

eFIGURE. Folate- and B vitamin-dependent one-carbon metabolism pathways

eTABLE 1. Periconceptual Vitamin Intake by Maternal Characteristics of Children with Typical Development (n=278) in the Childhood Autism Risks from Genetics and the Environment Study, Northern California, 2003–2009

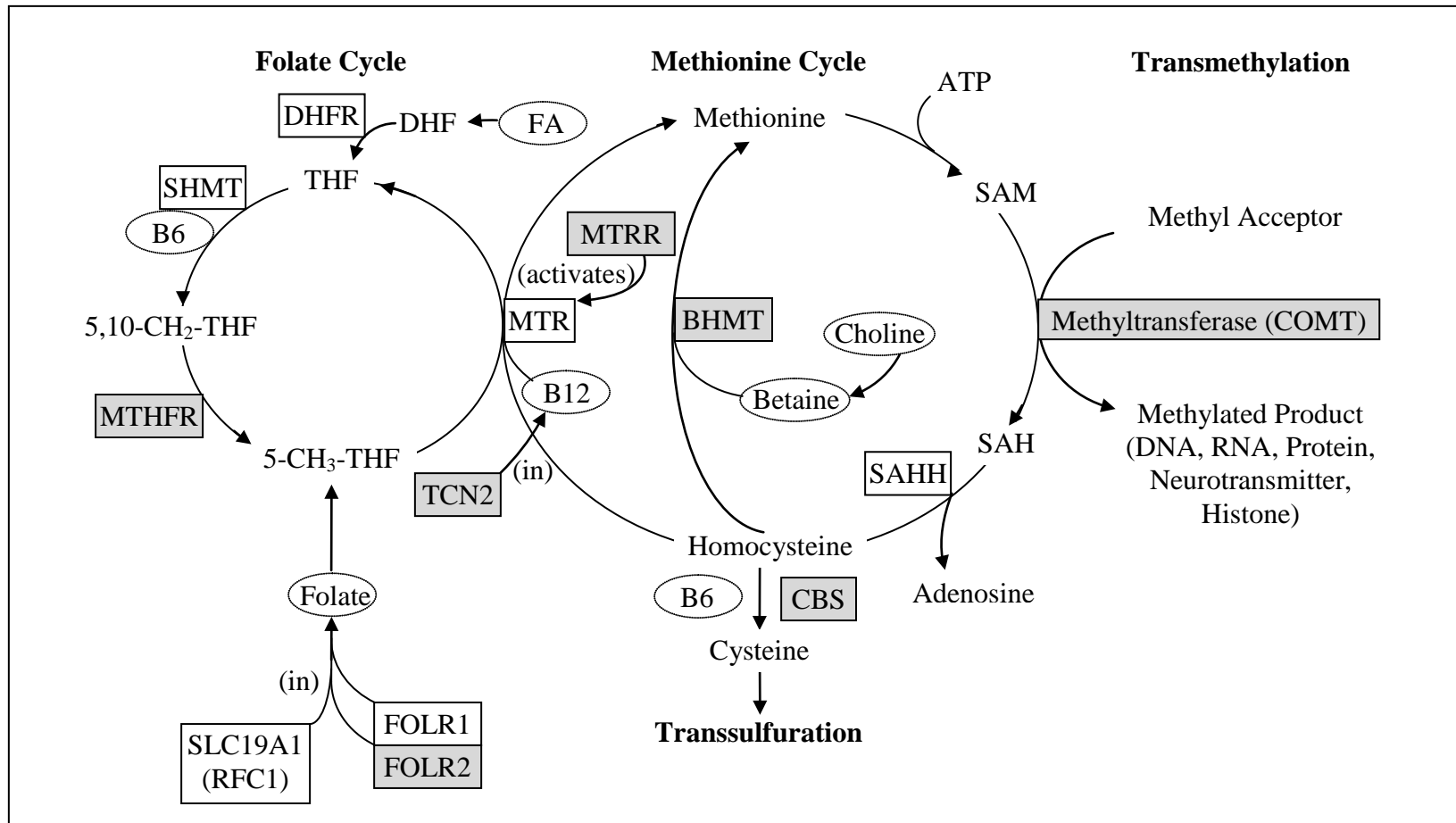
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eAPPENDIX. Interview questions for ascertaining vitamin intake before and during pregnancy



