this as the case, the activation or inhibition of related cortical regions is currently being explored to induce a measurable impact on vestibular feedback. One approach is transcranial magnetic stimulation (TMS), in which magnetic fields are induced in the target area, thereby stimulating or inhibiting regions on the cortex of the brain. The specific method used in this study was continuous theta burst stimulation (cTBS), which is designed to decrease cortical activity.[4] Thus, TMS was used to mimic lesions on the SMGp and the effects of its inhibition were investigated with respect to its impact on the SVV.

Up until recently, the SMGp was linked to eye torsion, or the twisting of the eye in its socket, which would have explained how the SVV changes with SMGp inhibition. SMGp inhibition induced a drift in SVV in the opposite direction as head tilt whereas the control showed SVV drift in the same direction as head tilt. This fit with the idea that the eye was rotating in the opposite direction after TMS application. It was found that TMS induced changes in the SVV, but eye torsion was not measurably affected by SMGp inhibition. Therefore, there may be another particular region of the SMGp that induces SVV changes which has yet to be localized and investigated. [5]

2 Problem Setup

It has been well established that TMS can be used for the inhibition of cortical brain activity for a variety of experimental setups. However, this can be a labor-intensive process due to the constant repositioning necessary to move the TMS applicator coil to target areas with the correct orientation. In addition, the potential for experimenters to make mistakes in positioning the coil could lead to erroneous application of non-target sites. Above this, there is no method of visualization once results have been found to localize activity to specific areas. Therefore, there is a need to automate TMS application for specified regions of the brain using a robotic tool so that mapping brain activity can be simplified. This project worked on one implementation that included a force feedback component to prevent TMS application from causing injury to subjects.

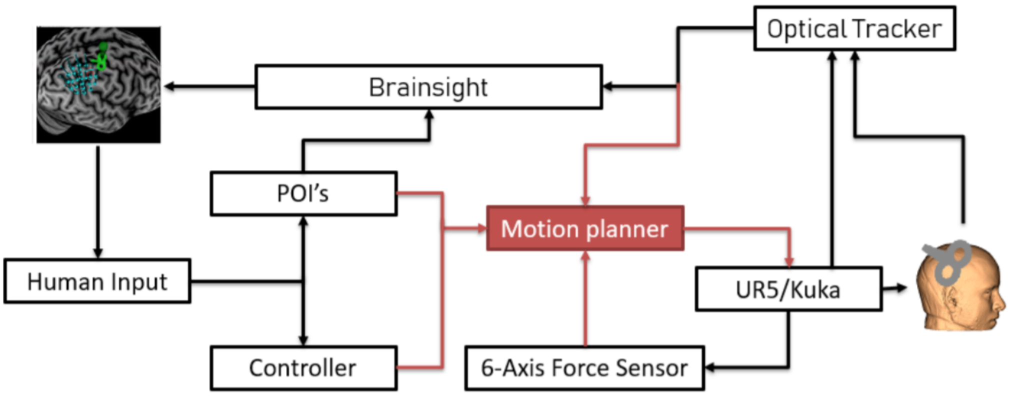

Figure 1: An outline for the function of the motion planner that was designed. The red inputs to the planner were designated as specific goals for this project

3 Technical Approach

A flowchart diagram of our approach is presented in Figure 1. Our goal was to implement the arrows in red, constructing a motion planner capable of directing movement of the coil to various points of interest (POI's). To walk through the process, we start with human input for coordinates where POI's should be located, based on brain scam imagery. To visualize the brain scan and the cortex of the subject, a software called Brainsight was used. The researcher using this tool would also be given a controller with which they could control the location of the coil. The motion planner would take inputs from either defined POI's or controller input and produce motion in either a UR5 or Kuka system. For this project, we decided to focus on a UR5 implementation but a Kuka system could be explored in the future provided the coil is not too heavy. The UR5 would then move the coil to a POI or specified location on the subject's head and provide force feedback information including the torque and pressure applied. This force information would be fed back to the motion planner which would reduce pressure by moving away from the subject if necessary. Above all components would be an optical tracker recording positions of the subject, the UR5, and the coil, each of which would have tracking markers. The location information would be sent back to Brainsight to help draw the position of the TMS coil over the grid location being measured.

