

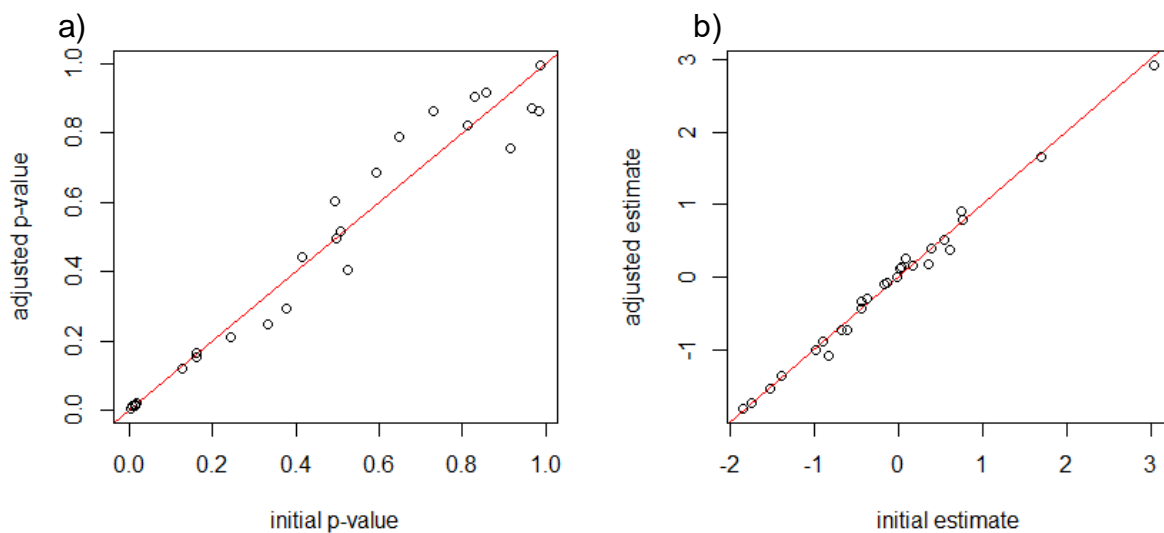
# Supporting Information

## ***ATP2C2* and *DYX1C1* are putative modulators of dyslexia-related MMR**

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### Supporting Information 1. DERET description