eFIGURE. Folate- and B vitamin-dependent one-carbon metabolism pathways. Enzymes are in boxes, vitamin substrates/cofactors are in ellipses. Shaded genes had variants examined for interactions in this study. Adapted from James et al, 2006. Abbreviations: DHFR, dihydrofolate reductase; DHF, dihydrofolate; FA, Folic acid; THF, tetrahydrofolate; SHMT, serine hydromethyltransferase; 5,10-CH₂-THF, 5,10-methylenetetrahydrofolate; MTHFR, methylenetetrahydrofolate reductase; 5-CH₃-THF, 5-methyltetrahydrofolate; SLC19A1, solute carrier family 19 member 1; FOLR1, folate receptor 1; FOLR2, folate receptor 2; MTR, 5-methyltetrahydrofolate-homocysteine methyltransferase; MTRR, 5-methyltetrahydrofolate-homocysteine methyltransferase reductase; TCN2, transcobalamin II; BHMT, betaine-homocysteine methyltransferase; SAM, S-adenosylmethionine; COMT, catechol-O-methyltransferase; SAH, S-adenosylhomocysteine; SAHH, SAH hydrolase; CBS, cystathionine beta synthase.

eTABLE 1. Periconceptual Vitamin Intake by Maternal Characteristics of Children with Typical Development (n=278) in the Childhood Autism Risks from Genetics and the Environment Study, Northern California, 2003–2009

Maternal Characteristic	Periconceptual Prenatal Vitamin ^a (n=159) No. (%)	Periconceptual Multivitamin ^{a,b} (n=18) No. (%)	Neither (n=61) No. (%)
Race/ethnicity			
Non-Hispanic white	110 (70)	12 (71)	29 (48)
Hispanic	24 (15)	3 (18)	18 (30)
Non-Hispanic black, Asian, mixed, and other	24 (15)	2 (12)	14 (23)
Age at child's birth (years)			
≤ 19	3 (2)	1 (6)	6 (10)
20-29	61 (39)	3 (17)	28 (46)
30-34	67 (42)	10 (56)	18 (30)
35 +	27 (17)	4 (22)	9 (15)
Birthplace			
United States	140 (88)	12 (67)	44 (72)
Mexico	2 (1)	1 (6)	11 (18)
Other	17 (11)	5 (28)	6 (10)
Education			
High school graduate or less	15 (9)	2 (11)	17 (28)
Some college, technical, vocational, associate degree	50 (31)	4 (22)	18 (30)
Bachelor, masters, professional, doctorate degree	94 (59)	12 (67)	26 (43)
Insurance delivery type			
Private	140 (88)	17 (94)	50 (82)
Government program	19 (12)	1 (6)	11 (18)
Intention to become pregnant			
Intended to become pregnant when she did	127 (80)	12 (67)	33 (56)
Indifferent about becoming pregnant at that time	15 (9)	3 (17)	11 (19)
Intended to become pregnant later	11 (7)	2 (11)	9 (15)
Did not intend to become pregnant at all	5 (3)	1 (6)	6 (10)
Cigarette smoking ^c			
No	142 (92)	16 (89)	50 (83)
Yes	12 (8)	2 (11)	10 (17)
Alcohol consumption ^c			
No	77 (51)	8 (53)	29 (50)
Yes	75 (49)	7 (47)	29 (50)

^a Any reported for the three months before pregnancy and the first month of pregnancy.

^b Mothers who reported both prenatal vitamin intake and multivitamin intake during this period were included under periconceptual prenatal vitamin and excluded from periconceptual multivitamin.

