<u>3. Behavioural results</u>

3.1. Between-group comparisons

Because there were many variables under statistical testing, a Family Wise Error (FWER) correction was adopted. We studied the pattern of between-variable correlations in the control group by means of Spearmann's rho tests. The Spearmann's rho correlation matrices are reported in table sm-1 and sm-2, respectively. The global level of significance of the two patterns of correlation was testes by means of Bartlett's sphericity test (Bartlett, 1937).

On the basis of the correlation matrices, we identified the following families of variables:

- Family 1: word-reading, pseudo-word reading, VOT task, picture naming, rhyme (d-prime); for this family the corrected alpha level was set to .01;
- Family 2: digit naming and spoonerisms; for this family the corrected alpha level was set to .025;
- Family 3: verbal and performance I.Q.; for this family the corrected alpha level was set to .025;
- Family 4: correct taps and lack of corrections; for this family the corrected alpha level was set to .025;
- Family 5: contrast discrimination for magnocellular stimuli, contrast discrimination for parvocellular stimuli, speed discrimination for magnocellular stimuli and coherent motion perception; for this family the corrected alpha level was set to .0125;
- Family 6: speed discrimination with parvocellular stimuli (alpha level .05 i.e. independent measure).

Below we report the uncorrected p value and we mark with (*) the p values meeting the aforementioned thresholds.

WAIS

The between-group difference for the **Global IQ** (Mann-Whitney U-test, Z-value = -2.13, p = .03, $|\mathbf{r}| = .33$) and **Performance IQ** (Mann-Whitney U-test, Z-value = -.34, p = .73, $|\mathbf{r}| = .05$) did not reach a corrected significance. In contrast, there was a between-group difference for the **verbal IQ** (Mann-Whitney U-test, Z-value = -2.89, p = .004*, $|\mathbf{r}| = .45$).

In particular, the analyses of single subtests showed that subjects with dyslexia made significantly more errors than controls in the **Arithmetics** (Mann-Whitney U-test, Z-value = -3.49, p < .001*, $|\mathbf{r}| = .54$), while in the **Similarities** (Mann-Whitney U-test, Z-value = -2.14, p = .032, $|\mathbf{r}| = .35$) and in the **Digit Span** (Mann-Whitney U-test, Z-value = -2.2, p = .03, $|\mathbf{r}| = .36$) there were trends. Of the

performance subtests, there was a trend for significance for the **Digit-Symbol Coding** (Mann-Whitney U-test, Z-value = -2.18, p = .029, |r| = .34) subtest only.

Reading

Dyslexics were significantly **slower** than controls in reading both **words** (Mann-Whitney U-test, Z-value = -5.24, p < .001*, $|\mathbf{r}| = .8$) and **pseudo-words** (Mann-Whitney U-test, Z-value = -5.38, p < .001*, $|\mathbf{r}| = .82$). Moreover, dyslexics made **more errors** than controls when reading both words (Mann-Whitney U-test, Z-value = -2.42, p = .015, $|\mathbf{r}| = .37$) and pseudo-words (Mann-Whitney U-test, Z-value = -2.03, p = .042, $|\mathbf{r}| = .31$) with trends for significance.

The lengthening of the reading reaction times was not caused by a generalized lengthening of vocal reaction times, as there was no significant group differences in a simple vocal reaction time for visual triggers (Mann-Whitney U-test, Z-value = -.24, p = .8, |r| = .04).

Phonology

Group differences were found in the **Spoonerism task**, the dyslexics being significantly slower than controls (Mann-Whitney U-test, Z-value = -4.58, p < .001*, $|\mathbf{r}| = .71$) and more prone to error (Mann-Whitney U-test, Z-value = -3.6, p < .001*, $|\mathbf{r}| = .53$). A similar difference was also present for the **digit naming** (Mann-Whitney U-test, Z-value = -3.55, p < .001*, $|\mathbf{r}| = .54$) and for the **picture naming tasks** (Mann-Whitney U-test, Z-value = -3.73, p < .001*, $|\mathbf{r}| = .57$), in that dyslexics were slower than controls.

