

212 **Supplementary Table 1: Hardy - Weinberg equilibrium test for *MTHFD1***
 213 **polymorphisms.**

Loci	Genotypes	Observations	Expectations	χ^2	P-value
rs11627387	AA	93	95.31	0.146	0.703
	AG	316	311.38		
	GG	252	254.31		
rs1076991	TT	368	370.50	0.268	0.604
	TC	253	248.00		
	CC	39	41.50		
rs2236224	GG	326	315.05	3.980	0.056
	GA	260	281.89		
	AA	74	63.05		
rs2236225	GG	375	371.44	0.545	0.460
	GA	241	248.12		
	AA	45	41.44		

214 *MTHFD1*: Methylene tetrahydrofolate dehydrogenase, cyclohydrolase, and
 215 formyl tetrahydrofolate synthetase 1.

216 **Supplementary Table 2: Comparison of *MTHFD1* polymorphisms in children.**

Loci	Genotypes/Allele	CG	HFG	χ^2	P-value
rs11627387	AA	47 (14.20)	46 (13.94)		
	AG	160 (48.34)	156 (47.27)	0.123	0.940
	GG	124 (37.46)	128 (38.79)		
	AG+GG	284 (85.80)	284 (86.06)	0.009	0.923
	A	254 (38.37)	248 (37.58)		
	G	408 (61.63)	412 (62.42)	0.088	0.766
rs1076991	TT	184 (55.76)	184 (55.76)		
	TC	128 (38.79)	125 (37.88)	0.266	0.875
	CC	18 (5.45)	21 (6.36)		
	TC+CC	146 (44.24)	146 (44.24)	0.000	1.000
	T	496 (75.16)	493 (74.70)		
	C	164 (24.85)	167 (25.30)	0.036	0.849
rs2236224	GG	164 (49.55)	162 (49.24)		
	GA	133 (40.18)	127 (38.60)	0.631	0.729
	AA	34 (10.27)	40 (12.16)		
	GA+AA	167 (50.45)	167 (50.76)	0.006	0.937
	G	461 (69.64)	451 (68.54)		
	A	201 (30.36)	207 (31.46)	0.186	0.666
rs2236225	GG	191 (57.70)	184 (55.76)		
	GA	118 (35.65)	123 (37.27)	0.255	0.880
	AA	22 (6.65)	23 (7.00)		
	GA+AA	140 (42.30)	146 (44.24)	0.255	0.614
	G	500 (75.53)	491 (74.39)		
	A	162 (24.47)	169 (25.61)	0.227	0.643

217 CG: Control group; HFG: High fluoride group; *MTHFD1*: Methylene tetrahydrofolate
 218 dehydrogenase, cyclohydrolase, and formyltetrahydrofolate synthetase 1.

219 **Supplementary Table 3: Regression analyses of *MTHFD1* polymorphisms and intelligence levels in the total group.**

Loci	Genotypes/Allele	Intelligence levels					
		High normal (<i>n</i> = 173)		Superior (<i>n</i> = 216)		Excellent (<i>n</i> = 182)	
		OR (95% CI)	<i>P</i> -value	OR (95% CI)	<i>P</i> -value	OR (95% CI)	<i>P</i> -value
Total (<i>n</i> = 683)							
rs11627387	AA	Reference		Reference		Reference	
	AG	0.489 (0.185–1.289)	0.148	1.043 (0.387–2.811)	0.933	1.066 (0.371–3.061)	0.906
	GG	0.579 (0.198–1.692)	0.318	2.071 (0.715–6.000)	0.180	1.792 (0.574–5.598)	0.316
	AG+GG	0.488 (0.196–1.217)	0.124	1.286 (0.505–3.273)	0.598	1.216 (0.448–3.300)	0.701
	A	Reference		Reference		Reference	
rs1076991	G	0.779 (0.482–1.257)	0.306	1.360 (0.860–2.153)	0.189	1.238 (0.762–2.012)	0.388
	TT	Reference		Reference		Reference	
	CT	0.700 (0.343–1.426)	0.326	0.845 (0.436–1.641)	0.620	0.847 (0.415–1.728)	0.648
	CC	1.562 (0.291–8.398)	0.603	1.902 (0.363–9.965)	0.477	3.294 (0.637–17.035)	0.155
	CT+TT	0.762 (0.384–1.512)	0.437	0.903 (0.475–1.718)	0.757	1.023 (0.517–2.023)	0.948
	T	Reference		Reference		Reference	
	C	0.878 (0.504–1.528)	0.645	0.986 (0.585–1.660)	0.957	1.193 (0.693–2.057)	0.524