^c Any reported for the period three months before pregnancy through the end of pregnancy.

eTABLE 2. Maternal and Child Genotypes by Periconceptual Prenatal Vitamin Intake and Risk for Autism Spectrum Disorder

Gene Variant		Periconceptual Prenatal Vitamin ^a	Genotype	Autism Spectrum Disorder ^b No. (%)	Typical Development No. (%)	OR ^c (95% CI)	Expected Joint OR: Additive Model	Expected Joint OR: Multiplicative Model
<i>MTHFR</i> 667	Maternal	Yes	CC+CT ^d	152 (50)	106 (57)	1.0	1.0	0.90
			TT	21 (7)	22 (12)	0.65 (0.33–1.3)		
		No	CC+CT	113 (37)	53 (29)	1.4 (0.90–2.1)		
			TT	17 (6)	4 (2)	3.4 (1.1–10.8)		
	Child	Yes	CC+CT ^d	152 (52)	103 (58)	1.0		
			TT	14 (5)	18 (10)	0.59 (0.28–1.3)		
		No	CC+CT	109 (37)	46 (26)	1.5 (0.96–2.3)	1.1	0.89
			TT	19 (6)	11 (6)	1.1 (0.48–2.5)		
<i>COMT</i> 472	Maternal	Yes	GG+GA ^d	127 (43)	109 (58)	1.0	2.5	3.0
			AA	40 (14)	20 (11)	1.6 (0.81–3.2)		
		No	GG+GA	106 (36)	50 (27)	1.9 (1.2–2.9)		
			AA	23 (8)	8 (4)	2.0 (0.78–5.3)		
	Child	Yes	GG+GA ^d	119 (41)	100 (56)	1.0		
			AA	45 (16)	22 (12)	1.8 (1.0–3.3)		
		No	GG+GA	94 (32)	54 (30)	1.4 (0.89–2.2)	2.2	2.5
			AA	32 (11)	4 (2)	7.3 (2.4–22.1)		
<i>CBS</i>	Maternal	Yes	GG ^d	109 (36)	88 (47)	1.0	1.6	1.7
			GT+TT	63 (21)	42 (22)	1.4 (0.80–2.5)		
		No	GG	73 (24)	40 (21)	1.2 (0.73–2.0)		
			GT+TT	57 (19)	18 (10)	3.2 (1.6–6.5)		
	Child	Yes	GG ^d	116 (39)	79 (43)	1.0		
			GT+TT	52 (18)	44 (24)	0.61 (0.34–1.1)		
		No	GG	84 (28)	40 (22)	1.3 (0.78–2.1)	0.90	0.79
			GT+TT	44 (15)	20 (11)	1.3 (0.62–2.6)		
<i>MTRR</i> 66	Maternal	Yes	AA ^d	58 (19)	36 (19)	1.0		
			AG+GG	120 (38)	97 (50)	0.88 (0.53–1.5)		
		No	AA	43 (14)	26 (13)	1.1 (0.54–2.1)	0.94	0.93
			AG+GG	92 (29)	35 (18)	1.7 (0.93–3.0)		

eTABLE 2. Continued

Gene Variant		Periconceptional Prenatal Vitamin ^a	Genotype	Autism Spectrum Disorder ^b No. (%)	Typical Development No. (%)	OR ^c (95% CI)	Expected Joint OR: Additive Model	Expected Joint OR: Multiplicative Model
<i>MTRR</i> 66	Child	Yes	AA ^d	48 (17)	40 (23)	1.0	2.1	2.4
			AG+GG	117 (40)	82 (46)	1.3 (0.77–2.2)		
		No	AA	41 (14)	19 (11)	1.8 (0.90–3.7)		
			AG+GG	84 (29)	36 (20)	2.0 (1.1–3.6)		
<i>BHMT</i> 716	Maternal	Yes	GG ^d	95 (31)	62 (33)	1.0	0.84	0.82
			GA+AA	79 (26)	67 (36)	0.77 (0.46–1.3)		
		No	GG	60 (20)	30 (16)	1.1 (0.59–1.9)		
			GA+AA	71 (23)	28 (15)	1.7 (0.91–3.1)		
	Child	Yes	GG ^d	82 (28)	57 (31)	1.0	1.2	1.1
			GA+AA	86 (29)	65 (36)	0.86 (0.52–1.4)		
		No	GG	65 (22)	33 (18)	1.3 (0.74–2.4)		
			GA+AA	61 (21)	26 (14)	1.5 (0.82–2.9)		
<i>FOLR2</i>	Maternal	Yes	GG+GA ^d	56 (20)	43 (24)	1.0	1.2	1.2
			AA	112 (39)	82 (46)	1.0 (0.61–1.7)		
		No	GG+GA	38 (13)	23 (13)	1.2 (0.59–2.3)		
			AA	81 (28)	29 (16)	2.0 (1.1–3.6)		
	Child	Yes	GG+GA ^d	67 (24)	46 (26)	1.0	1.6	1.6
			AA	96 (34)	75 (42)	0.93 (0.57–1.5)		
		No	GG+GA	47 (17)	19 (11)	1.7 (0.86–3.3)		
			AA	74 (26)	39 (22)	1.2 (0.71–2.2)		
<i>TCN2</i>	Maternal	Yes	CC ^d	62 (21)	41 (22)	1.0	1.8	1.7
			CG+GG	110 (36)	88 (47)	0.82 (0.47–1.4)		
		No	CC	39 (13)	12 (6)	2.0 (0.88–4.6)		
			CG+GG	91 (30)	46 (25)	1.2 (0.63–2.1)		
	Child	Yes	CC ^d	52 (18)	45 (25)	1.0	2.8	3.6
			CG+GG	115 (39)	74 (42)	1.6 (0.89–2.8)		
		No	CC	38 (13)	15 (8)	2.3 (1.0–5.0)		
			CG+GG	88 (30)	43 (24)	2.1 (1.1–3.9)		