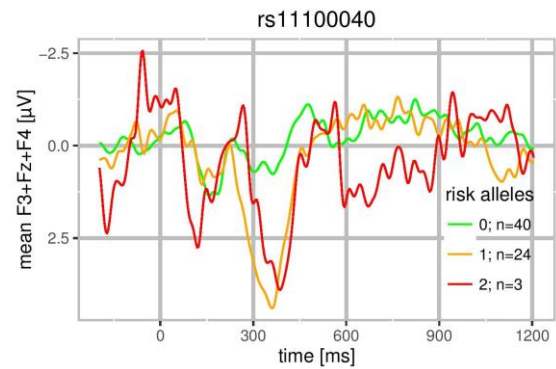
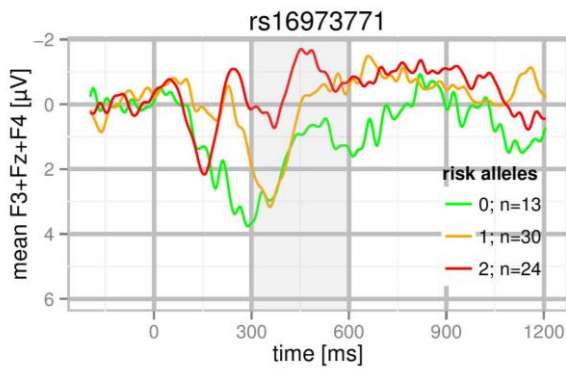
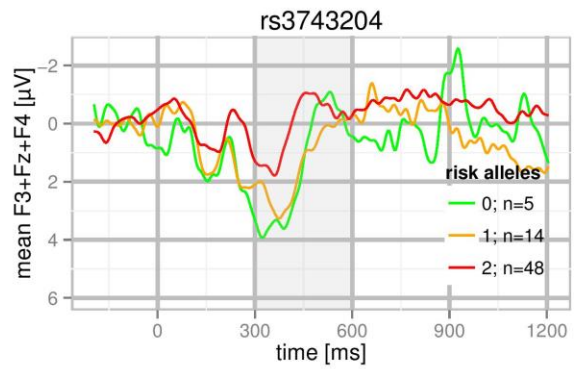
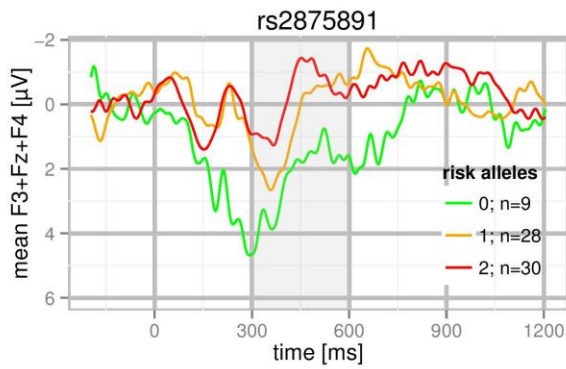
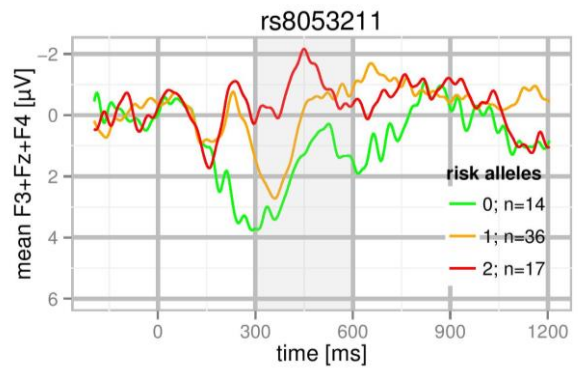
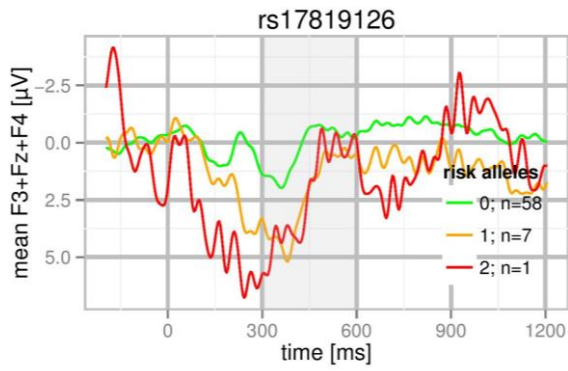
The text for third and fourth graders consists of ten sentences. Before writing the text from dictation, the text is completely read to the children once. When dictation begins, the first sentence is dictatated completely and after, segments (i.e., each consisting of three words on average) of the sentence are dictated to the child sequentially. After the segment of the sentence has been written down the next segment of the sentence is dictated. This procedure is continued for each of the following nine sentences. Spelling mistakes are enumerated for each sentence (one mistake is noted for words with at least one spelling mistake), summed up for the whole text, and translated into age-normed percentile ranks (PR).



**Supporting Figure 1. Correlation between the ADD-unadjusted and ADD-adjusted p-values (a) and ADD-unadjusted and ADD-adjusted effect sizes (b).**

Here, values of the ADD-unadjusted model are represented on the x-axes, whereas values of the ADD-adjusted model are shown on the y-axes.

The ADD-unadjusted model is specified as associations among SNPs and the late component of the MMR adjusted for poor spelling as used in the main analysis. The ADD-unadjusted model is the same but additionally includes ADD status as covariate.



**Supporting Figure 2. Difference waves (deviant-standard) for the mean of F3, Fz, F4 stratified according to the number of risk alleles for each of the nominal significant associated SNPs.**

**Supporting Table 1. Details of the spelling subgroups.** The p-values give the difference between the DERET > 10 and DERET ≤ 10 groups in the respective measures.

	DERET > 10	DERET ≤ 10	p-value
Boys : girls	28:25	10:4	0.243
Age	9.65 ± 0.53	9.54 ± 0.49	0.485
ADD	6	6	0.013
Nonverbal intelligence (mean IQ)	112 ± 9.7	106 ± 6.5	0.013

**Supporting Table 2. Overview of analyzed SNPs.** Presented are the SNPs with the respective gene, the minor allele frequency (MAF) of the genotyped SNP, the independent, tagging lead-SNP identified by clumping, the p-value, the estimate of the main effect and the risk allele of the respective SNP. SNPs were annotated with genes they were located in or if not applicable the nearest gene with the distance to the SNP in parentheses. SNP / gene informations are based on GRCh37.