rs2236224	GG	Reference		Reference		Reference	
	AG	0.611 (0.296–1.260)	0.182	0.889 (0.451–1.750)	0.733	1.158 (0.564–2.378)	0.689
	AA	0.519 (0.161–1.676)	0.273	1.104 (0.375–3.250)	0.857	0.729 (0.227–2.343)	0.596
	AG+GG	0.582 (0.296–1.145)	0.117	0.922 (0.490–1.738)	0.803	1.050 (0.536–2.058)	0.886
	G	Reference		Reference		Reference	
	A	0.641 (0.380–1.082)	0.096	0.969 (0.599–1.568)	0.899	0.953 (0.573–1.587)	0.854
rs2236225	GG	Reference		Reference		Reference	
	AG	0.756 (0.364–2.749)	0.455	1.036 (0.522–2.058)	0.919	1.291 (0.626–2.662)	0.489
	AA	0.334 (0.074–1.516)	0.155	0.907 (0.255–3.226)	0.880	0.799 (0.206–3.105)	0.746
	AG+GG	0.666 (0.332–1.335)	0.252	1.011 (0.530–1.931)	0.973	1.215 (0.613–2.406)	0.577
	G	Reference		Reference		Reference	
	A	0.651 (0.367–1.155)	0.142	0.985 (0.583–1.663)	0.954	1.080 (0.623–1.871)	0.763

220 Analyses were adjusted for age, gender, BMI, age at which pregnancy occurred, gestational weeks, birth modes, birth weight, and paternal and
221 maternal education level. Normal intelligence children were referenced ($n = 112$).

222 BMI: Body mass index; CI: Confidence interval; *MTHFD1*: Methylene tetrahydrofolate dehydrogenase, cyclohydrolase, and
223 formyltetrahydrofolate synthetase 1; OR: Odds ratio.

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228 **Supplementary Table 4: Regression analyses of *MTHFD1* polymorphisms and intelligence levels in the CG.**

Loci	Genotypes		Intelligence levels				
	/Allele	High normal (<i>n</i> = 85)		Superior (<i>n</i> = 113)		Excellent (<i>n</i> = 84)	
		OR (95% CI)	<i>P</i> -val ue	OR (95% CI)	<i>P</i> -val ue	OR (95% CI)	<i>P</i> -val ue
CG (<i>n</i> = 342)							
rs11627387	AA	Reference		Reference		Reference	
	AG	1.203 (0.280–5.177)	0.804	1.751 (0.382–8.028)	0.471	1.215 (0.231–6.394)	0.818
	GG	0.554 (0.122–2.525)	0.446	2.554 (0.565–11.552)	0.223	1.432 (0.272–7.534)	0.672
	AG+GG	0.652 (0.176–2.420)	0.523	1.814 (0.462–7.24)	0.393	1.126 (0.247–5.127)	0.878
	A	Reference		Reference		Reference	
rs1076991	G	0.708 (0.364–1.375)	0.308	1.278 (0.673–2.429)	0.453	0.944 (0.459–1.943)	0.875
	TT	Reference		Reference		Reference	
	CT	0.681 (0.253–1.833)	0.447	0.606 (0.241–1.525)	0.287	0.553 (0.189–1.613)	0.278
	CC	1.774 (0.160–19.679)	0.640	1.728 (0.164–18.188)	0.649	1.582 (0.134–18.624)	0.715
	CT+TT	0.732 (0.283–1.898)	0.521	0.666 (0.271–1.634)	0.375	0.633 (0.226–1.776)	0.385
rs2236224	T	Reference		Reference		Reference	
	C	0.888 (0.423–1.866)	0.755	0.817 (0.405–1.649)	0.573	0.801 (0.362–1.774)	0.584
	GG	Reference		Reference		Reference	

