1   **Adaptive plasticity in the healthy reading network investigated through combined**

2   **neurostimulation and neuroimaging**

3   Turker, S.[1], Kuhnke, P.[1,2], Schmid, F. R.[3], Cheung, V. K. M.[4], Zeidler, B.[5], Seidel, K. [1], Eckert,

4   L.[1], & G. Hartwigsen[1]

5   [1] Lise Meitner Research Group 'Cognition and Plasticity', Max Planck Institute for Human

6   Cognitive and Brain Sciences, Leipzig, Germany

7   [2] Wilhelm Wundt Institute for Psychology, University of Leipzig, Germany

8   [3] CBC Center for Brain and Cognition, Universitat Pompeu Fabra, Barcelona

9   [4] Institute of Information Science, Academia Sinica, Taipei, Taiwan

10   [5] Centre for Systematic Musicology, University of Graz, Austria

11   **Abstract (199 words).** The reading network in the human brain comprises several regions,

12   including the left inferior frontal cortex (IFC), ventral occipito-temporal cortex (vOTC) and dorsal

13   temporo-parietal cortex (TPC). The left TPC is crucial for phonological decoding, i.e., for learning

14   and retaining sound-letter mappings. Here, we tested the causal contribution of this area for reading

15   with repetitive transcranial magnetic stimulation (rTMS) and explored the response of the reading

16   network using functional magnetic resonance imaging (fMRI). 28 healthy adult readers overtly

17   read simple and complex words and pseudowords during fMRI after effective or sham TMS over

18   the left TPC. Behaviorally, effective stimulation slowed pseudoword reading. A multivariate

19   pattern analysis showed a shift in activity patterns in the left IFC for pseudoword reading after

20   effective relative to sham TMS. Furthermore, active TMS led to increased effective connectivity

21   from the left vOTC to the left TPC, specifically for pseudoword processing. The observed changes

22   in task-related activity and connectivity suggest compensatory reorganization in the reading

23   network following TMS-induced disruption of the left TPC. Our findings provide first evidence

24   for a causal role of the left TPC for overt pseudoword reading and emphasize the relevance of

25   functional interactions in the healthy reading network for successful pseudoword processing.

26

1. Introduction

Reading is a core feature of human communication and crucial for participating in everyday social life, work and interpersonal communication. Fluent reading is based upon multiple, hierarchically organized processes, including orthographic recognition, orthographic-phonological mapping (i.e., decoding), and semantic access (Xia et al., 2017). Known words, regardless their complexity, are usually automatically accessed as whole word forms in the mental lexicon (so-called sight word reading) (Ehri, 2005). Reading this sentence took you probably only a few seconds although you had to process the pronunciation and meaning of eighteen words consecutively and at a high speed. The single sounds that make up these words were most likely beyond your awareness, i.e., you did not have to look at single letters or decode them for reading the sentence. When reading pseudowords (i.e., words without any meaning), on the other hand, you rely considerably on the single sounds and/or the syllables they occur in. Therefore, reading (complex) pseudowords is more challenging for typical adult readers because it is a non-automatic reading process.

The universal reading network in the human brain supporting these processes comprises three major circuits: (i) the left inferior frontal cortex (IFC), (ii) the left dorsal temporo-parietal cortex (TPC) and (iii) the left ventral occipito-temporal cortex (vOTC) (Pugh et al., 2001; Rueckl et al., 2015). Neuroimaging studies suggest that the left IFC is involved in various processes, including attention and language functions (e.g., phonological output resolution; Taylor et al., 2013). The left TPC, often referred to as the 'decoding' center in the human brain, is responsible for the transformation of orthographic elements into associated phonological codes (Linkersdörfer et al., 2012). The last region, the left vOTC, shows growing sensitivity to print during reading acquisition (Chyl et al., 2021) and optimizes linguistic processing for quick access to familiar words by filtering out meaningless grapheme strings (e.g., pseudowords) (Gagl et al., 2020).

Although non-invasive brain stimulation (NIBS) studies have proliferated over the past two decades, only few studies have applied NIBS to specifically modulate reading-related processes, and practically none have explored the effect of NIBS on overt pseudoword reading (Turker & Hartwigsen, 2021a). Understanding the causal engagement and functional contribution of brain areas to reading, however, is vital to improve our understanding of the healthy reading network. Additionally, it can help uncover and alleviate potential deficits encountered by individuals with dyslexia (see Turker & Hartwigsen, 2021b). Existing NIBS studies with typical

57   readers provide first evidence for causal roles of reading-related regions to different reading

58   subprocesses (see summary in Turker & Hartwigsen, 2021a). For instance, the left anterior and

59   posterior IFC contribute to phonological and semantic aspects of reading, respectively (e.g., Devlin

60   et al., 2003; Gough et al., 2005; Hartwigsen et al., 2010 a,b). Other studies further highlight the

61   left vOTC as critical region for word processing (Duncan et al., 2010) but also confirm its

62   relevance for pseudoword processing (Pattamadilok et al., 2015). Finally, the left TPC was

63   identified as key area for phonological processes related to reading, in line with its expected role

64   as grapheme-phoneme-conversion center (e.g., Costanzo et al., 2012; Liederman et al., 2003).

65   However, existing NIBS studies on pseudoword reading focused on relatively simple bisyllabic

66   pseudowords and included few trials. Moreover, none of the previous studies used neuroimaging

67   to explore the underlying neuronal changes induced by neurostimulation. Consequently, the

68   underlying neural correlates of stimulation-induced modulation of the reading network remain

69   unclear.

70   Likewise, NIBS studies with atypical readers support the causal role of the left TPC to

71   reading, but neglect underlying neural changes and mechanisms (see review by Turker &

72   Hartwigsen, 2021b). Behaviorally, several single- or multiple-session studies with individuals with

73   dyslexia found NIBS-induced improvements in reading performance in low frequency word,

74   pseudoword and text reading after facilitation of the left TPC, or simultaneous inhibition of the

75   right TPC and facilitation of the left TPC (e.g., Costanzo et al., 2016, 2019; Lazzaro et al., 2020,

76   2021). This further supports the critical role of the left TPC for reading processing but leaves open

77   questions regarding potential NIBS-induced changes on the neural level, such as the potential of

78   NIBS to modify the reading network transiently or permanently.

79   What are the neural correlates of the observed NIBS-induced behavioral modulation of

80   reading performance in typical and atypical readers? On the one hand, facilitatory and inhibitory

81   NIBS most likely either in- or decrease functional brain activation in the targeted area, which

82   should in turn map onto changes in behavioral performance (Miniussi et al., 2013). Since

83   individuals with dyslexia across all age groups show less engagement of the left TPC during

84   reading when compared to typical readers (Richlan et al., 2011, 2013; Turker, 2018), it seems

85   likely that inhibitory NIBS should result in a deterioration of reading performance in typical

86   readers, whereas facilitation should help improve reading skills in atypical readers. On the other

3

87 hand, impairing a core node of a network most likely results in significant up- and down-
88 regulations in tightly connected brain regions, both in terms of functional activation and
89 connectivity (Sale et al., 2015). Such potential compensatory mechanisms should occur after
90 disruption of the targeted area, as described in previous combined TMS-fMRI studies in the
91 language network and may be correlated with changes in behavioral performance (see Hartwigsen
92 et al., 2013; Hartwigsen et al., 2017). Indeed, neuroimaging suggests that phonological deficits in
93 children with dyslexia could stem from a disruption of functional connectivity between the three
94 core reading areas (left IFC, vOTC and TPC) (van der Mark et al., 2011; Schurz et al., 2015),
95 highlighting the importance of considering within-network-interaction. In terms of reading, it
96 remains yet to be explored whether NIBS can alter functional activation and connectivity within
97 the reading network, and whether this directly maps onto reading performance.

98   In the present study, we tested: (i) the causal contribution of the left TPC for efficient word
99 and pseudoword reading by inducing a focal perturbation with repetitive transcranial magnetic
100 stimulation (rTMS); and (ii) explore the reading network's response to perturbation in terms of
101 functional activation and connectivity. We hypothesized that the inhibition of the left TPC would
102 lead to an increase in reading times and a decrease in accuracy for simple and complex
103 pseudowords, with a stronger effect on complex pseudowords. Our second hypothesis was that the
104 disruption of the left TPC should lead to an up-regulation of the left IFC and vOTC (i.e., higher
105 activation within these areas and higher functional coupling with the disrupted region), and
106 potentially also the contralateral right TPC (see Hartwigsen & Volz, 2021). This would be in line
107 with our hypotheses that a disruption of the reading circuit requires functional reorganization and
108 compensatory mechanisms to sustain reading. To test these hypotheses, we applied offline
109 effective or sham rTMS to the left TPC of healthy adults who then performed a reading task during
110 functional MRI. Subjects were asked to read aloud easy and complex words and pseudowords (see
111 **Figure 1**). As main findings, we observed that effective rTMS (relative to sham stimulation) led
112 to (1) slower speech onsets for pseudowords, (2) a shift in task-related activation patterns in the
113 left IFC during pseudoword reading, and (3) stronger task-related functional coupling between the
114 left vOTC and the left TPC.

4
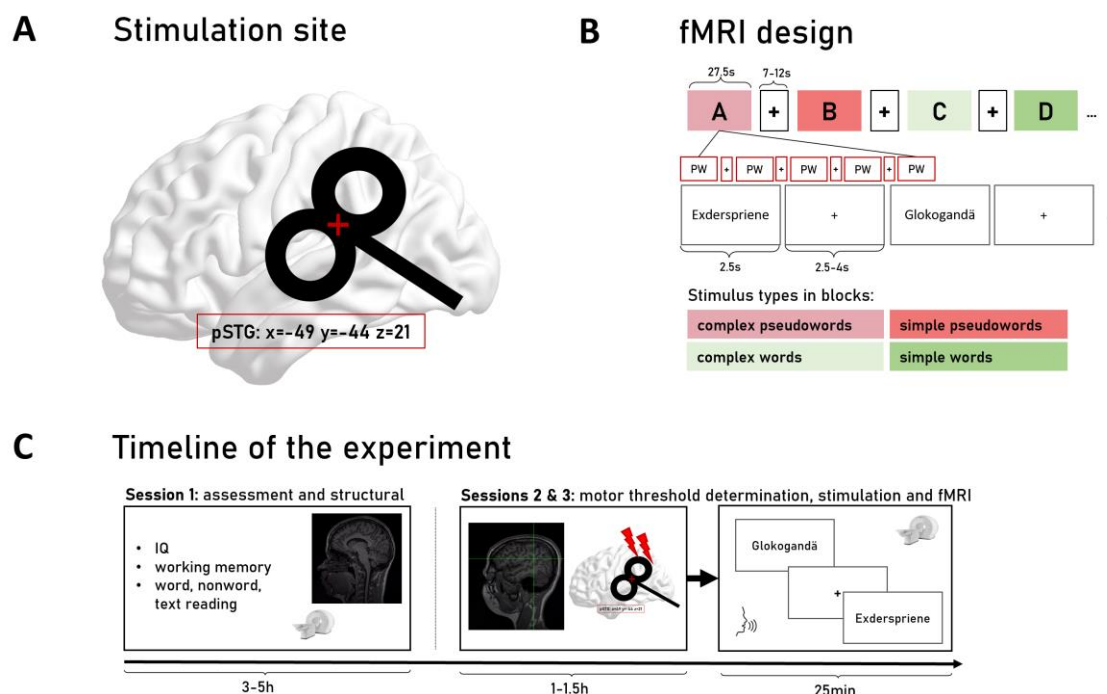
Figure 1 *Details on stimulation site (A), fMRI design (B) and timeline of the experiment (C).* The target was chosen based on previous meta-analyses and was situated in the left pSTG (-49/-44/21). During fMRI, subjects read simple and complex words and pseudowords (200 trials per scanning session; total duration: ~25 minutes).