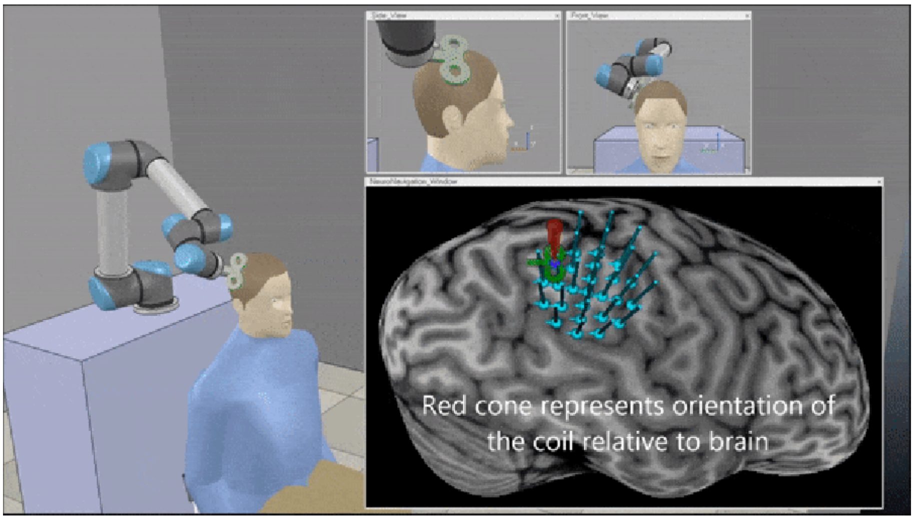

Figure 2: An outline for the function of the motion planner that was designed. The red inputs to the planner were designated as specific goals for this project

As part of our approach, we decided to develop a custom tool capable of holding the TMS coil in place, parallel to the end effector of the robot. The tool would grip the handle of the coil and place the center of the double loop at the target location. A basic illustration is provided in Figure 2. The coil would be held parallel to the cortex of the subject, determined prior to application by MRI scan and 3D reconstruction. The set of grid points to be scanned are also illustrated in Figure 2 on the bottom right overlayed over the 3D model of the subject's brain. This illustration was made at the beginning of the project so the force sensor and custom tool holder are not pictured on the end effector of the UR5.

3.1 Environment Setup

Figure 3: Above: An illustration of the bite bar setup where subjective visual vertical was assessed. Below: The subject's chair and the TMS coil station set up in the background.

This project was done in conjunction with the Vestibular and Ocular motor Research Laboratory (VORLAB) at the Johns Hopkins Medical Campus and with the Biomechanical and Image Guided

Surgical Systems (BIGSS) Lab at the Johns Hopkins Univerisity Homewood Campus in Baltimore, MD. The UR5 was not able to be moved into the VORLAB at the time of this paper's writing, but will hopefully be done soon. To work around this, the project was done in simulation except for the design of the tool holder itself. All other external resources such as Brainsight, the TMS coil, and the SVV assessment area were located in the VORLAB.

3.2 Unobstructed Linear Motion

To construct linear motion using the UR5 robot, a series of frame transformations were necessary to calculated end effector position given joint angles. The Jacobian, J, of the UR5 was calculated so that joint velocities could also be mapped to end effector velocities given the current position. Fortunately, both of these had been accomplished already for a standard UR5. Thus, the next step was to formulate a cost function, C, that would attempt to find the optimal route between two coordinate points, assuming they were in the same frame [1]. Our cost function was given to be the following:

$$C = \arg\min_{\Delta\vec{\theta}} \|J\Delta\vec{\theta} - \Delta\vec{y}\|$$

where $\Delta\vec{y}$ was the vector between two coordinates, setting up a linear path. This system was solved using least squares in MATLAB. However, there was an additional problem of adding constraints the system had to follow.