SNP	Gene	MAF	Lead SNP	p-value	Estimate	References	Coded as risk allele
rs17819126	<i>DYX1C1</i>	0.07		0.0037	3	Bates <i>et al.</i> , 2010; Paracchini <i>et al.</i> , 2011	minor
rs8053211	<i>ATP2C2</i>	0.48		0.0039	-1.8	Newbury <i>et al.</i> , 2009, 2011; Scerri <i>et al.</i> , 2011	major
rs11860694	<i>ATP2C2</i>	0.48	rs8053211	0.0096	1.7	Newbury <i>et al.</i> , 2009, 2011	minor
rs16973771	<i>ATP2C2</i>	0.42		0.0199	-1.4	Newbury <i>et al.</i> , 2009, 2011	major
rs2875891	<i>ATP2C2</i>	0.34		0.0146	-1.5	Newbury <i>et al.</i> , 2009, 2011	major
rs3743204	<i>DYX1C1</i>	0.17		0.0157	-1.7	Bates <i>et al.</i> , 2010; Becker <i>et al.</i> , 2013; Dahdouh <i>et al.</i> , 2009; Wigg <i>et al.</i> , 2004	major
rs8045507	<i>ATP2C2</i>	0.42	rs16973771	0.0199	-1.4	Newbury <i>et al.</i> , 2009, 2011	major
rs10246256	<i>CNTNAP2</i>	0.3		0.1606	-0.9	Newbury <i>et al.</i> , 2011; Vernes <i>et al.</i> , 2008	major
rs12533005	<i>FOXP2</i>	0.39		0.1268	-1	Peter <i>et al.</i> , 2011; Wilcke <i>et al.</i> , 2012	major
rs6564903	<i>CMIP</i>	0.41		0.1612	0.8	Newbury <i>et al.</i> , 2009, 2011; Scerri <i>et al.</i> , 2011	major
rs3935802	<i>CMIP</i>	0.38		0.2439	-0.7	Newbury <i>et al.</i> , 2009, 2011	minor
rs9461045	<i>TDP2</i> (1.1kb)	0.2		0.3333	0.8	Dennis <i>et al.</i> , 2009; Newbury <i>et al.</i> , 2011	minor
rs3212236	<i>TDP2</i> (1.7kb)	0.2	rs9461045	0.3333	0.8	Harold <i>et al.</i> , 2006; Newbury <i>et al.</i> , 2011	minor
rs6935076	<i>KIAA0319</i>	0.38		0.3766	-0.6	Becker <i>et al.</i> , 2013; Cope <i>et al.</i> , 2005; Couto <i>et al.</i> , 2010; Luciano <i>et al.</i> , 2007; Newbury <i>et al.</i> , 2011; Paracchini <i>et al.</i> , 2008; Scerri <i>et al.</i> , 2011	minor
rs555879	<i>MYO5B</i>	0.45		0.415	0.5	Scerri <i>et al.</i> , 2010	minor
rs685935	<i>DYX1C1</i>	0.41		0.4949	-0.4	Bates <i>et al.</i> , 2010; Paracchini <i>et al.</i> , 2011	minor
rs759178	<i>CNTNAP2</i>	0.48		0.498	-0.4	Vernes <i>et al.</i> , 2008; Whitehouse <i>et al.</i> , 2011	major
rs2710102	<i>CNTNAP2</i>	0.48	rs759178	0.498	-0.4	Newbury <i>et al.</i> , 2011; Peter <i>et al.</i> , 2011; Vernes <i>et al.</i> , 2008; Whitehouse, Bishop, Ang, Pennell, & Fisher, 2011	major
rs7201632	<i>CMIP</i>	0.43		0.508	0.4	Newbury <i>et al.</i> , 2009, 2011	major
rs3743205	<i>DYX1C1</i>	0.43		0.5253	-0.8	Becker <i>et al.</i> , 2013;	major