2. Results

2.1. Behavioral findings

We modelled the speech onset and accuracy of each trial using generalized linear mixed models (Tables 1-3). As fixed effects, the interaction between TMS (effective vs. sham), complexity (simple vs. complex stimuli), and stimulus type (words vs. pseudowords) and lower order terms were included in the model. A maximal random effects structure was used for each model to guard against inflated Type I errors. Results for speech onsets are displayed in **Tables 1 and 2** and visualized in **Figure 2**, results for reading accuracy are provided in **Table 3**.

The model shows that participants generally showed significantly longer speech onset times for pseudowords compared to words and for complex compared to simple stimuli. Likewise, subjects showed lower accuracy for pseudoword as compared to word reading. Significant complexity-by-pseudoword interactions furthermore indicated that these effects were enhanced for complex pseudowords. As for TMS effects, we found a marginally significant TMS-by-

130   pseudoword interaction (p=0.051) for speech onsets (**Table 1**). Step-down analyses (**Table 2**)

131   suggest that the effect was driven by a delay of 13 – 16 ms in pseudoword reading. Interestingly,

132   the TMS effect on pseudowords was significant when the model included random intercepts

133   (p=0.035), but not anymore when we included randoms slopes. This suggests large inter-individual

134   variability in TMS response, which makes effects that generalize to the population hard to detect.

135   We did not find any effect of TMS on reading accuracy (**Table 3**).

136
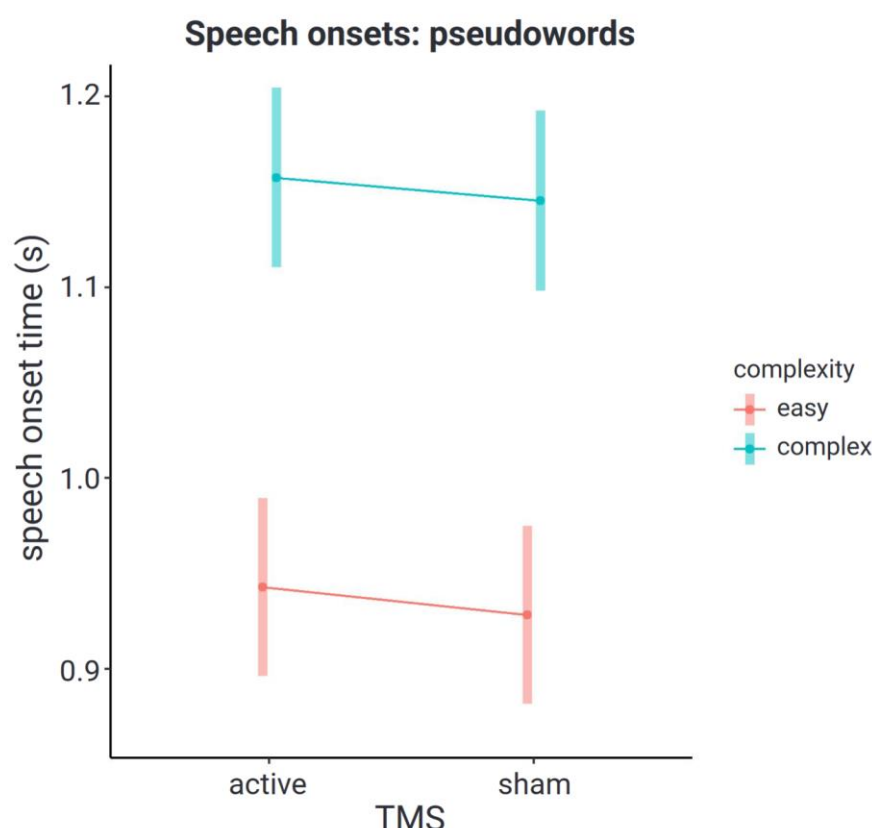
Figure 2 *TMS effect on pseudoword speech onsets* (active stimulation vs. sham stimulation) modelled by word complexity (0 = simple; 1= complex)

137   **Table 1** *Effects of TMS on speech onsets*. Speech onsets of each trial were modelled to follow a
138   Gamma distribution using a generalized linear mixed model. Significance of predictors were
139   assessed using the Wald test. *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$

Predictor	$\chi^2(1)$	p-value
Intercept	1614.6620	$< 2.20 \times 10^{-16}$ ***
TMS	0.0039	0.950
Complexity	64.2319	1.11×10^{-15} ***

6

Pseudoword	148.9187	$< 2.20 \times 10^{-16}$ ***
TMS x Complexity	1.9935	0.158
TMS x Pseudoword	3.7938	0.051
Complexity x Pseudoword	42.2177	8.17×10^{-11} ***
TMS x Complexity x Pseudoword	0.8281	0.363

Table 2 *Marginal effect of TMS (effective – sham) on speech onsets for pseudowords using step-down analysis*. Models with random subject intercepts and with or without random slopes for TMS were fitted. Significance predictors were assessed using the Wald test. *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$

| Condition	Mean TMS effect (ms)	SEM (ms)	z-score	p-value
Without TMS random slope				
Word	8.31	4.61	1.80	0.072
Pseudoword	13.07	6.19	2.11	0.035 *
With TMS random slope				
Word	5.34	16.67	0.32	0.749
Pseudoword	16.25	17.24	0.94	0.346

Table 3 *Effects of TMS on response accuracy*. Correct and incorrect responses of each trial were modelled using a binomial generalized linear mixed model. Significance predictors were assessed using the Wald test. *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$

Predictor	$\chi^2(1)$	p-value
Intercept	128.4377	$< 2.20 \times 10^{-16}$ ***
TMS	0.0020	0.964
Complexity	0.2867	0.592
Pseudoword	18.9644	1.33×10^{-5} ***
TMS x Complexity	0.0034	0.953
TMS x Pseudoword	0.0290	0.865
Complexity x Pseudoword	5.6493	0.017 *
TMS: Complexity x Pseudoword	0.0671	0.796

2.2. Functional activation

To explore differences in reading processing for stimulus type and complexity, we performed within-session univariate whole-brain analyses of the sham condition (see **Figure 3**). Pseudowords (bi- and four-syllabic) activated the left motor cortex, the left IFC, the bilateral posterior parietal cortices and the bilateral vOTC more than words. While activation of the motor cortex is most likely tied to higher articulation demands, the engagement of the other areas seems to be related to

154   higher reading demands as compared to word processing. Words, on the other hand, led to higher

155   activation in brain areas corresponding to the default mode network (DMN) (Smallwood et al.,

156   2021). These include the bilateral angular gyri, middle temporal gyri, middle frontal cortices, and

157   bilateral medial brain regions including the medial prefrontal cortices and the posteromedial

158   cortices. Since sight word reading is an automatized, higher-order cognitive task, it is little

159   surprising that word reading recruits areas of the DMN more strongly than pseudoword reading.

160   Especially since word reading is reliant upon lexical retrieval and semantic access, which are

161   known to depend on processing in the left angular gyrus and the left middle temporal cortex to left

162   anterior temporal lobe. Recently, the role of the posterior parietal cortex for reading was confirmed

163   in a few NIBS studies (Turker & Hartwigsen, 2021a for review). A stronger engagement of the

164   visual word form area and its homologue for pseudoword processing, on the other hand, have not

165   been explicitly discussed in research to date. Regarding complexity, we find primarily higher

166   activation for complex stimuli in the bilateral motor cortices, the bilateral superior temporal gyri

167   and areas within the posterior parietal cortex and occipital lobes.
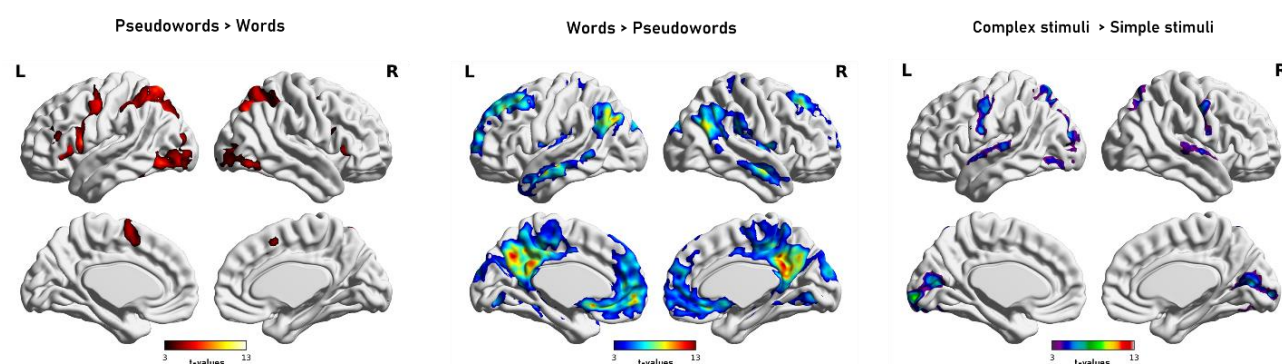
Figure 3 *Univariate contrast maps*. Results show functional brain activation differences due to stimulus type (pseudowords vs. words) and complexity ((complex pseudowords + complex words) > (simple pseudowords + simple words)) corrected at p<0.001 voxel-level and FWE-cluster-corrected at p<0.05.

