

However, long time would elapse before researchers started to use TMS not only for basic research on dyslexia but also for clinical applications.

TMS as clinical intervention technique

Within TMS protocols, Frye *et al.*^[56] were the first to hypothesize that high-frequency repetitive TMS could improve reading performance in people suffering from dyslexia by exciting underactive reading pathways in the brain. Previous neuroscientific research had shown that an improvement in reading in dyslexics was mediated by an increase in the activations of typically hypoactive left-hemisphere areas (also referred to as “normalization”) and by additional activation in the right hemisphere regions (also referred to as “compensation”).^[57]

Costanzo *et al.*^[58] conducted an intriguing study with high-frequency rTMS on 10 dyslexic adults,

who were native speakers of Italian, to test the hypothesis of exciting underactive reading pathways in dyslexics.^[56] They conducted 5-Hz TMS over both the left and the right inferior parietal lobules and the superior temporal gyrus (note that these areas had previously been found to improve reading in a TMS study on nondyslexics^[59]) in advance of reading words, nonwords, and text aloud. The results of the study showed that on the one hand, high-frequency rTMS stimulation over the left inferior parietal lobule led to a better performance in nonword reading; that is, the individuals with dyslexia made fewer errors. On the other hand, high-frequency rTMS stimulation over the left superior temporal gyrus resulted in faster word reading and better text reading. Interestingly, after the right inferior parietal lobule had been stimulated, the performances for nonword reading also increased. This intriguing study led