3.3 Additional Constraints

Immediately, we felt the best way to limit injury was to restrict the speed of the robot so experimenters would have time to react:

$$\|\Delta\vec{\theta}\| \leq \Delta\theta_{max}$$

The next constraint was force feedback. This was vital to the project to ensure that subjects would not feel extreme pressure against their heads during experimentation. Due to the time constraints, it was felt that a full implementation of the force feedback mechanism as originally planned could not be accomplished. Instead, a simple, spring-like force was implemented such that the tool would not get too close to the subject or target location. Thus, to add to our original cost function, we added a hard constraint to allow the head to repel the coil slightly. This is with constants that have not been measured at the time of this paper's writing. The updated cost function was changed to the following:

$$C = \arg\min_{\Delta\vec{\theta}} \|J\Delta\vec{\theta} - \Delta\vec{y}\|$$

such that:

$$\|\Delta\vec{\theta}\| \leq \Delta\theta_{max}$$
$$\Delta\vec{X} = J\Delta\vec{\theta}$$
$$\|K\Delta\vec{X}\| \leq F_{max}$$

where K was a matrix of chosen spring constants and F_max was the maximum allowable force, determined from experimental results.

As a result, this meant our original goal of keeping the tool tangent to the head could not feasibly be done. However if we were to construct additional constraints for this, we would likely get to the nearest point on the reconstruction of the subject's head, $\vec{p}$. We would then add a soft constraint to minimize the distance between coil position and $\vec{p}$, but first we would transform $\vec{p}$ to be in the same coordinate system as the robot. Thus, our new cost function would be:

$$C = \arg\min_{\Delta\vec{\theta}} \alpha\|\Delta\vec{X} - \Delta\vec{y}\| + \eta\|\vec{X} - F_{HeadToBase}F_{BaseToEE}\vec{p}\|$$

such that:

$$\|\Delta\vec{\theta}\| \leq \Delta\theta_{max}$$

[1]For points not in the same frame, an additional calculation had to be made to transform one point relative to the other. This process was accomplished separately, but should be redone with the custom tool design in mind

$$\Delta\vec{X} = J\Delta\vec{\theta}$$

$$\|K\Delta\vec{X}\| \leq F_{max}$$

and α and η would be experimentally determined. $F_{HeadToBot}$ would be calculated ahead of time knowing the positions of the subject and the robot base using the optical tracker. $F_{BaseToEE}$ is already known for standard UR5's and would be used to put $\vec{p}$ in the same coordinate frame as $\Delta\vec{X}$.

4 Results

4.1 Algorithm

Simulation was accomplished with Slicer, which allowed visualization of the UR5 given a set of joint angles. The path output from the MATLAB solution to the cost function previously detailed produced a direct path between specified points with reasonable accuracy. A manual check was able to show that the robot successfully moved linearly along a path in Slicer as well. As can be seen from the figure, the robot was able to converge to the desired location successfully.

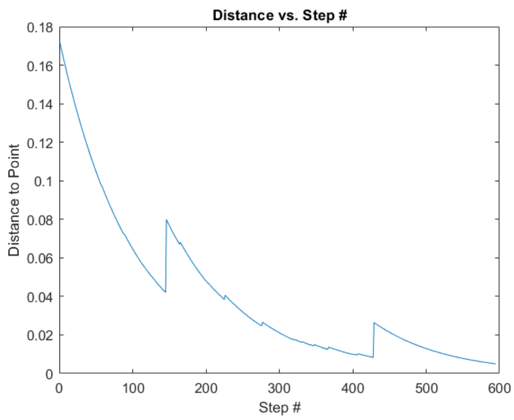

Figure 4: The distance from the desired position over several iterations until convergence.

4.2 Custom TMS Holder

To construct the TMS coil holder, we first needed to interface it with the force sensor and then interface the force sensor with the end effector of the UR5. Naturally, we constructed two separate parts that each each connect two others. The first was the connector between the UR5 end effector and the force sensor. The force sensor chosen was the KMS-40 six-axis force sensor which would allow us to make torque measurements in addition to contact forces. An illustration is shown in Figure 5.