	AG	0.900 (0.343–2.360)	0.830	1.044 (0.418–2.610)	0.926	1.220 (0.429–3.470)	0.709
	AA	0.922 (0.130–6.532)	0.935	2.601 (0.427–15.836)	0.300	0.626 (0.071–5.487)	0.672
	AG+AA	0.831 (0.330–2.089)	0.694	1.190 (0.496–2.856)	0.697	1.034 (0.382–2.801)	0.948
	G	Reference		Reference		Reference	
	A	0.846 (0.414–1.728)	0.645	1.276 (0.656–2.483)	0.473	0.890 (0.415–1.909)	0.764
rs2236225	GG	Reference		Reference		Reference	
	AG	0.791 (0.293–2.134)	0.643	1.290 (0.506–3.289)	0.593	1.520 (0.533–4.332)	0.434
	AA	1.562 (0.131–18.577)	0.724	4.046 (0.391–41.851)	0.241	0.804 (0.050–12.898)	0.877
	AG+AA	0.801 (0.306–2.095)	0.650	1.430 (0.581–3.523)	0.436	1.345 (0.487–3.717)	0.567
	G	Reference		Reference		Reference	
	A	0.891 (0.402–1.975)	0.775	1.495 (0.717–3.116)	0.284	1.108 (0.482–2.546)	0.810

229 Analyses were adjusted for age, gender, BMI, age at which pregnancy occurred, gestational weeks, birth modes, birth weight, and paternal and
 230 maternal education level. Normal intelligence children were referenced ($n = 60$).

231 BMI: Body mass index; CG: Control group; CI: Confidence interval; *MTHFD1*: Methylenetetrahydrofolate dehydrogenase, cyclohydrolase, and
 232 formyltetrahydrofolate synthetase 1; OR: Odds ratio.

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Models	<i>F</i>	<i>P</i>-value
Locus 1 * Locus 2	0.573	0.682
Locus 1 * Locus 3	1.901	0.151
Locus 1 * Locus 4	0.342	0.710
Locus 2 * Locus 3	0.319	0.865
Locus 2 * Locus 4	0.714	0.583
Locus 3 * Locus 4	0.406	0.666
Locus 1 * Locus 2 * Locus 3	1.362	0.181
Locus 1 * Locus 2 * Locus 4	1.726	0.059
Locus 1 * Locus 3 * Locus 4	1.340	0.238
Locus 2 * Locus 3 * Locus 4	0.602	0.827
Locus 1 * Locus 2 * Locus 3 * Locus 4	1.461	0.088
UF _{Cr} * Locus 1	0.785	0.456
UF _{Cr} * Locus 2	1.804	0.166
UF _{Cr} * Locus 3	0.957	0.385
UF _{Cr} * Locus 4	0.147	0.864
UF _{Cr} * Locus 1 * Locus 2	0.861	0.579
UF _{Cr} * Locus 1 * Locus 3	1.403	0.202
UF _{Cr} * Locus 1 * Locus 4	0.333	0.939
UF _{Cr} * Locus 2 * Locus 3	1.706	0.063
UF _{Cr} * Locus 2 * Locus 4	1.606	0.088
UF _{Cr} * Locus 3 * Locus 4	0.628	0.708
UF _{Cr} * Locus 1 * Locus 2 * Locus 3	1.669	0.021
UF _{Cr} * Locus 1 * Locus 2 * Locus 4	1.764	0.012
UF _{Cr} * Locus 1 * Locus 3 * Locus 4	1.807	0.368
UF _{Cr} * Locus 2 * Locus 3 * Locus 4	1.385	0.113
UF _{Cr} * Locus 1 * Locus 2 * Locus 3 * Locus 4	1.614	0.012

239 Analyses were adjusted for age, gender, BMI, age at which pregnancy occurred,
 240 gestational weeks, birth modes, birth weight, and paternal and maternal education
 241 level. BMI: Body mass index; Locus 1: rs11627387; Locus 2: rs1076991; Locus 3:
 242 rs2236224; Locus 4: rs2236225; UF_{Cr}: Urinary creatinine-adjusted urinary fluoride.