168   Regarding TMS effects, univariate whole-brain analyses showed no significant differences

169   in brain activation when comparing effective and sham TMS, not even for complex pseudowords

170   that have the highest decoding demand. To better understand this, we performed an exploratory

171   subject-specific analysis with individual subject maps thresholded at p<.001 (uncorrected) (**Figure

172   4**). Supporting our observation of large inter-individual variability in behavioral response to TMS,

173   participants also showed large differences in univariate brain activation involving up- and down-

174   regulation of the bilateral motor cortices and the occipital lobe bilaterally following effective TMS.

175   It is particularly striking that the increased and decreased activation in response to effective TMS

176   comprises largely overlapping areas in these regions. In other words, some individuals responded

177   with more and others with less activation in the bilateral motor areas, portions of the superior

178   temporal gyrus, and occipital areas in response to effective TMS as compared to sham TMS. These

179   preliminary analyses show that neural responses to TMS differ considerably between individuals,

180   which might explain the lack of group-level differences.

181
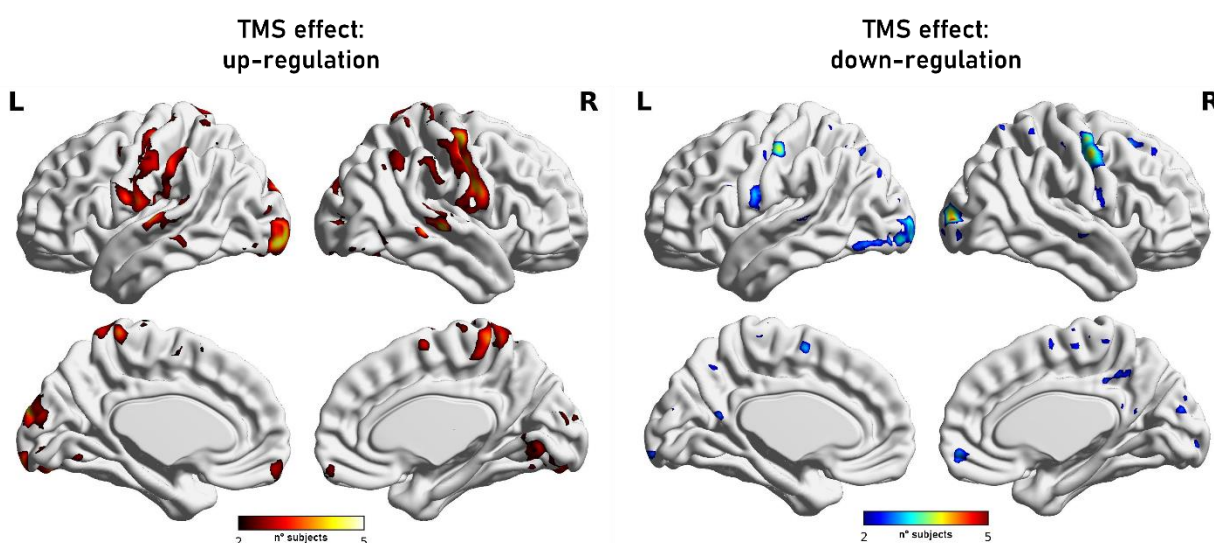
Figure 4. *Exploratory individual subject maps of functional activation in response to effective TMS as compared to sham.* Results on the left side show an up-regulation, i.e., a higher activation in brain areas after effective stimulation. Results on the right side show areas that responded to effective TMS with a down-regulation, i.e., with less brain activation. ($p<0.001$ uncorrected at the voxel level thresholded at 2 subjects; colour indicates number of subjects showing increase/decrease in the same voxel).

182   Since univariate analyses are often claimed to be insensitive to fine-grained differences in

183   multi-voxel activity patterns we additionally performed a multivariate pattern analysis (MVPA) to

184   investigate the effect of TMS on functional activation patterns within the core reading areas.

185   Specifically, we used a spherical 5-mm "searchlight" across the whole brain, and at each

186   searchlight location, we trained a machine learning classifier to decode between effective and sham

187   TMS across participants, separately for words and pseudowords. We found above-chance

188   between-subject decoding in the left posterior IFC selectively for pseudowords (**Figure 5**) (see a

189   discussion on the role of the left mid to posterior IFC for pseudoword processing in Turker &

190   Hartwigsen, 2021b). No effects were observed for word processing, supporting our hypothesis that

191   effective stimulation of the left TPC primarily influences pseudoword processing. These findings

192   indicate that effective TMS over the left TPC altered fine-grained multi-voxel activity patterns for

193   pseudoword reading in the left IFG (pars triangularis) by resulting in a shift of the task-related

194   activity pattern in that area.

195
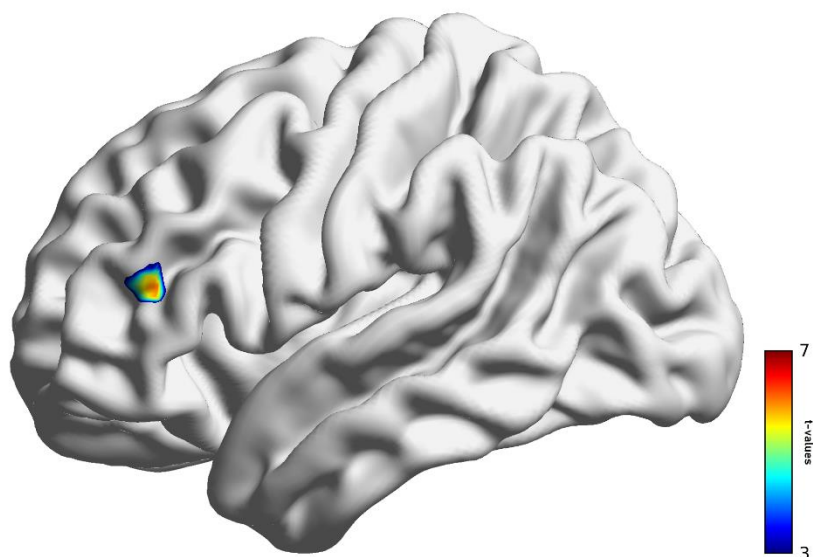
Figure 5 *Results for between-subject searchlight MVPA.* Following effective stimulation of the left TPC as compared to sham stimulation, we find a shift in functional activation patterns in the left IFC selectively for pseudoword reading. Activity patterns comprised beta estimates for each mini-block (see **Figure 1**) of every participant.

196   **2.3. Effective connectivity**

197   Finally, we performed Dynamic Causal Modeling (DCM) to map TMS-induced changes in

198   effective connectivity within the reading network. The DCM model included the core reading areas

199   (the left IFC, the left vOTC and the left TPC) that represent core nodes of the reading network that

200   were also active for pseudoword and word reading, independent of TMS. We performed a DCM

201   group analysis using Bayesian Model Reduction (Friston et al., 2016; Zeidman et al., 2019 a,b).

202   To this end, we first defined a 'full' DCM model for each subject. According to this model, all

203   three areas were bidirectionally connected, words and pseudowords could serve as driving inputs

10

204   to every region, and each between-region connection could be modulated by effective and sham

205   TMS. Bayesian Model Reduction then compared this full model to numerous reduced models.

206   Finally, we computed the Bayesian model average, which is the average of parameter values across

207   models weighted by each model's probability, and thresholded the BMA at 99% parameter

208   probability (see **Figure 6**).
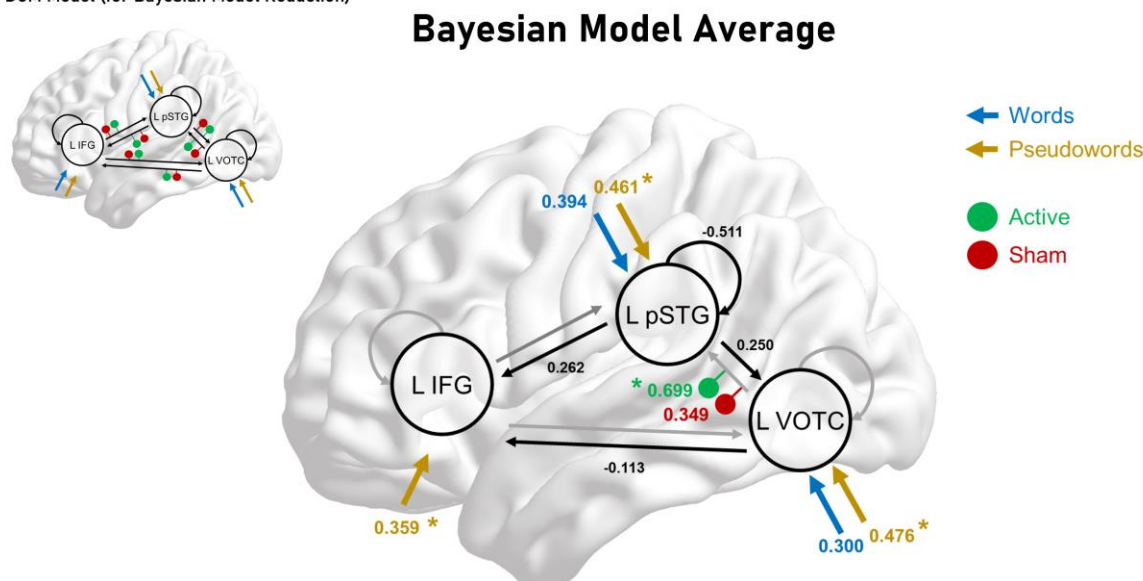
209
210   **Figure 6** *Dynamic causal modeling results.* *Left: The "full" DCM model that served as starting
211   point for Bayesian model reduction. Black arrows represent intrinsic connections, coloured arrows
212   denote driving inputs, and coloured dots represent modulatory inputs. Right:
213   The resulting Bayesian Model Average thresholded at 99% parameter probability. Driving and
214   between-region parameters are in units of Hz. Modulatory parameters in- or decrease connections
215   in an additive manner. *: Significantly stronger modulation than other parameters (/Pp /> 0.99).
216
217   We found strong evidence for intrinsic connectivity within all three areas and pseudowords

218   drove all three regions more strongly than words (Bayesian contrasts for TPC: *Pp*=0.999; IFG:

219   *Pp*=1.0; vOTC: *Pp*=1.0). Crucially, effective connectivity from the left vOTC to the left TPC was

220   significantly increased by effective TMS over the left TPC (modulation: 0.699; result: 0.464 Hz).

221   This modulation was much stronger for effective than for sham TMS (modulation: 0.349; result:

222   0.113 Hz; Bayesian contrast between active and sham TMS: *Pp*=1.0). In other words, a disruption

223   of the left TPC resulted in a stronger facilitatory drive from the left vOTC to the left TPC, which

224   can be interpreted as a compensatory mechanism (see Discussion).