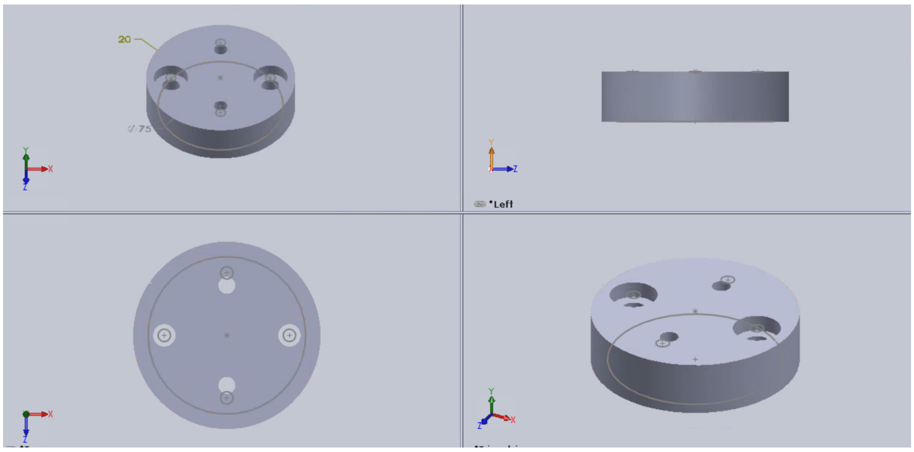

Figure 5: A CAD model of the interface between the end effector of the UR5 and the KMS-40 six-axis force sensor.

As can be seen from the CAD model, we made screw holes in a small disk designed to fit over the holes of the end effector and the holes of the force sensor. The force sensor used M4 screw heads and the UR5 used M8 screw heads. Models for these were found online to construct a validation assembly.

For the second part of the coil holder, we needed to attach the force sensor to the coil, but since the coil needed to be kept parallel to the end effector, we needed a way to grid it such that the double loop would stay offset, but parallel to the face of the force sensor. Ultimately, we chose a design where a loop would clsoe around the handle connecting the TMS coil to its cable. The loop could be tightened with screws to adjust the level of grip.

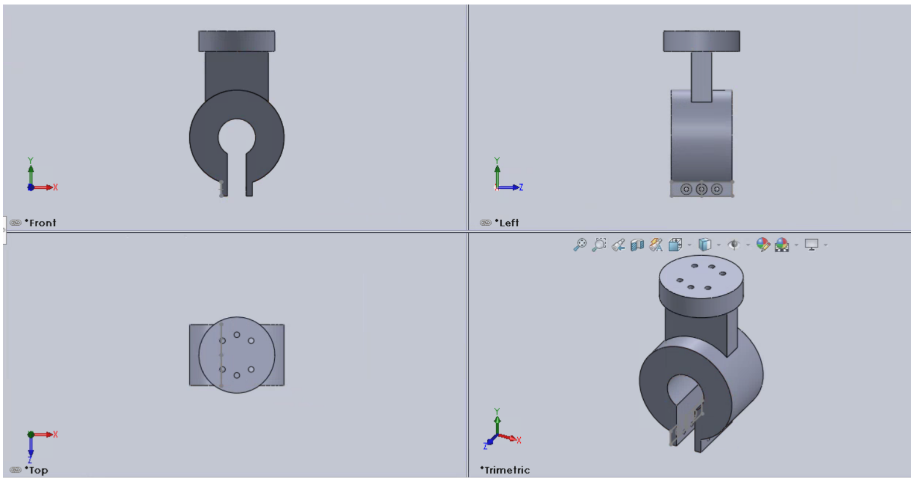

Figure 6: A CAD model of the coil holder that was attached to the force sensor.

An additional consideration had to be made for the flexibility of the handle, which we feared would cause the tool to sag while being held by the loop. For this reason a hard plastic covering was attached to fit over the handle, giving it rigidity and extra thickness. This was also tightened with M4 head screws. The whole part was assembled in SolidWorks before being 3D printed.