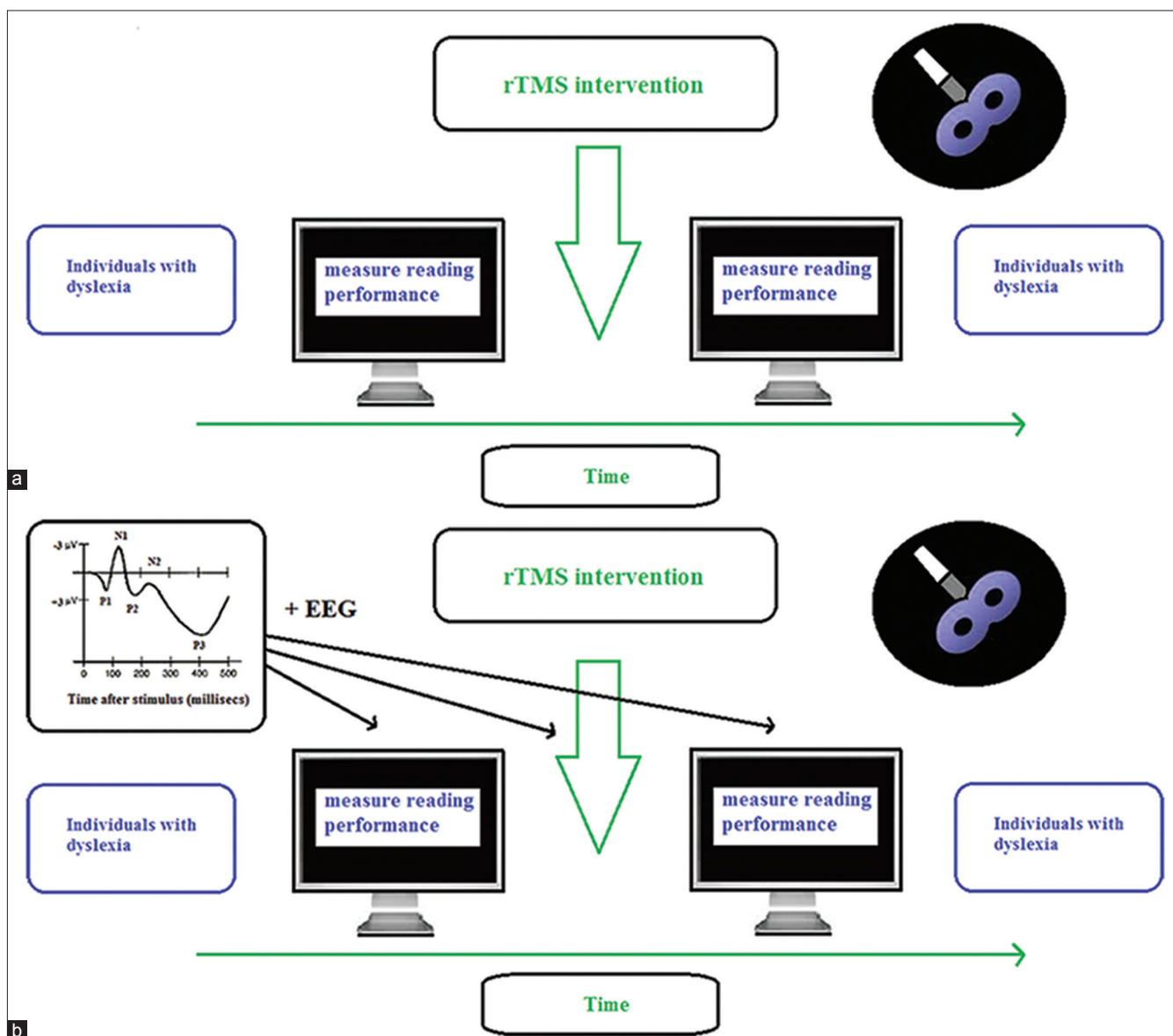


Figure 2: (a) One direction for future research aims to investigate the clinical usefulness of the rapid-rate transcranial magnetic stimulation intervention technique for treating individuals with dyslexia; (b) The second direction for future research aims to investigate the underlying neural working mechanisms (by using simultaneous electroencephalographic and transcranial magnetic stimulation) behind the rapid-rate transcranial magnetic stimulation intervention technique for treating individuals with dyslexia

to several important insights. First, these findings indicated that in individuals with dyslexia, the left superior temporal gyrus, and the left inferior parietal lobule did not have the same role when words, nonwords, and texts were read. Second, an important finding is that not only were left-lateralized improvements found in individuals with dyslexia, as one would expect, but also right inferior parietal lobule involvement, suggesting that additional compensatory recruitment^[57] exists in this area, were found in those individuals. For the first time, these results showed that distinctive facilitation of specific neural pathways (that were previously found to be less active in individuals with dyslexia)^[57] transiently improves the reading of words and texts, which is a fascinating finding, and could have far-reaching implications, for instance, the development of new treatments for dyslexia.^[58]

CONCLUSION

The primary aim of this study was to determine the contributions that TMS has made to different reading modalities. The second goal was to investigate whether TMS might be used as a future intervention technique to overcome reading problems associated with dyslexia. We have seen that rTMS turned out to be a valuable tool for investigating questions related to reading research, both on the word and the sentence-level. Moreover, it can be applied successfully in research on dyslexia. Recently, (high-frequency) rTMS has been used as a “clinical” intervention technique for treating dyslexia by improving the reading performance by exciting underactive reading pathways in the brain. This seems to be a very promising direction for developing new and better treatments for dyslexia [Figure 2a], as long as the safety of the individuals with dyslexia can be guaranteed and strict guidelines on brain stimulation are followed.^[60,61]

Moreover, a new development, the combination of brain stimulation by TMS with simultaneous electroencephalographic (EEG) imaging,^[62,63] offers new prospects for research on reading and dyslexia. The integration of TMS with EEG is able to give information on the causal link between brain activity and its underlying function and cortical reactivity and its connection with other areas in the brain. More importantly, it also gives a better time window on when particular neural actions occur in the brain.^[63] Therefore, this integration of TMS with EEG will give important additional neural information on reading abnormalities in individuals with dyslexia, as well as on the efficiencies and the underlying working mechanisms of future TMS dyslexia treatments [Figure 2b].

ACKNOWLEDGMENTS

We thank Prof. Jenny Thomson, Harvard Graduate School of Education, Cambridge, MA, USA, for vivid discussions on dyslexia that eventually resulted in the writing of the present review paper. Moreover, we thank Dr. Heike Staudte from the LVR-Klinik Bedburg-Hau, Kleve, Germany, for her insights regarding the possible clinical applications of high-frequency rTMS in individuals with dyslexia.