3. Discussion

11

The role of the left TPC for pseudoword reading

In our present study, we explored whether the left TPC, a critical region for acquiring and establishing sound-letter mappings, is causally involved in pseudoword processing in adult readers. In other words, we tested if the typically reading brain still relies on this brain region when confronted with a task that requires access to singles sounds and syllables. Our findings show that a disruption of the left TPC impacts pseudoword processing. An inhibition of this area with TMS led to an increase of speech onsets for pseudowords. These behavioral changes were underpinned by a modulation of task-related activity and connectivity in the larger network for reading, likely reflecting compensatory reorganization in the reading network which may have helped to maintain processing. While the absence of a TMS-induced modulation of task-related activation in the stimulated area may be surprising, previous work demonstrated compensatory reorganization in distributed networks after inhibitory TMS for language and other cognitive tasks (see Hartwigsen & Volz, 2021 for review). Moreover, the behavioral relevance of remote changes induced by TMS in the language network has also been shown (Hartwigsen et al., 2017).

Although our findings support earlier TMS studies reporting NIBS-induced deteriorations or improvements in phonological performance (Turker & Hartwigsen, 2021 a, b), our study is the first to provide direct evidence for a significant role of the left TPC for overt simple and complex pseudoword reading. The only comparable previous behavioral TMS study targeting the left TPC (Costanzo et al., 2012) reported an increase in reading accuracy but no differences in speech onsets. While facilitatory TMS effects on task performance are often interpreted as causal evidence for the contribution of the targeted area to a given task, such effects could also reflect the inhibition of task-irrelevant areas that compete for resources (Luber & Lisanby, 2014; see Bergmann & Hartwigsen, 2021 for discussion). The difference in the direction of results in the previous and present study is unclear. We believe that these differences could stem from a more precise neuronavigation in the present study, which may have resulted in targeting a different (sub-)region in our study, more complex stimuli (four instead of two or three syllables), a larger sample size and differences in stimulation parameters (continuous theta burst stimulation/cTBS instead of high-frequency rTMS). One other study tested pseudoword reading following TMS but in this language mapping study by Hauck and colleagues (2015a, b) several regions were targeted but no strong effect of TMS on the TPC could be found for pseudoword reading. Consequently, we here

255   provide first evidence that the left TPC is causally involved in pseudoword processing since

256   inhibitory TMS led to slower pseudoword reading and modulated communication within the

257   reading network.

258   The observed TMS effect confirms neuroimaging findings indicating that the left

259   TPC/inferior parietal cortex is still involved in spelling-sound conversion in adults (Taylor et al.,

260   2013), despite evidence of this area's contribution to various tasks including verbal working

261   memory (Jonides et al., 1998) and executive processing (Binder et al., 2005). However, it also

262   stands a bit in contrast to a meta-analysis on reading processing in child- and adulthood by Martin

263   et al. (2015), who reported a strong engagement of the left TPC in children, but no significant

264   activation in that area across neuroimaging studies with adults. Notably, the disruptive TMS effect

265   of the present study was significant for pseudowords only (although words showed a trend towards

266   delayed speech onsets). This observation may point to the relevance of the left TPC for

267   phonological processing during reading. Alternatively, the stronger effect on pseudoword reading

268   may have resulted from increased task difficulty for pseudoword relative to word reading. The

269   behavioral results further showed a strong interaction between complexity and pseudowords, but

270   this effect did not interact with TMS. Therefore, it is unlikely that the observed effect can

271   selectively be explained by general task complexity.

272   Why would we see differences in speech onsets and not reading times? Even when asked

273   to read written stimuli overtly, we process them before we start actual speech production, that is,

274   as soon as we see them, we process and thus read them (we are unable to "not read" visual stimuli).

275   Therefore, inhibiting an area that is crucial for access to letter-sound knowledge, will more likely

276   impair this inner, 'silent' reading process than the task of speech production, which relies heavily

277   on motor areas (Brown et al., 2005) and does not reflect reading mechanisms per se.

Adaptive plasticity within the reading network

279   The present study is the first study that mapped TMS-induced behavioral changes on reading

280   performance on the neural level with fMRI. Earlier research on language skills more generally

281   suggests that TMS leads to plastic after-effects, such as large-scale changes on the network level

282   affecting both local and remote activity within targeted networks, as well as interactions between

283   other involved networks (Hartwigsen & Volz, 2021). As such, the perturbed brain can flexibly

284   redistribute and functionally reorganize its computational capacities to compensate for the

13

285   disruption of an area or the network. The present study adds first evidence for compensatory
286   mechanisms within the typical reading network in terms of functional brain activation. We did not
287   detect any significant TMS-related differences with univariate measures of brain activation,
288   probably due to the observed strong interindividual variability in response to stimulation, which
289   has already been reported for motor excitability in previous studies (see Hamada et al., 2013).

290   Nevertheless, we found TMS-induced changes in fine-grained multi-voxel activity patterns
291   in the left IFC between effective and sham TMS, selectively for pseudoword (but not for word)
292   reading. In terms of the functional role of the left IFC for reading, theories hold that it is crucial
293   for phonological output resolution and rhyming during reading (Taylor et al., 2013; Brozdowski
294   & Booth, 2021), as well as attention and working memory (Corbetta et al., 2002; Tops & Boksem,
295   2011). With pseudowords having a higher decoding demand and thus requiring more effort,
296   specifically after inhibition of the left TPC, it is likely that differences in response patterns of the
297   left IFC at least partially stem from higher demands on attention, executive functions, and
298   cognitive control. Alternatively, the stronger contribution of left IFC to pseudoword reading after
299   disruption of the left TPC might also reflect a shift in the balance towards another key node for
300   reading, and thus reflect phonological processes per se. This explanation would be in line with
301   previous TMS studies showing flexible redistribution between homologous areas (e.g., Hartwigsen
302   et al., 2013; Jung & Lambon Ralph, 2016) or remote regions from the same specialized subnetwork
303   (Hallam et al., 2016) during different language tasks (e.g., Hartwigsen, 2016). A stronger
304   contribution of the left IFC after disruption of the left TPC likely reflects compensatory attempts
305   in the network which helped to maintain task processing at a high level and may have prevented
306   decreases in task accuracy.

307   Apart from the TMS-induced changes in response patterns, we found a shift in functional
308   coupling between the left vOTC and the left TPC in response to inhibition of the latter. After
309   effective TMS over the left TPC, as compared to sham stimulation, the left vOTC increased its
310   facilitatory drive onto the left TPC. This is particularly interesting since the left vOTC plays a key
311   role in orthographic processing and is vital for reading words and pseudowords (Jobard et al.,
312   2003, Turker & Hartwigsen, 2021a). A functional engagement of this region for pseudoword
313   processing could also be confirmed in the univariate analyses of this study. This observation of the
314   left vOTC exerting a stronger influence on the left TPC during pseudoword processing could be

14

315 interpreted as a compensatory mechanism. As such, functional connectivity between these two

316 areas is most likely vital for successful and efficient decoding, so that a disruption of the left TPC

317 requires an up-regulation of functional coupling to compensate for the increased demand posed by

318 the task. This highlights the importance of considering within-network interactions when exploring

319 TMS-induced effects on the neural level. When considering TMS-induced changes on task-related

320 activity and connectivity, it is important to bear in mind that TMS is not "lesioning" an area and

321 unlikely to completely "silence" processing in the targeted region. Consequently, a shift in the

322 balance between different nodes in the respective network with a stronger contribution of another

323 area may help to maintain processing at a relatively high level, despite the disruption (see

324 Hartwigsen, 2018).

325   Overall, the present study emphasizes the relevance of the three core reading areas for

326 pseudoword reading. It seems that the targeted region, the left TPC, is crucial for pseudoword

327 processing, most likely for the processing of very complex stimuli. However, the reading network

328 in typical adult readers is flexible enough to adapt to the disruption by increasing functional

329 coupling between the left vOTC and the left TPC, and at the same time shifting functional brain

330 activation in the left IFC. Since we still see a slight deterioration in pseudoword reading

331 performance, as hypothesized, neural plasticity seems to be only partially successful at

332 accommodating the induced disruption. This might still explain why the effects were not as large

333 as expected, and only slightly affected response efficiency but not accuracy. The observed small

334 behavioral effects most likely stem from large inter-individual variability in response to TMS. It

335 seems that TMS responses are largely variable between individuals, which makes group-level

336 analyses particularly challenging and explains both the small behavioral effects and the lack of

337 univariate whole-brain activation differences in our study.

338   With respect to the contribution of our data to theoretical reading models, our study can be

339 explained under the framework of two reading models, one being the connectionist framework of

340 reading (Seidenberg et al., 2005), the other the dual-cascaded model of reading (DRC; Coltheart

341 et al., 2001). The findings do not provide evidence for a hierarchical organization of the reading

342 network, but they suggest a constant interaction between reading areas, more in line with

343 connectionist accounts. Furthermore, the findings highlight that decoding recruits the left TPC,

344 which is in line with earlier assumptions that unfamiliar word and pseudoword reading rely upon

15

345   a dorsal reading stream, including recruitment of the vOTC, the left TPC and the left IFC (backed

346   by structural connectivity research, e.g., Cummine et al., 2015). Since we did not observe any

347   effects on word processing, this suggests that words might recruit a different route that does not

348   require the left TPC. However, words could also be too automatized and robustly presented in the

349   semantic lexicon as to respond to a TMS-induced disruption in the left TPC.

350   **4. Conclusion**

351   The present study provides first evidence that the left TPC is causally involved in overt

352   pseudoword reading and confirms adaptive plasticity within the reading network. By combining

353   rTMS with fMRI, we found that effective disruption led to (1) slower reading of pseudowords,

354   manifested as a delay in speech onsets for simple and complex pseudowords, (2) a change in

355   functional activation patterns in the left IFC as revealed by MVPA, and (3) an increase of

356   functional coupling between the left vOTC and the left TPC. The latter two can be interpreted as

357   compensatory mechanisms that show adaptive plasticity in the reading network in response to

358   perturbation.

359   In summary, we report neurophysiological changes in response to TMS at the level of task-

360   related activity and connectivity in addition to generally confirming earlier findings on causal

361   contributions of the left TPC to reading-related phonological processes (e.g., Liederman et al.,

362   2003; Costanzo et al., 2012). Even though we only used a single session intervention in this study,

363   we could still see immediate effects on the behavioral and neural levels. The present findings can

364   guide future studies and suggest new perspectives concerning the treatment of reading disorders,

365   e.g., by designing multiple-session interventions for individuals with reading impairments.