"Dorsal visual stream skills" tasks¹

Once the task specific correction was adopted, no significant group differences were seen any of the tasks designed to challenge the magnocellular visual system: the <u>contrast discrimination task</u> with low spatial frequency Gabors (Mann-Whitney U-test, Z-value = -.81, p = .42, |r| = .13) and the <u>coherent motion perception</u> (Mann-Whitney U-test, Z-value = -.28, p = .78, |r| = .05). There was a trend for significance in the <u>speed discrimination</u> (Mann-Whitney U-test, Z-value = -2.19, p = .03, |r| = .36) with low spatial frequency Gabors.

<u>The contrast discrimination task (Mann-Whitney U-test, Z-value = -.76, p = .45, $|\mathbf{r}| = .12$) and the speed discrimination task (Mann-Whitney U-test, Z-value = -.85, p = .4, $|\mathbf{r}| = .14$) with high spatial frequency Gabors, tests that should depend on the parvocellular system, were also not significant.</u>

¹ These tests were performed by 14 dyslexic subjects (6 subjects were no longer available for testing). While at a group level there were no difference with the normal controls, the prevalence of individual deficits in these tests was in the same low proportions reported by Ramus et al. (2003) on 16 subjects. In any event, all subjects did the fMRI test with the visual motion perception task and no difference was seen there either.

"Cerebellar" task

No between-group differences emerged in the motor/cerebellar task neither in the number of correct taps (Mann-Whitney U-test, Z-value = -.67, p = .5, |r| = .11), nor in the lack of corrections (Mann-Whitney U-test, Z-value = -.81, p = .42, |r| = .13).

3.2. Single-subject analyses (see table 1 for details)

<u>WAIS</u>: None of the dyslexic subjects showed a verbal IQ lower than controls, and only one dyslexic showed a performance IQ lower than controls.

<u>Vocal reaction times</u>: only one subject showed a generalized lengthening of vocal reaction times for visual stimuli (one normal control was also outside the normal range of distribution).

<u>Reading speed</u>: all subjects with dyslexia, with one exception, showed a lengthening of vocal reaction times for pseudo-word reading. Ten out of twenty subjects with dyslexia had a significantly prolonged reading times for real words.

<u>Phonology</u>: ten subjects with dyslexia showed a pathological performance in, at least, one phonological task: eight subjects showed a lengthening for the spoonerism task, four were slower than controls in the digit naming task and three in the picture naming task.

"Dorsal visual stream skills" and "cerebellar" tasks: three dyslexics showed a deficit in the contrast discrimination task for low-spatial frequency stimuli, none in the other visual/magnocellular tasks. In the "cerebellar" task, two dyslexics showed a lower performance than controls in at least one parameter.

4. fMRI results

4.1. Group activations for each task

4.1.1. Normal readers

<u>Pseudo-word reading:</u> The left inferior frontal cortex, the left precentral gyrus, the left temporal pole, the left middle temporal gyrus, the left superior and inferior parietal lobules, the left fusiform gyrus and the inferior occipital cortex, bilaterally, were activated during pseudo-word reading in controls (table sr-3a and figure 1: row 1, column A).

<u>Auditory rhyming</u>: Phonological awareness on spoken syllables was associated with left inferiorfrontal and middle and inferior temporal cortices activations in controls. A right-sided activation was present in the middle temporal gyrus (table sr-3b and figure 1: row 2, column A).

<u>Visual motion perception</u>: A bilateral pattern of activations including the precentral gyrus, the superior parietal lobule, the superior and middle occipital cortex, and the cerebellum was activated in controls during visual motion perception (table sr-3c and figure 1: row 3, column A). Right activations were observed in the middle and inferior frontal cortex, and in the superior, middle and inferior temporal gyri. The left superior frontal gyrus, and the left lingual gyrus were also activated.

<u>Motor learning</u>: The new motor sequence learning in controls was associated with a widespread cortico-subcortical activation involving the superior and middle frontal gyri, bilaterally, the right inferior frontal gyrus, the left SMA, and the left insula, the right supramarginal and inferior temporal gyrus, the supramarginal gyrus, the right precuneus, the inferior and superior parietal lobule and the cerebellum, bilaterally, and the left pallidum (table sr-3d and figure 1: row 4, column A).

Table sr-1: Brain activations in controls for the four tasks under consideration. The effects werethresholded at p < .05 corrected for multiple comparisons (FWE-corrected).