REFERENCES

1. Bolognini N, Pascual-Leone A, Fregni F. Using non-invasive brain stimulation to augment motor training-induced plasticity. *J Neuroeng Rehabil* 2009;6:8.
2. Devlin JT, Watkins KE. Stimulating language: insights from TMS. *Brain* 2007;130:610-22.
3. Jahanshahi M, Rothwell J. Transcranial magnetic stimulation studies of cognition: an emerging field. *Exp Brain Res* 2000;131:1-9.
4. Pascual-Leone A, Walsh V, Rothwell J. Transcranial magnetic stimulation in cognitive neuroscience-virtual lesion, chronometry, and functional connectivity. *Curr Opin Neurobiol* 2000;10:232-7.
5. Barker AT, Jalinous R, Freeston IL. Non-invasive magnetic stimulation of human motor cortex. *Lancet* 1985;1:1106-7.
6. Barker AT, Freestone IL, Jalinous R, Merton PA, Morton HB. Magnetic stimulation of the human brain. *J Physiol* 1985;369:3P.
7. Pascual-Leone A, Bartres-Faz D, Keenan JP. Transcranial magnetic stimulation: studying the brain-behaviour relationship by induction of ‘virtual lesions’. *Philos Trans R Soc Lond B Biol Sci* 1999;354:1229-38.
8. McCann UD, Kimbrell TA, Morgan CM, Anderson T, Geraci M, Benson BE, Wassermann EM, Willis MW, Post RM. Repetitive transcranial magnetic stimulation for posttraumatic stress disorder. *Arch Gen Psychiatry* 1998;55:276-9.
9. Pascual-Leone A, Valls-Solé J, Wassermann EM, Hallett M. Responses to rapid-rate transcranial magnetic stimulation of the human motor cortex. *Brain* 1994;117:847-58.
10. Pascual-Leone A, Rubio B, Pallardó F, Catalá MD. Rapid-rate transcranial magnetic stimulation of left dorsolateral prefrontal cortex in drug-resistant depression. *Lancet* 1996;348:233-7.
11. Zimerman M, Hummel FC. Non-invasive brain stimulation: enhancing motor and cognitive functions in healthy old subjects. *Front Aging Neurosci* 2010;2:149.
12. Freitas C, Farzan F, Pascual-Leone A. Assessing brain plasticity across the lifespan with transcranial magnetic stimulation: why, how, and what is the ultimate goal? *Front Neurosci* 2013;7:42.
13. Hamada M, Ugawa Y, Tsuji S; Effectiveness of rTMS on Parkinson’s Disease Study Group, Japan. High-frequency rTMS over the supplementary motor area improves bradykinesia in Parkinson’s disease: subanalysis of double-blind sham-controlled study. *J Neurol Sci* 2009;287:143-6.
14. Pascual-Leone A, Gates JR, Dhuna A. Induction of speech arrest and counting errors with rapid-rate transcranial magnetic stimulation. *Neurology* 1991;41:697-702.
15. Wada J, Rasmussen T. Intracarotid injection of sodium amytal for the lateralization of cerebral speech dominance: experimental and clinical observations. *J Neurosurg* 1960;17:266-82.
16. Loddenkemper T, Morris HH, Möddel G. Complications during the Wada test. *Epilepsy Behav* 2008;13:551-3.
17. Rösler J, Niraula B, Strack V, Zdunczyk A, Schilt S, Savolainen P, Lioumis P, Makela J, Vajkoczy P, Frey D, Picht T. Language mapping in healthy volunteers and brain tumor patients with a novel navigated TMS system: evidence of tumor-induced plasticity. *Clin Neurophysiol* 2014;125:526-36.
18. Epstein CM. Transcranial magnetic stimulation: language function. *J Clin Neurophysiol* 1998;15:325-32.