366   Overall, our study advances future experimental and translational applications of TMS in health

367   and disease.

368

369

5. Methods

5.1. Participants

Participants were young, healthy, right-handed adults (N = 28; 13 females; range: 18-40 years, M_{age}=25±4) with no prior history of psychiatric, neurological, hearing, or developmental disorders. All participants had nonverbal intelligence scores within the normal range or above (nonverbal IQ: ≥ 91; CFT 20-R; Weiß, 2019). Sample size was determined based on comparable previous TMS studies (e.g., Kuhnke et al., 2020). Participants were either recruited via the participants database of the Max Planck Institute for Human Cognitive and Brain Sciences Leipzig (MPI CBS), or flyers, posters, and social media. Participation in all sessions was required for the respective participant's data to be included in the study sample. Prior to participation, written informed consent was obtained from each subject. The study was performed according to the guidelines of the Declaration of Helsinki and approved by the local ethics committee of the University of Leipzig.

In accordance with the given governmental regulations and measures regarding the COVID-19 pandemic, participants were not allowed to have been to risk areas two weeks prior to study participation and were required to undergo a SARS-CoV-2 rapid antigen self-test upon arrival provided by the MPI CBS. Further, subjects were requested to sign a form stating that, in case of a positive result of the self-test, participation in the study had to be suspended.

5.2. Experimental procedure and behavioral reading assessment

The present study comprised one 3-hour behavioral testing session and two combined fMRI-TMS sessions (one for each TMS condition). During the behavioral testing session, we assessed nonverbal intelligence, working memory, and reading. However, for the present analysis, we only made sure that participants had normal nonverbal intelligence, reading and working memory. The *Culture Fair Test* (CFT 20-R; Weiß, 2019) was administered to test participants' nonverbal intelligence. Verbal working memory was measured through digit span forward and digit span backward taken from the *Wechsler Adult Intelligence Scale* (WAIS-I; Petermann & Petermann, 2011). Additionally, nonword span (Mottier Test in the ZLT II- Zürcher Lesetest; Petermann & Daseking, 2019) was assessed. The test was terminated if the subject could not repeat 50% of syllables in one trial block. Silent text reading was assessed with the LGVT 5–12+ (Schneider et

17

398   al., 2017), providing speed (number of words read), accuracy (ratio of filled gaps and correct items)

399   and comprehension scores (number of correctly inserted words).

400   The TMS-fMRI sessions were separated by at least 7 days to prevent carry-over effects of

401   TMS, and session order (sham or effective) was counterbalanced across participants. The study

402   employed a 2x2x2 within-subject design with the factors TMS (effective stimulation, sham

403   stimulation), stimulus type (words, pseudowords) and complexity (simple stimuli consisting of

404   two syllables, complex stimuli consisting of four syllables) (for details of the experimental

405   procedure, stimulation site and fMRI design, see **Figure 1**).

5.3. Transcranial magnetic stimulation (TMS)

407   To investigate the causal role of the left TPC for phonological processing, we applied "offline"

408   (i.e, before the task) continuous theta burst stimulation (cTBS). cTBS applies bursts of 3 stimuli

409   at 50 Hz repeated at intervals of 200 ms (5 Hz) for 40 seconds (total: 600 pulses) (Huang et al.,

410   2005). Offline protocols can induce adaptive changes in brain activity and connectivity that outlast

411   the stimulation for up to 60 minutes (Siebner & Rothwell, 2003). Participants underwent one

412   effective and one sham (placebo) session. The sham condition mirrored the effective condition in

413   terms of basic set-up and procedure, but a placebo coil (MCF-P-B65) was used, which features the

414   same mechanical outline and acoustic noise as the effective coil but reduces the magnetic field

415   strength by ~80%.

416   Intensity of the stimulation was set at 90% of the individual resting motor threshold (rMT)

417   The protocol for assessing the resting motor threshold was conducted in accordance with the

418   standardized procedure proposed by Schutter and van Honk (2006). This procedure applies

419   electromyography instead of purely visual observation of muscle twitch. rMT was determined as

420   the lowest stimulation intensity producing at least 5 motor evoked potentials of ≥50 µV in the

421   relaxed first dorsal interosseus muscle of the right hand when single-pulse TMS was applied over

422   the hand region of left primary motor cortex 10 times.

423   The specific MNI coordinates for the left TPC (x=-49, y=-44, z=21) were calculated from

424   three meta-analyses on reading impairments (Maisog et al., 2008; Richlan et al. 2009, 2011). To

425   precisely target these coordinates in each individual participant, they were transformed from MNI

426   to subject space using the *SPM12* software (Wellcome Trust Center for Neuroimaging, University

427   College London, UK). We then used stereotactic neuronavigation (TMS Navigator, Localite

428 GmbH, Sankt Augustin, Germany) to navigate the coil over the target area and maintain its location

429 throughout stimulation. For neuronavigation, participants' heads were co-registered onto their T1-

430 weighted MR image before the stimulation sessions. T1 scans were obtained beforehand with a 3T

431 MRI scanner (Siemens, Erlangen, Germany) using an MPRAGE sequence (176 slices in sagittal

432 orientation; repetition time: 2.3 s; echo time: 2.98 ms; field of view: 256 mm; voxel size: 1 x 1 $\times$

433 1 mm; no slice gap; flip angle: 9°; phase encoding direction: A/P).

5.4. Functional neuroimaging

Stimuli

436 We used an event-related mini-block design that used 400 stimuli altogether (200 simple and

437 complex words; 200 simple and complex pseudowords). In each session, participants read

438 randomly chosen 100 words (50 simple, 50 complex) and 100 pseudowords (50 simple, 50

439 complex) in mini-blocks (5 stimuli presented after another) aloud in the scanner (i.e., stimuli were

440 not repeated in the second session to avoid remembering pseudowords). The 200 simple word

441 stimuli consisted of two syllables and 4-6 letters and were taken from Schuster et al. (2015). As

442 complex words, we chose the first 100 most frequent 4-syllabic words (10-14 letters) from the dlex

443 database (http://www.dlexdb.de/). We excluded compound words and plurals but due to the small

444 number of available complex words we had to include a few 3-syllabic words and plurals (in

445 German the plural is usually constructed by adding a whole syllable). Pseudowords were then

446 designed using Wuggy (http://crr.ugent.be/programs-data/wuggy) based on the simple and

447 complex word lists. We excluded pseudowords that were too similar to real German words (<2

448 letters difference).

Neuroimaging

450 Functional MRI data were collected on a 3T Siemens Magnetom Skyra scanner (Siemens,

451 Erlangen, Germany) with a 32-channel head coil. Blood oxygenation level-dependent (BOLD)

452 images were acquired with a single-echo BOLD EPI sequence (repetition time [TR]: 2s, echo time

453 [TE]: 22ms; flip angle: 80°; field of view [FoV]: 204 mm; voxel size: $2.5 \times 2.5 \times 2.5$ mm;

454 bandwidth: 1794 Hz/Px; phase encoding direction: A/P; acceleration factor: 3). B0 field maps were

455 acquired for susceptibility distortion correction using a spin-echo BOLD EPI sequence (TR:

456 8000ms; TE:50ms; flip angle: 90°; bandwidth: 1794 Hz/Px).

457   During fMRI, stimuli were presented for 2.5 seconds. We jittered the between-stimulus-

458   interval, as well as the between-mini-block-interval. Each block lasted for 27.5 seconds and

459   participants were in the scanner for around 25 minutes (see **Figure 1**). Subjects were instructed to

460   read out all stimuli as fast and correct as they could with as little head movement as possible.

461   Subjects' in-scanner responses were recorded and manually preprocessed with audacity. Speech

462   on- and offsets were determined with Praat by four independent raters, two analyzing each

463   audiofile in 50% of cases. We computed an interrater reliability >0.85 suggesting that

464   determination of speech on- and offsets was very similar between raters. For the following

465   analyses, we averaged speech onsets across raters if they were rated by more than one person.

466   Accuracy for all trials was checked by a third person.

467   **5.5. Data analysis**

468   **5.5.1. Linear Mixed Model**

469   Speech onsets and response accuracy of each trial were analysed with generalised linear mixed

470   models (GLMM) using glmmTMB 1.1.2.3 (Brooks et al., 2017) in R 4.0.5. To circumvent the need

471   to transform reaction times to satisfy normality assumptions, reading times were modelled using a

472   Gamma distribution with the identity link function (Lo & Andrews, 2015). The accuracy of each

473   trial (correct versus incorrect) was modelled as a binary response using a binomial distribution and

474   logit link function. All models included as fixed effects the three-way interaction between TMS

475   (sham/active), Pseudoword (pseudoword/word), and Complexity (simple/complex), and all lower

476   order terms. A maximal random effects structure was used for all models with subject as the

477   grouping variable to avoid inflated Type I errors (Barr et al., 2013). The resulting GLMM for

478   speech onsets included random intercepts, and random slopes for the interaction between TMS,

479   Complexity and Pseudoword, as well as all lower order terms. Likewise, random intercepts and

480   random slopes for TMS and Complexity were included in the GLMM for response accuracy. The

481   significance of each variable was assessed using the Wald test, and marginal effects were

482   calculated using a step-down simple effects analysis.

483   **5.5.2. fMRI analysis**

484   *Preprocessing*

485   MRI preprocessing was performed using *fMRIprep* (version 20.2.1; Esteban et al. 2019).

486   Anatomical T1-weighted images were corrected for intensity non-uniformity (using

487   *N4BiasFieldCorrection* from ANTs 2.3.3), skull-stripped (using *antsBrainExtraction* from ANTs

488   2.3.3), segmented into gray matter, white matter and cerebrospinal fluid (using *fast* in FSL 5.0.9),

489   and normalized to MNI space (MNI152NLin2009cAsym; using *antsRegistration* in ANTs 2.3.3).

490   Brain surfaces were reconstructed using *reconall* (FreeSurfer 6.0.1).

491   Functional BOLD images were co-registered to the anatomical image (using *bbregister* in

492   FreeSurfer 6.0.1), distortion corrected based on B0-fieldmaps (using *3dQwarp* in AFNI

493   20160207), slice-timing corrected (using *3dTshift* from AFNI 20160207), motion corrected (using

494   *mcflirt* from FSL 5.0.9), normalized to MNI space (via the anatomical-to-MNI transformation),

495   and smoothed with a 5 mm^3 FWHM Gaussian kernel (using *SPM12*; Wellcome Trust Centre for

496   Neuroimaging; http://www.fil.ion.ucl.ac.uk/spm/). Moreover, physiological noise regressors were

497   extracted using the anatomical version of *CompCor* (aCompCor, Behzadi et al., 2007).