^a Any reported for the three months before pregnancy and the first month of pregnancy.

^b Autism spectrum disorder was defined using the criteria of Risi et al, 2006, which requires: 1) meeting the cutoff for autism spectrum disorder on ADOS Module 1 or 2; 2) meeting the cutoff for Abnormality of Development at ≤ 36 months on the ADI-R; *and* 2) meeting the criteria on Social and Communication domains on the ADI-R, *or* meeting criteria on Social and within 2 points on Communication, *or* meeting criteria on Communication and within 2 points on Social Criteria, *or* being within 1 point of cutoffs on both Social and Communication domains.

^c ORs adjusted for maternal education and child's birth year. ORs for maternal *COMT* 472 adjusted for child genotype. Maternal and child *CBS* adjusted for one another. Maternal and child *BHMT* adjusted for one another. Maternal and child *TCN2* adjusted for one another.

^d Reference category.

eTABLE 3. Associations between Maternal Periconceptional Vitamin Intake and Risk for Autism Spectrum Disorder

Periconceptional Vitamin Intake ^a	Autism Spectrum Disorder ^b (n=429) No. (%)	Typical Development (n=278) No. (%)	OR ^c (95% CI)	Weighted OR ^c (95% CI)
Prenatal Vitamin				
None ^d	176 (46)	70 (31)		
Any	209 (54)	159 (69)	0.59 (0.41–0.84)	0.57 (0.38–0.87)
Prenatal Vitamin Frequency ^e				
None ^d	176 (46)	70 (31)		
Irregular or < 4 days/week	12 (3)	7 (3)	0.66 (0.24–1.8)	0.88 (0.32–2.4)
4 Days/week – daily	185 (48)	138 (60)	0.61 (0.42–0.88)	0.58 (0.37–0.88)
> Daily	12 (3)	14 (6)	0.38 (0.17–0.89)	0.44 (0.18–1.1)
Test for trend ^f			<i>P</i> < .0001	<i>P</i> < .0001
Multivitamin ^g				
None ^d	173 (84)	91 (83)		
Any	34 (16)	18 (17)	1.1 (0.56–2.1)	1.1 (0.50–2.3)

^a Any reported for the three months before pregnancy and the first month of pregnancy.

^b Autism spectrum disorder was defined using the criteria of Risi et al, 2006, which requires: 1) meeting the cutoff for autism spectrum disorder on ADOS Module 1 or 2; 2) meeting the cutoff for Abnormality of Development at ≤ 36 months on the ADI-R; *and* 2) meeting the criteria on Social and Communication domains on the ADI-R, *or* meeting criteria on Social and within 2 points on Communication, *or* meeting criteria on Communication and within 2 points on Social Criteria, *or* being within 1 point of cutoffs on both Social and Communication domains.

^c Odds ratios adjusted for maternal education and child's birth year.

^d Reference category.

^e Frequency categories determined *a priori* based on similar vitamin metabolite levels for those taking supplements regularly (most days/week) and those taking them daily. If those with 4-6 days/week are moved to the second category, the test for trend remains significant (*P* < .0001).