19. Broca P. New observation of aphemia caused by a lesion of the posterior half of the second and third left frontal convolutions. *Bull Soc Anat Paris* 1861;6:398-407.
20. Wernicke C. *Der aphasische Symptomenkomplex*. Breslau: Cohn and Weigert; 1874.
21. Mugnaini D, Lassi S, La Malfa G, Albertini G. Internalizing correlates of dyslexia. *World J Pediatr* 2009;5:255-64.
22. Cogo-Moreira H, Andriolo RB, Yazigi L, Ploubidis GB, Brandão de Ávila CR, Mari JJ. Music education for improving reading skills in children and adolescents with dyslexia. *Cochrane Database Syst Rev* 2012;8:CD009133.
23. Lopes J. Biologising reading problems: the specific case of dyslexia. *Contemp Soc Sci* 2012;7:215-29.
24. de Beer J, Engels J, Heerkens Y, van der Klink J. Factors influencing work participation of adults with developmental dyslexia: a systematic review. *BMC Public Health* 2014;14:77.
25. Young AW. Methodological and theoretical bases of visual hemifield studies. In: Beaumont JG, editor. *Divided Visual Field Studies of Cerebral Organization*. London: Academic Press; 1982.
26. Ellis AW, Young AW, Anderson C. Modes of word recognition in the left and right cerebral hemispheres. *Brain Lang* 1988;35:254-73.
27. Skarratt PA, Lavidor M. Magnetic stimulation of the left visual cortex impairs expert word recognition. *J Cogn Neurosci* 2006;18:1749-58.
28. Ellis AW, Brooks J, Lavidor M. Evaluating a split fovea model of visual word recognition: effects of case alternation in the two visual fields and in the left and right halves of words presented at the fovea. *Neuropsychologia* 2005;43:1128-37.
29. Lavidor M, Hayes A, Shillcock R, Ellis AW. Evaluating a split processing model of visual word recognition: effects of orthographic neighborhood size. *Brain Lang* 2004;88:312-20.
30. Ellis AW, Brysbaert M. Split fovea theory and the role of the two cerebral hemispheres in reading: a review of the evidence. *Neuropsychologia* 2010;48:353-65.
31. Brysbaert M. The importance of interhemispheric transfer for foveal vision: a factor that has been overlooked in theories of visual word recognition and object perception. *Brain Lang* 2004;88:259-67.
32. Hsiao JH, Shillcock R, Lavidor M. A TMS examination of semantic radical combinability effects in Chinese character recognition. *Brain Res* 2006;1078:159-67.
33. Stoeckel C, Gough PM, Watkins KE, Devlin JT. Supramarginal gyrus involvement in visual word recognition. *Cortex* 2009;45:1091-6.
34. Price CJ, Moore CJ, Humphreys GW, Wise RJ. Segregating semantic from phonological processes during reading. *J Cogn Neurosci* 1997;9:727-33.
35. Nakamura K, Hara N, Kouider S, Takayama Y, Hanajima R, Sakai K, Ugawa Y. Task-guided selection of the dual neural pathways for reading. *Neuron* 2006;52:557-64.
36. Tomasino B, Fink GR, Sparing R, Dafotakis M, Weiss PH. Action verbs and the primary motor cortex: a comparative TMS study of silent reading, frequency judgments, and motor imagery. *Neuropsychologia* 2008;46:1915-26.
37. Hoffman P, Jefferies E, Lambon Ralph MA. Ventrolateral prefrontal cortex plays an executive regulation role in comprehension of abstract words: convergent neuropsychological and repetitive TMS evidence. *J Neurosci* 2010;30:15450-6.
38. Binder JR, Desai RH, Graves WW, Conant LL. Where is the semantic system? A critical review and meta-analysis of 120 functional neuroimaging studies. *Cereb Cortex* 2009;19:2767-96.
39. Manenti R, Cappa SF, Rossini PM, Miniussi C. The role of the prefrontal cortex in sentence comprehension: an rTMS study. *Cortex* 2008;44:337-44.
40. Caplan D, Vijayan S, Kuperberg G, West C, Waters G, Greve D, Dale AM. Vascular responses to syntactic processing: event-related fMRI study of relative clauses. *Hum Brain Mapp* 2002;15:26-38.
41. Hashimoto R, Sakai KL. Specialization in the left prefrontal cortex for sentence comprehension. *Neuron* 2002;35:589-97.