Univariate analyses

499   We performed a whole-brain random-effects group analysis based on the general linear model

500   (GLM), using the two-level approach in *SPM12*. At the first level, individual participant data were

501   modeled separately. The participant-level GLM included regressors for the 4 experimental

502   conditions, modelling trials as box car functions (2.5 s duration) convolved with the canonical

503   HRF. Only correct trials were analyzed, error trials were modeled in a separate regressor-of-no-

504   interest. Nuisance regressors included 24 motion regressors (the 6 base motion parameters + 6

505   temporal derivatives of the motion parameters + 12 quadratic terms of the motion parameters and

506   their temporal derivatives), individual regressors for time points with strong volume-to-volume

507   movement (framewise displacement > 0.9; Siegel et al. 2014), and the top 10 aCompCor regressors

508   explaining the most variance in physiological noise. The data were subjected to an AR(1) auto-

509   correlation model to account for temporal auto-correlations, and high-pass filtered (cutoff 128 s)

510   to remove low-frequency noise.

511   Contrast images for each participant were computed at the first level. At the second level,

512   these contrast images were submitted to one-sample or paired t-tests (to test for interactions). For

513   all second-level analyses, a gray matter mask was applied, restricting statistical tests to voxels with

514   a gray matter probability > 0.1 (MNI152NLin2009cAsym gray matter template in *fMRIprep*). All

515   activation maps were thresholded at a voxel-wise $p < 0.001$ and a cluster-wise $p < 0.05$ FWE-
516   corrected.

Multivariate pattern analysis (MVPA)

518   As univariate analyses are insensitive to information represented in fine-grained, multi-voxel
519   activation patterns (Haxby et al., 2014), we additionally performed a multivariate pattern analysis
520   (MVPA) using *The Decoding Toolbox* (Hebart et al., 2015) implemented in *Matlab* (version
521   2021a). Our MVPA aimed to test whether effective TMS over TPC, as compared to sham TMS,
522   modulated activity patterns in the stimulated or other, remote brain regions. We employed
523   searchlight MVPA, moving a spherical region-of-interest (or "searchlight") of 5 mm radius
524   through the entire brain (Kriegeskorte et al., 2006). At each searchlight location, a machine-
525   learning classifier (an L2-norm support vector machine; C=1) aimed to decode between effective
526   and sham TMS, separately for words and pseudowords. We used leave-one-*participant*-out cross
527   validation (CV), training on the activation patterns from n-1 participants and testing on the left-
528   out participant (yielding 28 CV-folds). For statistical inference, we performed a permutation test
529   across the accuracy-minus-chance maps of the different CV-folds (using *SnPM13*; as proposed by
530   Wang et al., 2021), thresholded at a voxel-wise $p < 0.001$ and a cluster-wise $p < 0.05$ FWE-
531   corrected (as in our univariate analyses). Activity patterns comprised beta estimates for each mini-
532   block of every participant.

Dynamic Causal Modelling (DCM)

534   Finally, we performed dynamic causal modelling (DCM; Friston et al., 2003) to investigate TMS-
535   induced changes in effective connectivity (i.e., directed causal influences) between the core nodes
536   of the reading network. DCM estimates a model of effective connectivity between brain regions
537   to predict a neuroimaging time series. A DCM consists of three types of parameters: 1) "intrinsic"
538   (i.e., condition-independent) directed connections between brain regions, 2) "modulatory inputs"
539   that change connection strengths during a certain experimental manipulation, and 3) "driving
540   inputs" that drive activity in the network. The goal of DCM is to optimize a tradeoff between
541   model fit (of the predicted to observed time series) and complexity (i.e., deviation of model
542   parameters from their prior expectations), measured by the model evidence (Kahan & Foltynie,
543   2013; Zeidman et al., 2019a).

22

544   We performed a two-level analysis using Parametric Empirical Bayes (PEB) and Bayesian

545   Model Reduction (BMR)—the current "standard practice for group DCM studies" (Friston et al.,

546   2016). At the first level, a "full model" was specified and estimated for each participant (see

547   Results section). Regions included in the model were the left TPC (the stimulated region), left

548   vOTC, and left IFG. The three regions were defined functionally in each individual participant as

549   the top 10% most activated voxels for [all sham trials > rest] within 20 mm spheres around the

550   MNI peak coordinates in a meta-analysis of reading in adults (Martin et al., 2015): left TPC = -49

551   -44 21; left IFG = -52 20 18; left vOTC = -42 -68 -22. All regions were restricted to the cerebral

552   gray matter. The first eigenvariate of the BOLD time series of each region was extracted and

553   adjusted for effects-of-interest (all experimental conditions) using our participant-level GLM (see

554   Univariate analyses). DCM inputs were mean-centered, so that the intrinsic connections reflected

555   the mean connectivity across experimental conditions (Zeidman et al., 2019a).

556   At the second level, DCM parameters of individual participants were entered into a GLM—

557   the PEB model—that decomposed interindividual variability in connection strengths into group

558   effects and random effects (Zeidman et al., 2019b). BMR then compared the full model against

559   numerous reduced models that had certain parameters "switched off" (i.e., prior mean and variance

560   set to 0) (Friston et al., 2016). Finally, we computed the Bayesian model average (BMA), the

561   average of parameter values across models weighted by each model's posterior probability (Pp)

562   (Penny et al., 2007). This approach is preferred over exclusively assessing the parameters of the

563   "best" model as it accommodates uncertainty about the true underlying model (Friston et al., 2016;

564   Dijkstra et al., 2017). The BMA was thresholded to only retain parameters with a Pp > 99% (cf.

565   Zeidman et al., 2019b; Kuhnke et al., 2021). For each modulatory input, we calculated the resulting

566   connectivity value (in Hz) using formula 3 in Zeidman et al. (2019a). Finally, to determine whether

567   one experimental condition modulated a certain connection more strongly than another, we directly

568   compared different parameters on the same connection using Bayesian contrasts (Dijkstra et al.,

569   2017; Kuhnke et al., 2021).

570   **6. Acknowledgements**

572   **7. Competing interests**

573 The authors declare no competing financial or nonfinancial interests.

574 **8. Bibliography**

575 Barr, D. & Levy, R., Scheepers, C. & Tily, H. J. (2013). Random effects structure for confirmatory

576 hypothesis testing: Keep it maximal. *Journal of Memory and Language, 68*(3). 255-278.

577 https://doi.org/10.1016/j.jml.2012.11.001

578 Bergmann TO, Hartwigsen G. Inferring Causality from Noninvasive Brain Stimulation in

579 Cognitive Neuroscience. *Journal of Cognitive Neuroscience* 33(2), 195-225. doi:

580 10.1162/jocn_a_01591.

581 Binder, J. R., Westbury, C. F., McKiernan, K. A., Possing, E. T. & Medler, D. A. (2005). Distinct

582 brain systems for processing concrete and abstract concepts. *Journal of Cognitive*

583 *Neuroscience, 17*(6), 905-917. 10.1162/0898929054021102

584 Brooks, M. E., Kristensen, K., van Benthem, K. J., Magnusson, A., Berg, C. W., Nielsen, A.,

585 Skaug, H. J., Maechler, M. & Bolker, B. M. (2017). GlmmTMB balances speed and

586 flexibility among packages for zero-inflated generalized linear mixed modeling. *The R*

587 *Journal*, 9(2), 378–400. https://doi.org/10.32614/RJ-2017-066

588 Brown, S., Ingham, R. J., Ingham, J. C., Laird, A. R., & Fox, P. T. (2005). Stuttered and fluent

589 speech production: An ALE meta-analysis of functional neuroimaging studies. *Human*

590 *Brain Mapping, 25*(1), 105–117. https://doi.org/10.1002/hbm.20140

591 Brozdowski, C. & Booth, J. (2021). Reading skill correlates in frontal cortex during semantic and

592 phonological processing. *PsyArXiv.* 10.31234/osf.io/d3mj7

593 Behzadi, Y., Restom, K., Liau, J., & Liu, T. T. (2007). A component based noise correction method

594 (CompCor) for BOLD and perfusion based fMRI. *NeuroImage, 37*(1), 90–101.

595 https://doi.org/10.1016/j.neuroimage.2007.04.042

596 Chyl, K., Fraga González, G., Brem, S. & Jednoróg, K. (2021). Brain dynamics of (a)typical

597 reading development: A review of longitudinal studies. *npj Science of Learning,*

598 *6*(1), 1-9. https://doi.org/10.1038/s41539-020-00081-5

599 Coltheart, M., Rastle, K., Perry, C., Langdon, R., & Ziegler, J. (2001). DRC: A dual route cascaded

600 model of visual word recognition and reading aloud. *Psychological Review, 108*(1),

601 204- 256. https://doi.org/10.1037/0033-295X.108.1.fpeter204

602   Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in
603   the brain. *Nature reviews Neuroscience, 3*(3), 201–215. https://doi.org/10.1038/nrn755

604   Costanzo, F., Menghini, D., Caltagirone, C. & Oliveri, M. (2012). High frequency rTMS over the
605   left parietal lobule increases non-word reading accuracy. *Neuropsychologia,*
606   *50*(11), 2645- 2651. https://doi.org/10.1016/j.neuropsychologia.2012.07.017

607   Costanzo, F., Varuzza, C., Rossi, S., Sdoia, S., Varvara, P., Oliveri, M., Giacomo, K., VIcari, S.
608   & Menghini, D. (2016). Evidence for reading improvement following tDCS treatment in
609   children and adolescents with dyslexia. *Restorative Neurology and Neuroscience, 34*(2),
610   215–226. 10.3233/RNN-150561

611   Costanzo, F., Rossi, S., Varuzza, C., Varvara, P., Vicari, S. & Menghini, D. (2019). Long-lasting
612   improvement following tDCS treatment combined with a training for reading in children
613   and adolescents with dyslexia. *Neuropsychologia, 130*, 38–43.
614   https://doi.org/10.1016/j.neuropsychologia.2018.03.016

615   Cummine, J., Dai, W., Borowsky, R., Gould, L., Rollans, C., & Boliek, C. (2015). Investigating
616   the ventral-lexical, dorsal-sublexical model of basic reading processes using diffusion
617   tensor imaging. *Brain Structure and Function*, *220*(1), 445-455.
618   https://doi.org/10.1007/s00429-013-0666-8

619   Devlin, J. T., Matthews, P. M. & Rushworth, M. F. (2003). Semantic
620   processing in the left inferior prefrontal cortex: A combined
621   functional magnetic resonance imaging and transcranial
622   magnetic stimulation study. *Journal of Cognitive Neuroscience, 15*(1), 71–84.
623   https://doi.org/10.1162/089892903321107837