^f Two-sided *p* value for test of trend.

^g Mothers who reported intake of prenatal vitamins during this period were excluded.

eTABLE 4. Weighted Analyses Results for Selected Maternal and Child Genotypes by Periconceptional Prenatal Vitamin Intake and Risk for Autism and Autism Spectrum Disorder

Gene Variant		Periconceptional Prenatal Vitamin ^a	Genotype	Autism OR ^b (95% CI)	Autism Spectrum Disorder ^c OR ^b (95% CI)
<i>MTHFR</i> 667	Maternal	Yes	CC+CT ^d	1.0	1.0
			TT	0.64 (0.27–1.5)	0.54 (0.25–1.2)
		No	CC+CT	1.2 (0.69–2.0)	1.4 (0.83–2.2)
			TT	3.7 (0.78–17.7)	2.7 (0.57–12.9)
	Child	Yes	CC+CT ^d	1.0	1.0
			TT	0.76 (0.28–2.1)	0.78 (0.33–1.9)
		No	CC+CT	1.5 (0.90–2.6)	1.6 (0.99–2.7)
			TT	0.38 (0.12–1.2)	0.86 (0.34–2.2)
<i>COMT</i> 472	Maternal	Yes	GG+GA ^d	1.0	1.0
			AA	1.3 (0.51–3.2)	1.4 (0.64–3.3)
		No	GG+GA	1.7 (0.96–3.0)	1.9 (1.1–3.2)
			AA	1.6 (0.51–4.8)	2.0 (0.71–5.5)
	Child	Yes	GG+GA ^d	1.0	1.0
			AA	1.7 (0.80–3.5)	1.7 (0.87–3.5)
		No	GG+GA	1.2 (0.67–2.1)	1.4 (0.84–2.3)
			AA	9.7 (2.4–38.9)	9.4 (2.4–37.7)
<i>CBS</i>	Maternal	Yes	GG ^d	1.0	1.0
			GT+TT	1.1 (0.52–2.2)	1.5 (0.80–2.9)
		No	GG	1.0 (0.55–2.0)	1.2 (0.69–2.2)
			GT+TT	2.5 (1.1–5.9)	3.4 (1.5–7.8)
	Child	Yes	GG ^d	1.0	1.0
			GT+TT	0.62 (0.29–1.3)	0.57 (0.29–1.1)
		No	GG	1.2 (0.65–2.3)	1.4 (0.76–2.4)
			GT+TT	1.1 (0.46–2.5)	1.1 (0.49–2.3)
<i>MTRR</i> 66	Maternal	Yes	AA ^d	1.0	1.0
			AG+GG	0.90 (0.49–1.7)	0.99 (0.56–1.7)
		No	AA	0.87 (0.38–2.0)	1.0 (0.49–2.2)
			AG+GG	1.8 (0.88–3.8)	2.0 (1.0–4.0)
	Child	Yes	AA ^d	1.0	1.0
			AG+GG	1.3 (0.68–2.4)	1.3 (0.75–2.4)
		No	AA	1.9 (0.81–4.4)	2.1 (0.94–4.5)
			AG+GG	1.7 (0.82–3.4)	1.9 (0.98–3.6)
<i>BHMT</i> 716	Maternal	Yes	GG ^d	1.0	1.0
			GA+AA	0.94 (0.50–1.8)	0.77 (0.43–1.4)
		No	GG	1.0 (0.50–2.2)	1.1 (0.56–2.2)
			GA+AA	1.7 (0.82–3.6)	1.7 (0.86–3.3)
	Child	Yes	GG ^d	1.0	1.0
			GA+AA	0.81 (0.43–1.5)	0.87 (0.49–1.5)
		No	GG	1.1 (0.53–2.2)	1.3 (0.65–2.5)
			GA+AA	1.5 (0.69–3.3)	1.7 (0.8–3.4)