42. Cacciari C, Bolognini N, Senna I, Pellicciari MC, Miniussi C, Papagno C. Literal, fictive and metaphorical motion sentences preserve the motion component of the verb: a TMS study. *Brain Lang* 2011;119:149-57.
43. Scorolli C, Jacquet PO, Binkofski F, Nicoletti R, Tessari A, Borghi AM. Abstract and concrete phrases processing differentially modulates cortico-spinal excitability. *Brain Res* 2012;1488:60-71.
44. Acheson DJ, Hagoort P. Stimulating the brain's language network: syntactic ambiguity resolution after TMS to the inferior frontal gyrus and middle temporal gyrus. *J Cogn Neurosci* 2013;25:1664-77.
45. Goswami U. Sensory theories of developmental dyslexia: three challenges for research. *Nat Rev Neurosci* 2015;16:43-54.
46. Nelson JM, Lindstrom W, Foels PA. Test anxiety among college students with specific reading disability (Dyslexia): nonverbal ability and working memory as predictors. *J Learn Disabil* 2015;48:422-32.
47. Hadzibeganovic T, van den Noort M, Bosch P, Perc M, van Kralingen R, Mondt K, Coltheart M. Cross-linguistic neuroimaging and dyslexia: a critical view. *Cortex* 2010;46:1312-6.
48. Siegel LS. Perspectives on dyslexia. *Paediatr Child Health* 2006;11:581-7.
49. Boets B, Op de Beeck HP, Vandermosten M, Scott SK, Gillebert CR, Mantini D, Bulthe J, Sunaert S, Wouters J, Ghesquiere P. Intact but less accessible phonetic representations in adults with dyslexia. *Science* 2013;342:1251-4.
50. Bruck M. Word-recognition skills of adults with childhood diagnoses of dyslexia. *Dev Psychol* 1990;26:439-54.
51. Shaywitz SE, Fletcher JM, Holahan JM, Schneider AE, Marchione KE, Stuebing KK, Francis DJ, Pugh KR, Shaywitz BA. Persistence of dyslexia: the Connecticut Longitudinal Study at adolescence. *Pediatrics* 1999;104:1351-9.
52. Shaywitz SE. Dyslexia. *N Engl J Med* 1998;338:307-12.
53. Habib M, Giraud K. Dyslexia. *Handb Clin Neurol* 2013;111:229-35.
54. Joly-Pottuz B, Mercier M, Leynaud A, Habib M. Combined auditory and articulatory training improves phonological deficit in children with dyslexia. *Neuropsychol Rehabil* 2008;18:402-29.
55. Coslett HB, Monsul N. Reading with the right hemisphere: evidence from transcranial magnetic stimulation. *Brain Lang* 1994;46:198-211.
56. Frye RE, Rotenberg A, Ousley M, Pascual-Leone A. Transcranial magnetic stimulation in child neurology: current and future directions. *J Child Neurol* 2008;23:79-96.
57. Hoeft F, McCandliss BD, Black JM, Gantman A, Zakerani N, Hulme C, Lyytinen H, Whitfield-Gabrieli S, Glover GH, Reiss AL, Gabrieli JD. Neural systems predicting long-term outcome in dyslexia. *Proc Natl Acad Sci U S A* 2011;108:361-6.
58. Costanzo F, Menghini D, Caltagirone C, Oliveri M, Vicari S. How to improve reading skills in dyslexics: the effect of high frequency rTMS. *Neuropsychologia* 2013;51:2953-9.
59. Costanzo F, Menghini D, Caltagirone C, Oliveri M, Vicari S. High frequency rTMS over the left parietal lobe increases non-word reading accuracy. *Neuropsychologia* 2012;50:2645-51.
60. Gutches A. Plasticity of the aging brain: new directions in cognitive neuroscience. *Science* 2014;346:579-82.
61. van den Noort M, Lim S, Bosch P. Recognizing the risks of brain stimulation. *Science* 2014;346:1307.
62. Thut G, Pascual-Leone A. Integrating TMS with EEG: how and what for? *Brain Topogr* 2010;22:215-8.
63. Miniussi C, Thut G. Combining TMS and EEG offers new prospects in cognitive neuroscience. *Brain Topogr* 2010;22:249-56.

Cite this article as: Noort Mv, Struys E, Bosch P. Transcranial magnetic stimulation research on reading and dyslexia: a new clinical intervention technique for treating dyslexia?. *Neuroimmunol Neuroinflammation* 2015;2(3):145-52.

Source of Support: Nil. **Conflict of Interest:** No.

Received: 05-11-2014; **Accepted:** 23-12-2014