				MNI	Coordinates						
	X	у	z	Z score	X	у	Z	Z score			
Brain regions		I eft he	mispher	0		Right hemisphere					
Drain regions		Lett lie	Control			Mgnt	nennspi				
		a Pse		l reading							
Inf. frontal gyrus, pars orbitalis	-40	30	-2	7.37							
ini. nontai gyrus, pars oronans	-38	30	-6	7.30							
Inf. frontal gyrus, pars triangularis	-38	50	-0	7.50	60	22	22	4.46			
	50	14	16	7.54	00	22	22	4.40			
Inf. frontal, pars opercularis	-50 -48	14 12	16 22								
Deventer1				7.46							
Precentral gyrus	-44	2	30	6.67							
	-48	0	50	6.13							
Sup. temporal pole	-52	12	-4	6.17							
	-52	14	-10	6.05							
Mid. temporal gyrus	-64	-42	2	5.91	62	-32	-6	4.63			
Hippocampus	-26	-22	-10	4.59							
	-24	-26	-10	4.55							
Sup. parietal lobule	-30	-64	52	4.57							
Inf. parietal lobule	-52	-44	52	6.11							
ini. puriour iosuio	-44	-42	42	4.93							
Fuciform gurus	-42	-42 -56	-20								
Fusiform gyrus											
Mid. occipital gyrus	-26	-68	40	4.74							
Inf. occipital gyrus	-26	-98	-8	>8							
	26	-100	-2	>8							
Cerebellum	-38	-48	-24	>8	32	-80	-24	4.73			
	-40	-70	-20	>8							
Amygdala	-26	2	-20	4.55							
	-28	-2	-20	4.50							
		b. Ai	uditory ri	hvming							
Inf. frontal gyrus, pars triangularis	-48	18	24	5.62							
Mid. temporal gyrus	-60	-18	-8	6.18	58	-36	-2	4.75			
inia. temporar gyras	00	10	0	0.10	60	-14	-10	4.43			
Inf. tomporal avrus	-52	-48	-20	4.71	00	-14	-10	4.45			
Inf. temporal gyrus	-32										
	24			perception							
Sup. frontal gyrus	-24	-10	54	6.69		_					
Mid. frontal gyrus					48	-2	56	6.53			
Inf Frontal gyrus, pars triangularis					40	22	30	4.47			
Precentral gyrus	-52	0	46	4.81	26	-8	54	7.01			
					56	6	42	6.21			
Sup. temporal gyrus					58	-36	16	7.24			
Mid. temporal gyrus					46	-68	2	>8			
Inf. temporal gyrus					44	-48	-24	7.22			
Sup. parietal lobule	-22	-60	64	>8	22	-58	60	>8			
Sup. parlear looule	-26	-52	64	>8	32	-42	58	>8			
Sup. occipital gyrus	-20 -24	-32	30	>8	26	-42 -86	32	>8			
Sup. occipital gyrus	-24	-00	50	>0	26 24						
Mid a spinitel and	10	70	0	. 0		-88	18	7.82			
Mid. occipital gyrus	-46	-78	0	>8	26	-86	14	7.76			
.	-24	-88	22	>8							
Lingual gyrus	-12	-82	-12	7.32							
Cerebellum	-40	-70	-20	7.21	20	-74	-30	4.60			
					18	-72	-28	4.43			
		d.M	Aotor lea	rning							
Sup. frontal gyrus	-22	-8	60	7.14	24	0	54	>8			
	-24	-4	56	7.14							
Mid. frontal gyrus	-38	30	30	6.07	40	36	30	7.71			
Since nonun Bjrub	50	50	20	0.07	10	20	20				

	-38	50	14	5.20				
Inf. frontal gyrus, pars opercularis					48	10	16	6.92
					52	10	22	6.82
Supplementary Motor Area	-4	0	58	7.01				
Insula	-32	16	0	7.34				
Supramarginal gyrus					40	-38	42	>8
Inf. temporal gyrus					56	-48	-18	6.65
					56	-52	-16	6.60
Precuneus					22	-56	-28	5.85
Sup. parietal lobule	-20	-58	66	>8	36	-54	56	>8
					16	-66	60	7.62
Inf. parietal lobule	-46	-38	56	>8	50	-38	52	>8
Cerebellum	-2	-80	-20	6.27	4	-74	-12	6.51
	-26	-62	-30	4.74				
Pallidum	18	0	0	6.93				

4.1.2. Subjects with dyslexia

<u>Pseudo-word reading</u>: Activations in the left inferior frontal cortex, in the left precentral gyrus, in the left SMA, in the left temporal pole, in the middle and inferior occipital cortex, bilaterally, and in the cerebellum were observed in dyslexics during pseudo-word reading (table sr-4a and figure 1: row 1, column B).