eTABLE 4. Continued

Gene Variant		Periconceptional Prenatal Vitamin ^a	Genotype	Autism OR ^b (95% CI)	Autism Spectrum Disorder ^c OR ^b (95% CI)
<i>FOLR2</i>	Maternal	Yes	GG+GA ^d	1.0	1.0
			AA	1.5 (0.77–2.8)	1.4 (0.76–2.6)
		No	GG+GA	1.3 (0.53–3.0)	1.4 (0.61–3.0)
			AA	2.7 (1.3–5.8)	2.7 (1.3–5.5)
	Child	Yes	GG+GA ^d	1.0	1.0
			AA	1.2 (0.63–2.1)	0.98 (0.56–1.7)
		No	GG+GA	1.6 (0.70–3.7)	1.5 (0.71–3.3)
<i>TCN2</i>	Maternal	Yes	CC ^d	1.0	1.0
			CG+GG	1.0 (0.50–2.1)	0.87 (0.46–1.7)
		No	CC	2.0 (0.73–5.4)	1.9 (0.77–4.7)
			CG+GG	1.3 (0.58–2.8)	1.3 (0.63–2.6)
	Child	Yes	CC ^d	1.0	1.0
			CG+GG	1.7 (0.86–3.5)	1.5 (0.78–2.8)
		No	CC	2.7 (1.0–6.8)	2.7 (1.2–6.3)
			CG+GG	1.9 (0.84–4.3)	1.8 (0.88–3.8)

^a Any reported for the three months before pregnancy and the first month of pregnancy.

^b Weighted. ORs adjusted for maternal education and child's birth year. ORs for maternal *COMT* 472 adjusted for child genotype. Maternal and child *CBS* adjusted for one another. Maternal and child *BHMT* adjusted for one another. Maternal and child *TCN2* adjusted for one another.

^c Autism spectrum disorder was defined using the criteria of Risi et al, 2006, which requires: 1) meeting the cutoff for autism spectrum disorder on ADOS Module 1 or 2; 2) meeting the cutoff for Abnormality of Development at ≤ 36 months on the ADI-R; and 2) meeting the criteria on Social and Communication domains on the ADI-R, or meeting criteria on Social and within 2 points on Communication, or meeting criteria on Communication and within 2 points on Social Criteria, or being within 1 point of cutoffs on both Social and Communication domains.

^d Reference category.

eTABLE 5. Main Findings for Children of Non-Hispanic White Mothers

Gene Variant		Periconceptional Prenatal Vitamin ^a	Genotypes	Autism No. (%)	Typical Development No. (%)	OR ^b (95% CI)	Expected Joint OR: Additive Model	Expected Joint OR: Multiplicative Model
<i>MTHFR</i> 667	Maternal	No	All ^c	54 (35)	35 (24)	1.0	NA	NA
		Yes	All	100 (65)	110 (76)	0.65 (0.39–1.1)		
		Yes	CC+CT ^c	72 (55)	72 (63)	1.0		
			TT	13 (10)	16 (14)	0.74 (0.32–1.7)		
			CC+CT	38 (29)	24 (21)	1.4 (0.75–2.7)		
			TT	7 (5)	3 (3)	2.5 (0.57–10.6)		
	Child	Yes	CC+CT ^c	77 (59)	68 (62)	1.0	0.99	0.93
			TT	8 (6)	15 (14)	0.54 (0.21–1.4)		
			CC+CT	37 (28)	23 (21)	1.3 (0.70–2.5)		
			TT	8 (6)	3 (3)	2.0 (0.47–8.5)		
		No	GG+GA ^c	89 (45)	109 (58)	1.0		
			AA	26 (13)	20 (11)	1.7 (0.72–4.1)		
<i>COMT</i> 472	Maternal	Yes	GG+GA	70 (35)	50 (27)	1.9 (0.98–3.8)	2.6	3.3
			AA	13 (7)	8 (4)	3.1 (0.54–17.5)		
			GG+GA ^c	58 (46)	67 (60)	1.0		
			AA	24 (19)	16 (14)	1.9 (0.91–4.1)		
		No	GG+GA	31 (24)	24 (22)	1.4 (0.72–2.8)		
			AA	14 (11)	4 (4)	4.2 (1.3–14.1)		
	Child	Yes	GG+GA ^c	58 (46)	67 (60)	1.0	2.4	2.7
			AA	24 (19)	16 (14)	1.9 (0.91–4.1)		
			GG+GA	31 (24)	24 (22)	1.4 (0.72–2.8)		
			AA	14 (11)	4 (4)	4.2 (1.3–14.1)		
		No	GG+GA	31 (24)	24 (22)	1.4 (0.72–2.8)		
			AA	14 (11)	4 (4)	4.2 (1.3–14.1)		
<i>CBS</i>	Maternal	Yes	GG ^c	58 (44)	56 (48)	1.0	1.1	1.1
			GT+TT	27 (21)	33 (28)	1.1 (0.48–2.3)		
			GG	23 (18)	16 (14)	1.1 (0.48–2.5)		
			GT+TT	23 (18)	11 (9)	3.0 (1.1–8.0)		
		No	GG	23 (18)	16 (14)	1.1 (0.48–2.5)		
			GT+TT	23 (18)	11 (9)	3.0 (1.1–8.0)		
	Child	Yes	GG ^c	58 (45)	50 (45)	1.0	0.92	0.77
			GT+TT	26 (20)	34 (30)	0.57 (0.26–1.3)		
			GG	26 (20)	15 (13)	1.4 (0.61–3.0)		
			GT+TT	18 (14)	13 (12)	1.2 (0.44–3.3)		
		No	GG	26 (20)	15 (13)	1.4 (0.61–3.0)		
			GT+TT	18 (14)	13 (12)	1.2 (0.44–3.3)		