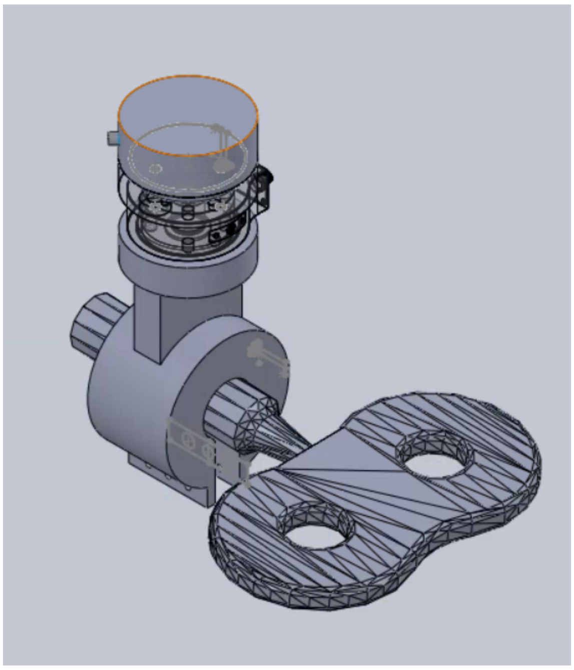

Figure 7: A CAD assembly showing all parts linked together to hold the TMS coil.

The final result after 3D printing is shown in the figure below:

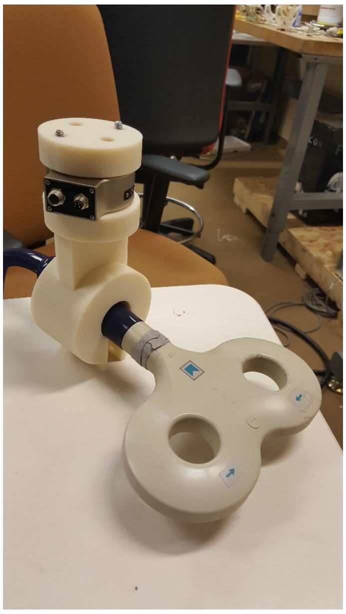

Figure 8: The fully assembled model without the UR5.

5 Significance

The process of TMS application over a grid area on the cortex of the brain has been shown to be difficult to automate, but the steps taken by this project demonstrate its practicality. Although we were specifically studying the SMGp, there is evidence to suggest that other regions of the brain could be investigated in the same fashion. We successfully managed to achieve the original minimum deliverables and the adjusted expected deliverables. The maximum deliverables unfortunately required additional time to achieve due to the investment made into printing the custom tool holder. However, all components are now in place for the maximum goals to be achieved with approximately 2 more months of work. It is still necessary to gain approval from the necessary review boards as to whether the automatic procedure is safe enough to use for other experiments. Also, the procedure will have to be fine tuned to adjust the weighting parameters for the soft constraints and to find the maximum allowable forces. Future plans for this project would include attempting to keep the orientation of the coil constant relative to the individual's head and to improve the force feedback. Tangency to the subject's head will also be a difficult issue to resolve, but given the code and parts made by this project, it is certainly possible.

6 Acknowledgements

I would like to thank Dr. Amir Kheradmand, Dr. Jorge Otero-Millan, Farshid Alambeigi, and Rachel Hegeman for their contributions towards the completion of this project. Additional thanks goes out to Dr. David S. Zee and Dr. Mehran Armand for guidance and for supporting the project. I'd also like to thank Dr. Russell Taylor and Ehsan Azimi for feedback and for running Computer Integrated Surgery II, through which this project was conducted.

Management Summary

This project was conducted by an individual (myself), working in tandem with several others from the VORLAB and the BIGSS Lab. In terms of code, the BIGSS Lab provided packages that I was able to make use of to run Slicer and the forward kinematics of the UR5. The VORLAB provided workspace, the TMS coil, and models that were used while building the simulation environment. The deliverables for the project were as follows: *Minimum Deliverables*

1. Develop control algorithms to move the TMS coil in simulation reliably between given points (no safety concerns, linear motion only).

2. Documentation of control algorithms and motion planning

Expected Deliverables

1. Add constraints to robot path planning to ensure patient safety with force feedback

2. Create custom tool holder for TMS coil in conjunction with six-axis force sensor and robot

3. Documentation of safety constraint code and motion adjustments

Maximum Deliverables

1. Move the TMS coil reliably between many head locations on the physical robotic system

2. Document implementation in full robotic system, including installation instructions

Of these, all of the minimum and expected deliverables were completed and the installation instructions from the maximum deliverables were written. However, these were after adjustment after the checkpoint presentation during which it was realized that the custom tool took priority over the algorithm so it would be possible to collect force data. Prior to this, the expected deliverables were to have the full implementation of safety constraints and there was no need for a custom tool.