SNP	Gene	MAF	Lead SNP	p-value	Estimate	References	Coded as risk allele
						Dahdouh <i>et al.</i> , 2009; Lim, Ho, Chou, & Waye, 2011; Newbury <i>et al.</i> , 2011; Taipale <i>et al.</i> , 2003; Wigg <i>et al.</i> , 2004	
rs793862	<i>DCDC2</i>	0.3		0.5947	-0.4	Becker <i>et al.</i> , 2013; Ludwig <i>et al.</i> , 2008; Meng <i>et al.</i> , 2005; Scerri <i>et al.</i> , 2011; Schumacher <i>et al.</i> , 2006; Wilcke <i>et al.</i> , 2009	minor
rs7765678	<i>DCDC2</i>	0.08		0.6492	0.6	Lind <i>et al.</i> , 2010	major
rs12606138	<i>NEDD4L</i>	0.4		0.7294	0.4	Scerri <i>et al.</i> , 2010	major
rs2179515	<i>KIAA0319</i>	0.33		0.8117	0.2	Becker <i>et al.</i> , 2013; Cope <i>et al.</i> , 2005	major
rs807701	<i>DCDC2</i>	0.4		0.8311	-0.1	Becker <i>et al.</i> , 2013; Ludwig <i>et al.</i> , 2008; Schumacher <i>et al.</i> , 2006; Wilcke <i>et al.</i> , 2009	minor
rs1419228	<i>DCDC2</i>	0.19		0.8552	-0.2	Lind <i>et al.</i> , 2010; Paracchini <i>et al.</i> , 2011	minor
rs2143340	<i>KIAA0319</i>	0.19		0.9142	0.1	Francks <i>et al.</i> , 2004; Luciano <i>et al.</i> , 2007; Newbury <i>et al.</i> , 2011; Paracchini <i>et al.</i> , 2008, 2011	minor
rs8094327	<i>NEDD4L</i>	0.13	rs12606138	0.9665	0	Scerri <i>et al.</i> , 2010	minor
rs1000585	<i>EVA1A</i> (26kb)	0.41		0.982	0	Anthoni <i>et al.</i> , 2007; Newbury <i>et al.</i> , 2011	minor
rs761100	<i>KIAA0319</i>	0.41		0.9874	0	Becker <i>et al.</i> , 2013; Harold <i>et al.</i> , 2006; Ludwig <i>et al.</i> , 2008; Newbury <i>et al.</i> , 2011	minor
rs11100040	<i>FTH1P21</i> (79kb)	0.23		0.0306	1.6	Roeske <i>et al.</i> , 2011	
rs4234898	<i>FTH1P21</i> (70kb)	0.14		0.1711	1.2	Roeske <i>et al.</i> , 2011	

**Supporting Table 3. Literature-screen for eQTL-effects.** Displayed are the SNP with their respective gene, the linkage ( $R^2$ ) to the eQTL, the gene which expression is affected by the eQTL, the tissue the effect was observed and the respective study. If the eQTL and the tested SNP are identical, the eQTL is shown in bold.

SNP	Gene	eQTL	$R^2$	D'	Affected gene	Tissue	Study
rs3743204	<i>DYX1C1</i>	<b>rs3743204</b>	1.00	1.00	<i>DYX1C1</i>	Blood	Heinzen <i>et al.</i> , 2008
rs3743204	<i>DYX1C1</i>	chr15_55765580_I	0.31	0.82	<i>DYX1C1-CCPGI</i>	Brain (Cerebellum)	GTEC Consortium,, 2015
rs3743204	<i>DYX1C1</i>	rs8040756	0.57	0.90	<i>CCPGI</i>	Blood	Fehrmann <i>et al.</i> , 2011
rs3743204	<i>DYX1C1</i>	rs8040756	0.57	0.90	<i>PIGB</i>	Blood	Fehrmann <i>et al.</i> , 2011
rs3743204	<i>DYX1C1</i>	rs8037056	0.44	0.98	<i>PIGB</i>	Monocytes	Zeller <i>et al.</i> , 2010
rs17819126	<i>DYX1C1</i>	<b>rs17819126</b>	1.00	1	<i>PIGB</i>	Blood	Westra <i>et al.</i> , 2013
rs17819126	<i>DYX1C1</i>	rs4774760	0.30	1	<i>PIGB</i>	Monocytes	Zeller <i>et al.</i> , 2010
rs17819126	<i>DYX1C1</i>	rs11857829	0.95	1	<i>RAB27A</i>	Blood	Fehrmann <i>et al.</i> , 2011
rs17819126	<i>DYX1C1</i>	rs11855084	0.95	1	<i>RAB27A</i>	Blood	Westra <i>et al.</i> , 2013
rs11100040	<i>FTHIP21</i> (79kb)	<b>rs11100040</b>	1.00	1	<i>PTPRU</i>	Blood	Fehrmann <i>et al.</i> , 2011
rs11100040	<i>FTHIP21</i> (79kb)	<b>rs11100040</b>	1.00	1	<i>PTPRU</i>	Blood	Westra <i>et al.</i> , 2013