<u>Auditory rhyming:</u> A larger activation pattern including the left middle and inferior frontal cortex, the left precentral gyrus, the left temporal pole, the left middle and inferior temporal cortex, the precuneus, bilaterally, the right superior parietal lobule, the left inferior parietal lobule, and the right angular gyrus was seen in dyslexics (table sr-4b and figure 1: row 2, column C).

<u>Visual motion perception</u>: A pattern including the precentral gyrus, bilaterally, the right superior and middle temporal cortex, the right-superior and left-inferior parietal lobule, the middle occipital cortex, bilaterally, and the right inferior occipital gyrus was seen in the dyslexics during the motion perception task (table sr-4c and figure 1: row 3, column B).

<u>Motor learning</u>: A pattern of activations including the left superior frontal gyrus, the middle frontal gyrus, bilaterally, the left precentral gyrus, the right SMA, the right middle cingulate cortex, the insula, bilaterally, the left postcentral cortex, the right inferior and middle temporal cortex, the right supramarginal gyrus, the left precuneus, the right superior and inferior parietal lobule, the right calcarine, and the cerebellum, bilaterally, was observed in dyslexics during the motor learning task (table sr-4d and figure 1: row 4, column B).

Table sr-2.: Brain activations in subjects with dyslexia for the four tasks under consideration.The effects were thresholded at p < .05 corrected for multiple comparisons (FWE-corrected).

-	MNI Coordinates									
-	x	у	Z	Z score	x	у	Z	Z score		
Brain regions		Left he	mispher	9	Right hemisphere					
			Dyslexie	S						
		a. Psei	udo-word	l reading						
nf. frontal gyrus, pars triangularis	-40	26	2	5.86						
nf. frontal gyrus, pars opercularis	-50	12	2	5.36						
Precentral gyrus	-52	0	46	7.82						
27	-58	2	22	5.52						
Supplementary Motor Area	-4	8	58	6.23						
Sup. temporal pole	-52	12	-4	5.31						
/lid. occipital gyrus	-				34	-94	2	6.85		
nf. occipital gyrus	-26	-98	-8	>8	24	-100	-2	>8		
ini occipital gjias	20	20	0	20	36	-92	-6	6.51		
Cerebellum	-40	-72	-22	5.44	28	-66	-32	4.61		
	10		uditory rl		20	50	52	1.01		
Iid. frontal gyrus, pars orbitalis	-38	46	ланогу п -6	4.43						
nf. frontal gyrus, pars orbitalis	-36 -36	40	-0 -4	4.45						
nf. frontal gyrus, pars triangularis	-30 -40	40 16	-4 26	4.40 6.82						
in. nomai gyrus, pars triangularis	-40 -42	28		6.28						
)			14	6.28 5.26						
Precentral gyrus	-36	6	34							
Sup. temporal pole	-44	18	-24	5.15						
6 1	-32	14	-22	4.61						
Aid. temporal gyrus	-60	-16	-10	7.31						
	-58	-36	0	7.29						
nf. temporal gyrus	-50	-20	-18	6.55						
	-50	-50	-12	5.83						
Precuneus	-4	-72	38	5.01	4	-60	42	4.92		
	-4	-76	56	4.50						
Sup. parietal lobule					34	-76	52	4.97		
nf. parietal lobule	-28	-70	48	7.67						
-	-42	-42	42	4.59						
Angular gyrus					36	-72	54	4.93		
<u> </u>		c. Visua	l motion	perception						
Precentral gyrus	-34	-4	50	5.52	48	-2	48	6.15		
	-50	0	40	4.82	28	-6	54	5.71		
up. temporal gyrus	20	v			60	-36	14	5.54		
Aid. temporal gyrus					46	-66	4	>8		
Sup. parietal lobule					28	-50	58	7.20		
nf. parietal lobule	-28	-50	56	7.66	20	-50	50	1.20		
ni. parletar lobale	-32	-38	42	6.12						
Aid. occipital gyrus	-32 -44	-38 -72	42	>8	30	-80	32	6.04		
and. occipital gyrus	-44 -26	-72 -78	$\frac{2}{28}$	>8 6.67	30 30	-80 -86	52 24	6.04 5.43		
nf oppinitel gumus	-20	-/0	20	0.07						
nf. occipital gyrus			1	:	44	-82	-6	5.65		
	24		Motor lea	0						
up. frontal gyrus	-24	-6	58	6.93		00	22	0		
Aid. frontal gyrus	-36	44	16	6.44	36	38	22	>8		
	-42	26	34	5.77	28	8	58	7.32		
recentral gyrus	-30	-14	64	>8						
upplementary Motor Area					4	6	58	7.62		
/lid. Cingulum					6	24	42	7.42		
nsula	-32	18	-4	7.27	36	24	-4	>8		
1	-42	-32	48	>8						
Postcentral gyrus	-+2	52	40	20						
Aid. temporal gyrus	-42	52	40	20	62	-26	-12	5.60		