For next steps, it will be necessary to constrain the coil path of motion so its orientation is maintained as much as possible. This is so that the robot does not try to rotate around the side of the subject's head and the coil remains parallel to the cortex. The force feedback algorithm could also be improved so that tangency to the head could be maintained. Once the UR5 is moved into the VORLAB, it will become possible to test these implementations out of simulation so further debugging will be possible.

Over the course of this project, I learned more about the practical applications of the knowledge I gained from CIS I. I had to use frame transformations and had to set constraints over motion, two techniques we had gone over in lecture and homework. I also gained skills in using CAD, which I had previously only done for simple objects. Moving to more complex models was initially challenging, but I feel more comfortable using SolidWorks now. I also learned the basics of Slicer over ROS, which could be useful for understanding older robotics research.

Technical Appendices

All code and manuals can be found via the link on the project webpage in a Bitbucket repository. The CAD files are also in the same repository along with the code and copies of all reports/presentations. The models are separated into folders and the "Full Assembly" contained every coil holder part put together.

References

[1] Naik Chetana and Rane Jayesh. Subjective Visual Vertical in Various Vestibular Disorders by Using a Simple Bucket Test. *Indian Journal of Otolaryngology and Head & Neck Surgery*, 67(2):180–184, June 2015.

[2] A. Kheradmand, A. Lasker, and D. S. Zee. Transcranial Magnetic Stimulation (TMS) of the Supramarginal Gyrus: A Window to Perception of Upright. *Cerebral Cortex*, 25(3):765–771, March 2015.

[3] Jorge Otero-Millan, Dale C. Roberts, Adrian Lasker, David S. Zee, and Amir Kheradmand. Knowing what the brain is seeing in three dimensions: A novel, noninvasive, sensitive, accurate, and low-noise technique for measuring ocular torsion. *Journal of Vision*, 15(14):11, October 2015.

[4] Lizbeth Cárdenas-Morales, Dennis A. Nowak, Thomas Kammer, Robert C. Wolf, and Carlos Schönfeldt-Lecuona. Mechanisms and Applications of Theta-burst rTMS on the Human Motor Cortex. *Brain Topography*, 22(4):294–306, January 2010.

[5] Jorge Otero-Millan, Ariel Winnick, and Amir Kheradmand. Exploring the Role of Temporoparietal Cortex in Upright Perception and the Link With Torsional Eye Position. *Frontiers in Neurology*, 9, April 2018.

[6] Cristiana Borges Pereira, Aline Kozoroski Kanashiro, Fernanda Martins Maia, and Egberto Reis Barbosa. Correlation of impaired subjective visual vertical and postural instability in Parkinson's disease. *Journal of the Neurological Sciences*, 346(1-2):60–65, November 2014.

[7] Darío H. Scocco, Judith N. Wagner, Juan Racosta, Anabel Chade, and Oscar S. Gershanik. Subjective visual vertical in Pisa syndrome. *Parkinsonism & Related Disorders*, 20(8):878–883, August 2014.

[8] Michael C. Brodsky and Jonathan M. Holmes. Torsional augmentation for the treatment of lateropulsion and torticollis in partial ocular tilt reaction. *Journal of American Association for Pediatric Ophthalmology and Strabismus*, 16(2):141–144, April 2012.

[9] David A. Gorelick, Abraham Zangen, and Mark S. George. Transcranial magnetic stimulation in the treatment of substance addiction: TMS as addiction treatment. *Annals of the New York Academy of Sciences*, pages n/a–n/a, July 2014.

[10] Shalini Narayana, Andrew C. Papanicolaou, Amy McGregor, Frederick A. Boop, and James W. Wheless. Clinical Applications of Transcranial Magnetic Stimulation in Pediatric Neurology. *Journal of Child Neurology*, 30(9):1111–1124, August 2015.

[11] Simone Rossi, Mark Hallett, Paolo M. Rossini, and Alvaro Pascual-Leone. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. *Clinical Neurophysiology*, 120(12):2008–2039, December 2009.