**Supporting Table 4. Known and predicted regulatory elements for all associated SNPs.** Displayed is the full output of the RegulomeDB.

SNP	Hits
rs16973771	Motifs Footprinting 8988t NF-1, Motifs PWM NF-1, Chromatin_Structure DNase-seq 8988t, Chromatin_Structure DNase-seq Ips, Chromatin_Structure Diffa14d DNase-seq H7es, Chromatin_Structure DNase-seq K562G1phase, Chromatin_Structure DNase-seq Lncap, Chromatin_Structure Nabut DNase-seq K562, Chromatin_Structure DNase-seq K562, Chromatin_Structure Saha1u72hr DNase-seq K562, Chromatin_Structure DNase-seq H7es, Protein_Binding ChIP-seq K562 EZH2
rs3743204	Chromatin_Structure Lenticon DNase-seq Fibroblgm03348, Chromatin_Structure DNase-seq Adultcd4th0, Chromatin_Structure Ifna4h FAIRE Helas3, Chromatin_Structure DNase-seq Fibrobl, Chromatin_Structure DNase-seq Ipsnihi7, Chromatin_Structure DNase-seq Htr8, Chromatin_Structure DNase-seq K562, Chromatin_Structure Tam10030 DNase-seq Ishikawa, Chromatin_Structure DNase-seq Fibropag08395, Chromatin_Structure Andro DNase-seq Lncap, Chromatin_Structure DNase-seq Gcbcell, Chromatin_Structure DNase-seq Hpde6e6e7, Chromatin_Structure DNase-seq Mel2183, Chromatin_Structure DNase-seq Cil, Chromatin_Structure FAIRE Helas3, Chromatin_Structure Est10nm30m DNase-seq Ishikawa, Chromatin_Structure DNase-seq Cd20ro01794, Chromatin_Structure DNase-seq Ipsnihi11, Chromatin_Structure DNase-seq Ips, Chromatin_Structure DNase-seq Mcf7, Chromatin_Structure DNase-seq Heartoc, Chromatin_Structure Ifng4h FAIRE Helas3, Chromatin_Structure DNase-seq Fibrop, Chromatin_Structure DNase-seq UrotsaUt189, Chromatin_Structure DNase-seq Panisd, Chromatin_Structure DNase-seq Fibroblgm03348, Chromatin_Structure DNase-seq Cerebellumoc, Chromatin_Structure DNase-seq Gm10266, Chromatin_Structure DNase-seq Nhek, Chromatin_Structure DNase-seq Sknsh, Chromatin_Structure Hypoxlaccn DNase-seq Mcf7, Chromatin_Structure DNase-seq T47d, Chromatin_Structure DNase-seq Gliobla, Chromatin_Structure DNase-seq A549, Chromatin_Structure DNase-seq Huh7, Chromatin_Structure DNase-seq Lncap, Chromatin_Structure DNase-seq Helas3, Chromatin_Structure DNase-seq Gm19238, Chromatin_Structure DNase-seq Cerebrumfrontaloc, Chromatin_Structure DNase-seq Hbvsmc, Chromatin_Structure Ifna4h DNase-seq Helas3, Chromatin_Structure FAIRE Nhek, Chromatin_Structure DNase-seq Hek293t, Chromatin_Structure DNase-seq Urotsa, Chromatin_Structure Est10nm30m DNase-seq T47d, Chromatin_Structure DNase-seq Gm12891, Chromatin_Structure DNase-seq Rwpe1, Chromatin_Structure DNase-seq Gm19239, Chromatin_Structure DNase-seq Huh75, Chromatin_Structure DNase-seq Gm19240, Chromatin_Structure DNase-seq Osteobl, Chromatin_Structure Est10nm30m DNase-seq Ecc1, Chromatin_Structure DNase-seq Phte, Chromatin_Structure DNase-seq Naivebcell, Chromatin_Structure DNase-seq Olfneurosphere, Chromatin_Structure DNase-seq Stellate, Chromatin_Structure