Inf. temporal gyrus					58	-30	-14	5.61
Supromorginal gurus					54 42	-48 -30	-20 42	4.95 >8
Supramarginal gyrus Precuneus	-10	-52	74	4.48	42	-30	42	>0
	-10	-52	74	4.40	• •			
Sup. parietal lobule					38	-60	60	>8
					16	-66	62	7.15
Inf. parietal lobule					46	-46	50	>8
Calcarine sulcus					12	-76	12	5.23
Cerebellum	-8	-82	-24	5.29	22	-52	-30	5.87
	-28	-60	-30	5.03	4	-62	-12	5.72

4.2. Conjunctions of the group effects: commonalities between controls and dyslexics

Pseudo-word silent reading

Both controls and dyslexics activated during pseudo-word reading the left inferior frontal cortex, the left precentral gyrus, the left superior temporal pole, the inferior occipital gyrus, bilaterally, and the left cerebellar hemisphere (table sr-5a. and figure 2: row 1, column C).

Auditory rhyming

Phonological awareness for spoken syllables was associated with activation in the left middle and inferior temporal and inferior frontal cortices, in both controls and dyslexics. A right-sided activation was present in the middle temporal gyrus (table sr-5b and figure 2: row 2, column C).

Visual motion perception task

Comparison of the moving Gabor patches with the stationary ones evoked a significant activation in the lateral occipito-temporal cortex bilaterally (including area MT/V5) in both controls and subjects with dyslexia. In addition, there was robust bilateral activation in the dorsal posterior-parietal and dorsal-premotor cortices normally involved in eye movement control (table sr-5c and figure 2: row 3, column C).

Motor sequence learning task

The new-sequence motor learning was associated with a widespread cortico-subcortical activation involving the left superior frontal cortex, the middle frontal gyrus, bilaterally, the right inferior frontal gyrus, the left SMA, the insula, bilaterally, the left postcentral gyrus, the right inferior temporal and supramarginal gyri, the left precuneus, the right inferior and superior parietal lobule, and the cerebellum, bilaterally, in both controls and dyslexics, as assessed by conjunction analyses (table sr-5d and figure 2: row 4, column C).

Table sr-3: Brain activations observed in both controls and dyslexics in the fMRI tasks (conjunction effects at p< .05 FWE-corrected). *: V5/MT