624   Dijkstra, N., Zeidman, P., Ondobaka, S., van Gerven, M., & Friston, K. (2017). Distinct top-down
625   and bottom-up brain connectivity during visual perception and imagery. *Scientific*
626   *Reports, 7*(1), Article 5677. https://doi.org/10.1038/s41598-017-05888-8

627   Duncan, K. J., Pattamadilok, C., & Devlin, J. T. (2010). Investigating occipito-temporal
628   contributions to reading with TMS. *Journal of Cognitive Neuroscience, 22*(4), 739–750.
629   https://doi.org/10.1162/jocn.2009.21207

630   Ehri, L. C. (2005). Development of Sight Word Reading: Phases and Findings. In M. J. Snowling
631   & C. Hulme (Eds.), *The science of reading: A handbook* (pp. 135–154). Blackwell
632   Publishing. https://doi.org/10.1002/9780470757642.ch8

633   Esteban, O., Markiewicz, C. J., Blair, R. W., Moodie, C. A., Isik, A. I., Erramuzpe, A., Kent, J.
634   D., Goncalves, M., DuPre, E., Snyder, M., Oya, H., Ghosh, S. S., Wright, J., Durnez, J.,
635   Poldrack, R. A., & Gorgolewski, K. J. (2019). fMRIPrep: A robust preprocessing pipeline
636   for functional MRI. *Nature methods*, *16*(1), 111–116. https://doi.org/10.1038/s41592-018-
637   0235-4

638   Friston, K. J., Harrison, L., & Penny, W. (2003). Dynamic causal modelling. *NeuroImage, 19*(4),
639   1273–1302. https://doi.org/10.1016/s1053-8119(03)00202-7

640   Friston, K., Brown, H. R., Siemerkus, J., & Stephan, K. E. (2016). The dysconnection
641   hypothesis. *Schizophrenia   Research,   176*(2-3),   83–
642   94. https://doi.org/10.1016/j.schres.2016.07.014

643   Gagl, B., Sassenhagen, J., Haan, S., Gregorova, K., Richlan, F., & Fiebach, C. J. (2020). An
644   orthographic   prediction   error   as   the   basis   for   efficient   visual   word
645   recognition. *NeuroImage, 214*,   116727.
646   https://doi.org/10.1016/j.neuroimage.2020.116727

647   Gough, P. M., Nobre, A. C. & Devlin, J. T. (2005). Dissociating linguistic processes in the left
648   inferior frontal cortex with transcranial magnetic stimulation. *Journal of Neuroscience*
649   *25*(35), 8010–8016. https://doi.org/10.1523/JNEUROSCI.2307-05.2005

650   Hallam, G. P., Whitney, C.; Hymers, M., Gouws, A. D. & Jefferies, E. (2016). Charting the effects
651   of TMS with fMRI: Modulation of cortical recruitment within the distributed network
652   supporting   semantic   control.   *Neuropsychologia,   93*,   40-52.
653   https://doi.org/10.1016/j.neuropsychologia.2016.09.012

654   Hamada, M., Murase, N., Hasan, A., Balaratnam, M., & Rothwell, J. C. (2013). The role of
655   interneuron networks in driving human motor cortical plasticity. *Cerebral Cortex, 23*(7),
656   1593–1605.   https://doi.org/10.1093/cercor/bhs147

657   Hartwigsen, G. (2016). Adaptive plasticity in the healthy language network: Implications for
658   language   recovery   after   stroke. *Neural   Plasticity, 2016,*   1–18.
659   https://doi.org/10.1155/2016/9674790

660   Hartwigsen G. (2018). Flexible Redistribution in cognitive cetworks. *Trends   in   Cognitive*
661   *Sciences, 22(*8), 687–698. https://doi.org/10.1016/j.tics.2018.05.008

662   Hartwigsen, G., & Volz, L. J. (2021). Probing rapid network reorganization of motor and language
663   functions via neuromodulation and neuroimaging. *NeuroImage, 224*, Article 117449.

664   https://doi.org/10.1016/j.neuroimage.2020.117449

665   Hartwigsen, G., Price, C., Baumgaertner, A., Geiss, G., Koehnke, M., Ulmer, S. & Siebner, H. R.

666   (2010a). The right posterior inferior frontal gyrus contributes to phonological word

667   decisions in the healthy brain: Evidence from dual-site TMS. *Neuropsychologia, 48*(10),

668   3155-3163. https://doi.org/10.1016/j.neuropsychologia.2010.06.032

669   Hartwigsen G, Baumgaertner A, Price, C. J., Koehnke, M., Ulmer, S. & Siebner, H. R. (2010b).

670   Phonological decisions require both the left and right supramarginal gyri. *PNAS, 107*(38),

671   16494–16499.   https://doi.org/10.1073/pnas.1008121107

672   Hartwigsen, G., Saur, D., Price, C. J., Ulmer, S., Baumgaertner, A., & Siebner, H. R. (2013).

673   Perturbation of the left inferior frontal gyrus triggers adaptive plasticity in the right

674   homologous area during speech production. *PNAS, 110*(41), 16402-16407.

675   https://doi.org/10.1073/pnas.1310190110

676   Hartwigsen, G., Bzdok, D., Klein, M., Wawrzyniak, M., Stockert, A., Wrede, K.,Classen, J. &

677   Saur, D. (2017). Rapid short-term reorganization in the language network. *ELife, 6*.

678   10.7554/eLife.25964

679   Hauck, T., Tanigawa, N., Probst, M., Wohlschlaeger, A., Ille, S., Sollmann, N., Maurer, S.,

680   Zimmer, C., Ringel, F., Meyer, B. & Krieg, S. M. (2015a). Stimulation frequency

681   determines the distribution of language positive cortical regions during navigated

682   transcranial magnetic brain stimulation. *BMC Neuroscience, 16*(5), 1-14. 10.1186/s12868-

683   015-0143-9

684   Hauck, T., Tanigawa, N., Probst, M., Wohlschlaeger, A., Ille, S., Sollmann, N., Maurer, S.,

685   Zimmer, C., Ringel, F., Meyer, B. & Krieg, S. M. (2015b). Task type affects location of

686   language: Positive cortical regions by repetitive navigated transcranial magnetic

687   stimulation   mapping.   *PLOS   One,   10*(4),   1-21.

688   https://doi.org/10.1371/journal.pone.0125298

689   Haxby, J. V., Connolly, A. C. & Swaroop Guntupalli, J. (2014). Decoding neural

690   representational spaces using multivariate pattern analysis. *Annual Review of*

691   *Neuroscience, 37*(1), 435-456.   https://doi.org/10.1146/annurev-neuro-062012-170325

692   Hebart, M. N., Görgen, K., & Haynes, J. D. (2015). The Decoding Toolbox (TDT): A versatile

693   software package for multivariate analyses of functional imaging data. *Frontiers in*

694   *Neuroinformatics*, *8*(88). https://doi.org/10.3389/fninf.2014.00088

695   Huang, Y. Z., Edwards, M. J., Rounis, E., Bhatia, K. P., & Rothwell, J. C. (2005). Theta burst
696   stimulation of the human motor cortex. *Neuron, 45*(2), 201-206.
697   https://doi.org/10.1016/j.neuron.2004.12.033

698   Jobard, G., Crivello, F. & Tzourio-Mazoyer, N. (2003). Evaluation of the dual route theory of
699   reading: A metanalysis of 35 neuroimaging studies. *Neuroimage, 20*(2), 693-712.
700   https://doi.org/10.1016/S1053-8119(03)00343-4

701   Jonides, J., Smith, E., Marshuetz, C., Koeppe, R., & Reuter-Lorenz, P. (1998). Inhibition in verbal
702   working memory revealed by brain activity. *PNAS, 95*(14), 8410-8413.
703   https://doi.org/10.1073/pnas.95.14.8410

704   Jung, J. Y. & Lambon Ralph, M. A. (2016). Mapping the dynamic network interactions
705   underpinning cognition: A cTBS-fMRI study of the flexible adaptive neural system for
706   semantics. *Cerebral Cortex, 26*(8), 3580–3590. 10.1093/cercor/bhw149

707   Kahan, J., & Foltynie, T. (2013). Understanding DCM: ten simple rules for the
708   clinician. *NeuroImage, 83*, 542–549. https://doi.org/10.1016/j.neuroimage.2013.07.008

709   Kriegeskorte, N., Goebel, R. & Bandettini, P. (2006). Information-based functional brainmapping.
710   *PNAS, 103*(10), 3863–3868. https://doi.org/10.1073/pnas.0600244103

711   Kuhnke, P., Beaupain, M. C., Cheung, V. K. M., Weise, K., Kiefer, M., & Hartwigsen, G. (2020).
712   Left posterior inferior parietal cortex causally supports the retrieval of action knowledge.
713   *Neuroimage, 219*, Article 117041. https://doi.org/10.1016/j.neuroimage.2020.117041

714   Kuhnke, P., Kiefer, M. & Hartwigsen, G. (2021). Task-Dependent Functional and Effective
715   Connectivity during Conceptual Processing. *Cerebral Cortex, 31*(7), 3475–
716   3493. https://doi.org/10.1093/cercor/bhab026

717   Lazzaro, G., Costanzo, F., Varuzza, C., Rossi, S., Matteis, M. & Menghini, D. (2020). Individual
718   differences modulate the effects of tDCS on reading in children and adolescents with
719   dyslexia. *Scientific Studies of Reading, 25*(6), 470-485.
720   https://doi.org/10.1080/10888438.2020.1842413

721   Lazzaro, G., Bertoni, S., Menghini, D., Costanzo, F., Franceschini, S., Varuzza, C., Ronconi, L.,
722   Battisti, A., Gori, S., Facoetti, A., & Vicari, S. (2021). Beyond reading modulation:
723   Temporo-parietal tdcs alters visuo-spatial attention and motion perception in
724   dyslexia. *Brain Sciences, 11*(2), 1-17. https://doi.org/10.3390/brainsci11020263

725   Liederman, J., McGraw Fischer, J. & Schulz, M. (2003). The role of motion direction selective
726   extrastriate regions in reading: A transcranial magnetic stimulation study. *Brain and*
727   *Language,   85*(1):   140-155.   https://doi.org/10.1016/S0093-934X(02)00550-3

728   Petermann, F. & Daseking, M. (2019). Zürcher Lesetest – II: Weiterentwicklung des Zürcher
729   Lesetests (ZLT) von Maria Linder und Hans Grissemann. Göttingen, Germany: Hogrefe.