DNase-seq Gm13977, Chromatin_Structure DNase-seq Imr90, Chromatin_Structure Lentimyod DNase-seq Fibroblgm03348, Chromatin_Structure DNase-seq Gm10248, Chromatin_Structure DNase-seq Hepg2, Chromatin_Structure Hypoxlac DNase-seq Mcf7, Chromatin_Structure DNase-seq Ipscwru1, Chromatin_Structure DNase-seq Hsmmfshd, Chromatin_Structure DNase-seq Hsmmemb, Chromatin_Structure DNase-seq Fibropag20443, Chromatin_Structure DNase-seq Medullod341, Chromatin_Structure DNase-seq Medullo, Chromatin_Structure Serumfree DNase-seq Aosmc, Chromatin_Structure DNase-seq Gm20000, Chromatin_Structure Dm002p1h DNase-seq Ecc1, Chromatin_Structure DNase-seq Gm12892, Chromatin_Structure DNase-seq Hsmm, Chromatin_Structure DNase-seq Fibropag08396, Chromatin_Structure DNase-seq Gm12878, Chromatin_Structure DNase-seq Monocd14, Chromatin_Structure Znf4g7d3 DNase-seq K562, Chromatin_Structure DNase-seq Panislets, Chromatin_Structure DNase-seq Gm13976, Protein_Binding shLuc ChIP-seq CD36 GATA1, Protein_Binding 02pct ChIP-seq A549 REST, Protein_Binding ChIP-seq GM12878 SIN3A, Protein_Binding shbrg1 ChIP-seq CD36 GATA1, Protein_Binding ChIP-seq PFSK-1 SIN3A, Protein_Binding ChIP-seq HeLa-S3 SMARCC1, Protein_Binding tnfa ChIP-seq GM15510 NFKB1, Protein_Binding ChIP-seq K562 SAP30, Protein_Binding 02pct ChIP-seq A549 SIN3A, Protein_Binding ChIP-seq K562 RFX3, Protein_Binding ChIP-seq HeLa-S3 CEBPB
rs17819126	Chromatin_Structure DNase-seq Monocd14ro1746, Chromatin_Structure DNase-seq Monocd14
rs8053211	Chromatin_Structure DNase-seq K562, Chromatin_Structure Saha1u72hr DNase-seq K562, Chromatin_Structure DNase-seq Mcf7, Chromatin_Structure Nabut DNase-seq K562, Chromatin_Structure DNase-seq Hmec
rs2875891	Chromatin_Structure DNase-seq Monocd14ro1746, Chromatin_Structure DNase-seq Monocd14
rs11100040	No data

**Supplementary Table 5. Expression characteristics of the associated genes.** Expression levels according to protein detection and RNA detection are displayed. Protein expression was stratified according to tissue and cell type. RNA expression levels were categorized into low (1-10 FPKM), medium (10-50 FPKM) or high (>50 FPKM) RNA abundance.

<b>Region</b>	<b><i>DYX1C1</i></b>	<b><i>ATP2C2</i></b>
<i>Protein level</i>		
cerebellum / cells in granular layer	not detected	not detected
cerebellum / cells in molecular layer	medium	not detected
cerebellum / Purkinje cells	medium	not detected
cerebral cortex / endothelial cells	low	medium
cerebral cortex / glial cells	low	not detected
cerebral cortex / neuronal cells	medium	low
cerebral cortex / neuropil	not detected	not detected
hippocampus / glial cells	not detected	not detected
hippocampus / neuronal cells	medium	not detected
lateral ventricle / glial cells	medium	not detected
lateral ventricle / neuronal cells	medium	medium
<i>RNA level</i>		
cerebral cortex	low	low



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