				MNI Co	ordinates					
	x	у	Z	Z score	x	у	Z	Z score		
Brain regions		Left he	mispher	•e	Right hemisphere					
				d reading	Right hemisphere					
Inf. frontal gyrus, pars triangularis	-40	26	2	5.9						
Inf. frontal gyrus, pars opercularis	-50	12	2	5.4						
	-58	6	16	4.8						
Precentral gyrus	-48	0	50	6.1						
	-52	6	46	6.1						
Sup. temporal pole	-52	12	-4	5.3						
Inf. occipital gyrus	-26	-98	-8	>8	24	-100	-2	>8		
					34	-94	-2	6.7		
Cerebellum	-40	-72	-22	5.4						
			uditory r	hyming						
Inf. frontal gyrus, pars triangularis	-48	20	26	5.6						
Mid. temporal gyrus	-60	-18	-8	6.2	58	-36	-2	4.8		
					60	-14	-10	4.4		
Inf. temporal gyrus	-52	-48	-20	4.7						
			l motion	perception						
Sup. frontal gyrus	-24	-8	56	6.2						
Precentral gyrus	-46	-2	48	4.6	48	-2	48	6.0		
	-52	0	44	4.5	28	-6	54	5.7		
Sup. temporal gyrus					60	-36	14	5.5		
Supramarginal gyrus	-44	-40	32	4.7						
Sup. parietal lobule					28	-50	58	7.2		
Inf. parietal lobule	-28	-50	56	7.7						
Mid. temporal gyrus					46	-66	4	>8*		
Mid. occipital gyrus	-44	-72	2	>8*	30	-80	32	6.0		
	-26	-78	28	6.7	30	-86	24	5.4		
Inf. occipital gyrus					44	-82	-6	5.7		
~ ~ ~			Motor le	0						
Sup. frontal gyrus	-26	-8	60	6.9	40	20	20			
Mid. frontal gyrus	-42	26	34	5.8	40	38	28	7.6		
	-38	50	14	5.2	28	8	58	7.3		
					56	-40	-16	5.2		
Supramarginal gyrus	10	50		4.5	42	-30	42	>8		
Precuneus	-10	-52	74	4.5						
	-14	-48	76	4.4	20	E.C.	E.C.	7.0		
Sup. parietal lobule					38	-56	56	7.8		
T.C					16	-66	62	7.2		
Inf. parietal lobule	0	02	24	5.2	46	-44	52	>8		
Cerebellum	-8	-82	-24	5.3	22	-54	-30	5.7		
	-26	-62	-30	4.7	4	-64	-14	5.6		

 Table sr-4: Marsbar results are reported for all ROIs from Paulesu et al. 2014.

		C>D READING				C>D READING > RHYMING				C>D READING > "MAGNO"				
ROI LABEL	Stereotactic coordinates of ROIs centroids	Contrast value	t statistic	Uncorrected P	Corrected P	Contrast value	t statistic	Uncorrected P	Corrected P	Contrast value	t statistic	Uncorrected P	Corrected P	
L5 - Fusiform gyrus	-41 -60 -18	.55	3.88	< .001	< .001	.48	2.44	.008	.07	.53	2.51	.006	.06	
L6 - Inf. temporal gyrus	-50 -61 -9	.50	4.00	< .001	< .001	.52	2.93	.002	.02	.64	3.44	< .001	< .001	
L23 - Inf. temporal gyrus	-45 -49 -15	.35	4.78	< .001	< .001	0.38	3.68	< .001	.001	.40	3.65	< .001	.002	
L86 - Mid. temporal gyrus	-58 -58 6	.31	2.54	.006	.05	0.24	1.39	.08	.54	.29	1.58	.06	.41	
L89 - Supramarginal gyrus	-55 -47 35	.14	1.39	.08	.54	0.19	1.33	.09	.58	.16	1.08	.145	.75	
L30 - Inf. parietal lobule	-43 -40 46	.24	2.36	.01	.08	0.40	2.82	.003	.02	.30	2.03	.02	.18	
L34 - Sup. parietal lobule	-19 -67 54	.14	.99	.16	.79	.36	1.79	.04	.29	04	17	.57	1.00	
L38 - Precentral gyrus	-41 -5 42	03	35	.64	1.00	01	10	.54	1.00	.11	.84	.2	.87	
L16 - SMA	-5 -4 62	12	99	.84	1.00	06	39	.65	1.00	.01	.03	.49	1.00	

Figure Caption

Figure SF-1: Graphic representation of the nine control-specific clusters reported by Paulesu and colleagues in a meta-analysis on developmental dyslexia and used in this work for small volume correction.

Figure SF-2: Graphic representation of the latency gradient for controls and dyslexics in pseudoword reading, word reading and picture naming.

Figure SF 3: The scatter plots (with the SEMs in red) for the 1-OTC cluster hypoactivated in dyslexics and used for Marsbar analyses.

Figure SF 4-12: The scatter plots (with the SEMs in red) for the nine ROIs from Paulesu et al. (2014) used for Marsbar analyses.