730   Linkersdörfer, J., Lonnemann, J., Lindberg, S., Hasselhorn, M. & Fiebach, C. J. (2012). Grey
731   matter alterations co-localize with functional abnormalities in developmental dyslexia: An
732   ALE meta-analysis. *PLOS One, 7*(8), 1–10. https://doi.org/10.1371/journal.pone.0043122

733   Lo, S. & Andrews. S. (2015). To transform or not to transform: using generalized linear mixed
734   models to analyse reaction time data. *Frontiers in Psychology, 6*, Article 1171.
735   10.3389/fpsyg.2015.01171

736   Luber, B., & Lisanby, S. H. (2014). Enhancement of human cognitive performance using
737   transcranial magnetic stimulation (TMS). *Neuroimage, 85,* 961–970. DOI:
738   https://doi.org/10.1016/j.neuroimage.2013.06.007.

739   Maisog, J. M., Einbinder, E. R., Flowers, D. L., Turkeltaub, P. E., & Eden, G. F. (2008). A meta-
740   analysis of functional neuroimaging studies of dyslexia. *Annals of the New York Academy*
741   *of Sciences*, *1145*(1), 237-259.

742   Martin, A., Schurz, M., Kronbichler, M., & Richlan, F. (2015). Reading in the brain of children
743   and adults: A meta-analysis of 40 functional magnetic resonance imaging studies. *Human*
744   *Brain   Mapping, 36*(5),   1963–1981.   https://doi.org/10.1002/hbm.22749

745   Miniussi, C., Harris, J. A., & Ruzzoli, M. (2013). Modelling non-invasive brain stimulation in
746   cognitive neuroscience. *Neuroscience and Biobehavioral Reviews, 37*(8), 1702–1712.
747   https://doi.org/10.1016/j.neubiorev.2013.06.014

748   Moll, K. & Landerl, K. (2014). SLRT-II: Lese- und Rechtschreibtest – Weiterentwicklung des
749   Salzburger Lese- und Rechtschreibtests (SLRT). Bern, Switzerland: Huber.

750   Pattamadilok, C., Bulnes, L. C., Devlin, J. T., Bourguignon, M., Morais, J., Goldman, S. &
751   Kolinsky, R. (2015). How early does the brain distinguish between regular words, irregular
752   words, and pseudowords during the reading process? Evidence from neurochronometric
753   TMS.   *Journal   of   Cognitive   Neuroscience,   27*(6),   1259-1274.
754   https://doi.org/10.1162/jocn_a_00779

755   Penny, W., Flandin, G. & Trujillo-Barreto, N. (2007). Bayesian comparison of spatially

756   regularised general linear models. *Human Brain Mapping, 28*(4), 275-93.
757   0.1002/hbm.20327

758 Petermann, F. & Petermann, U. (2011). WISC-IV. Wechsler Intelligence Scale for Children–
759   Fourth Edition. Frankfurt, Germany: Pearson.

760 Pugh, K. R., Mencl, W. E., Jenner, A. R., Katz, L., Frost, S. J., Lee, J. R., Shawitz, S. E. &
761   Shaywitz, B. A. (2001). Neurobiological studies of reading and reading disability. *Journal*
762   *of Communication Disorders, 32,* 479–492.
763   https://doi.org/10.1016/S00219924(01)00060-0

764 Taylor, J. S., Rastle, K., & Davis, M. H. (2013). Can cognitive models explain brain activation
765   during word and pseudoword reading? A meta-analysis of 36 neuroimaging
766   studies. *Psychological Bulletin*, *139*(4), 766–791. https://doi.org/10.1037/a0030266

767 Richlan, F., Kronbichler, M., & Wimmer, H. (2009). Functional abnormalities in the dyslexic
768   brain: A quantitative meta-analysis of neuroimaging studies. *Human brain mapping*,
769   *30*(10), 3299-3308. https://doi.org/10.1002/hbm.20752

770 Richlan, F., Kronbichler, M., & Wimmer, H. (2011). Meta-analyzing brain dysfunctions in
771   dyslexic children and adults. *NeuroImage, 56*(3), 1735–1742.
772   https://doi.org/10.1016/j.neuroimage.2011.02.040

773 Richlan, F., Kronbichler, M., & Wimmer, H. (2013). Structural abnormalities in the dyslexic brain:
774   A meta-analysis of voxel-based morphometry studies. *Human Brain Mapping, 34*(11),
775   3055–3065. https://doi.org/10.1002/hbm.22127

776 Rueckl, J. G., Paz-Alonso, P. M., Molfese, P. J., Kuo, W. J., Bick, A., Frost, S. J., ... & Frost, R.
777   (2015). Universal brain signature of proficient reading: Evidence from four contrasting
778   languages. *Proceedings of the National Academy of Sciences*, *112*(50), 15510-15515.
779   https://doi.org/10.1073/pnas.1509321112

780 Sale, M. V., Mattingley, J. B., Zalesky, A. & Cocchi, L. (2015). Imaging human brain networks to
781   improve the clinical efficacy of non-invasive brain stimulation. *Neuroscience and*
782   *Biobehavioral Reviews, 57,* 187-198. https://doi.org/10.1016/j.neubiorev.2015.09.010

783 Schneider, W., Schlagmüller, M., Ennemoser, M. (2017). Lesegeschwindigkeits- und
784   Verständnistest für die Klassen 5-12+. Göttingen, Germany: Hogrefe.

785 Schurz, M., Wimmer, H., Richlan, F., Ludersdorfer, P., Klackl, J., & Kronbichler, M. (2015).
786   Resting-State and task-based functional brain connectivity in developmental
787   dyslexia. *Cerebral Cortex, 25*(10), 3502–3514. https://doi.org/10.1093/cercor/bhu184

788 Schuster, S., Hawelka, S., Richlan, F., Ludersdorfer, P., & Hutzler, F. (2015). Eyes on words: A
789   fixation-related fMRI study of the left occipito-temporal cortex during self-paced silent
790   reading of words and pseudowords. *Scientific reports*, *5*(1), 1-11.
791   https://doi.org/10.1038/srep12686

792 Schutter, D. J., & van Honk, J. (2006). An electrophysiological link between the cerebellum,
793   cognition and emotion: Frontal theta EEG activity to single-pulse cerebellar
794   TMS. *NeuroImage, 33*(4), 1227–1231. https://doi.org/10.1016/j.neuroimage.2006.06.055

795 Seidenberg, M. S. (2005). Connectionist models of word reading. *Current Directions in*
796   *Psychological Science, 14*(5), 238-242. https://doi.org/10.1111/j.09637214.2005.00372.x.

797 Siebner, H. R. & Rothwell, J. (2003). Transcranial magnetic stimulation: New insights into
798   representational cortical plasticity. *Experimental Brain Research, 148*(1), 1–16.
799   https://doi.org/10.1007/s00221-002-1234-2

800 Siegel, J., Power, J., Dubis, J., Vogel, A., Church, J., Schlaggar, B. & Petersen, S. (2014).
801   Statistical improvements in functional magnetic resonance imaging analyses produced
802   by censoring high-motion data points. *Human Brain Mapping, 35*(5), 1981-1996.
803   10.1002/hbm.22307

804 Smallwood, J., Bernhardt, B. C., Leech, R., Bzdok, D., Jefferies, E. & Margulies, D. S., (2021).
805   The default mode network in cognition: a topographical perspective. *Nature Reviews*
806   *Neuroscience,   22,   503-513.   10.1038/s41583-021-00474-4

807 Tops, M., & Boksem, M. A. (2011). A potential role of the inferior frontal gyrus and anterior insula
808   in cognitive control, brain rhythms, and event-related potentials. *Frontiers in*
809   *Psychology, 2*, Article 330. https://doi.org/10.3389/fpsyg.2011.00330

810 Turker, S. (2018). Exploring the neurofunctional underpinnings of developmental dyslexia: A
811   review focussing on dyslexic children. In E. Luef & M. Marin (Eds.), *The talking*
812   *species* (p. 495). Uni Graz Press.

813 Turker, S., & Hartwigsen, G. (2021a). Exploring the neurobiology of reading through non-invasive
814   brain stimulation: A review. *Cortex. 141,* 497–521.
815   https://doi.org/10.1016/j.cortex.2021.05.001

816 Turker, S., & Hartwigsen, G. (2021b). The use of noninvasive brain stimulation techniques to
817 improve reading difficulties in dyslexia: A systematic review. *Human Brain Mapping.*
818 *43*(3), 1157-1173. https://doi.org/10.1002/hbm.25700

819 van der Mark, S., Klaver, P., Bucher, K., Maurer, U., Schulz, E., Brem, S., Martin, E., & Brandeis,
820 D. (2011). The left occipitotemporal system in reading: Disruption of focal fMRI
821 connectivity to left inferior frontal and inferior parietal language areas in children with
822 dyslexia. *NeuroImage, 54*(3), 2426–2436.
823 https://doi.org/10.1016/j.neuroimage.2010.10.002

824 Wang, Q., Akram, H., Muthuraman, M., Gonzalez-Escamilla, G., Sheth, S. A., Oxenford, S., Yeh,
825 F. C., Groppa, S., Vanegas-Arroyave, N., Zrinzo, L., Li, N., Kühn, A., & Horn, A. (2021).
826 Normative vs. patient-specific brain connectivity in deep brain
827 stimulation. *NeuroImage*, *224*, Article 117307.
828 https://doi.org/10.1016/j.neuroimage.2020.117307

829 Weiß, R. (2019). Grundintelligenztest Skala 2 – Revision (CFT 20-R) mit Wortschatztest (WS)
830 und Zahlenfolgentest (ZF) – Revision (WS/ZF-R). Göttingen, Germany: Hogrefe.

831 Xia, Z., Hancock, R., & Hoeft, F. (2017). Neurobiological bases of reading disorder Part I:
832 Etiological investigations. *Language And Linguistics Compass, 11*(4).
833 https://doi.org/10.1111/lnc3.12239

834 Zeidman, P., Jafarian, A.,Corbin, N., Seghier, M., Razi, A., Price, C. & Friston, K.. (2019a). A
835 guide to group effective connectivity analysis, part 1: First level analysis with DCM for
836 fMRI. *NeuroImage, 200*, 174-190. https://doi.org/10.1016/j.neuroimage.2019.06.031

837 Zeidman, P., Amirhossein, J., Seghier, M. L., Litvak, V., Cagnan, H., Price, C. J. & Friston, K. J.
838 (2019b). A guide to group effective connectivity analysis, part 2: Second level analysis
839 with PEB. *NeuroImage, 200*, 12-25. https://doi.org/10.1016/j.neuroimage.2019.06.032