eTABLE 5. Continued

Gene Variant		Periconceptional Prenatal Vitamin ^a	Genotypes	Autism No. (%)	Typical Development No. (%)	OR ^b (95% CI)	Expected Joint OR: Additive Model	Expected Joint OR: Multiplicative Model
<i>MTRR</i> 66	Maternal	Yes	AA ^c	25 (18)	22 (18)	1.0	0.83	0.83
			AG+GG	63 (46)	69 (58)	0.85 (0.42–1.7)		
		No	AA	10 (7)	9 (8)	0.98 (0.32–3.0)		
			AG+GG	38 (28)	20 (17)	1.6 (0.69–3.7)		
	Child	Yes	AA ^c	18 (14)	21 (19)	1.0	1.4	1.5
			AG+GG	65 (51)	62 (57)	1.3 (0.62–2.8)		
		No	AA	10 (8)	9 (8)	1.1 (0.35–3.5)		
			AG+GG	35 (27)	16 (15)	2.5 (1.0–6.2)		
<i>BHMT</i> 716	Maternal	Yes	GG ^c	41 (31)	43 (37)	1.0	1.3	1.3
			GA+AA	45 (34)	45 (39)	1.0 (0.53–2.0)		
		No	GG	21 (16)	15 (13)	1.2 (0.50–3.0)		
			GA+AA	25 (19)	12 (10)	2.0 (0.82–5.0)		
	Child	Yes	GG ^c	37 (29)	38 (34)	1.0	1.6	1.6
			GA+AA	49 (38)	45 (41)	1.0 (0.53–2.0)		
		No	GG	22 (17)	16 (14)	1.5 (0.64–3.7)		
			GA+AA	21 (16)	12 (11)	1.7 (0.65–4.3)		
<i>FOLR2</i>	Maternal	Yes	GG+GA ^c	26 (21)	25 (23)	1.0	1.2	1.1
			AA	57 (46)	61 (56)	0.95 (0.48–1.9)		
		No	GG+GA	9 (7)	6 (6)	1.2 (0.35–4.1)		
			AA	33 (26)	17 (16)	1.9 (0.81–4.4)		
	Child	Yes	GG+GA ^c	35 (27)	28 (25)	1.0	1.6	1.4
			AA	49 (38)	55 (50)	0.74 (0.39–1.4)		
		No	GG+GA	12 (9)	5 (5)	1.9 (0.56–6.4)		
			AA	32 (25)	22 (20)	1.1 (0.49–2.3)		
<i>TCN2</i>	Maternal	Yes	CC ^c	27 (21)	28 (24)	1.0	3.0	2.6
			CG+GG	56 (43)	60 (52)	0.82 (0.37–1.8)		
		No	CC	12 (9)	4 (3)	3.2 (0.75–13.5)		
			CG+GG	34 (26)	23 (20)	1.1 (0.43–2.7)		

eTABLE 5. Continued

Gene Variant		Periconceptional Prenatal Vitamin ^a	Genotypes	Autism No. (%)	Typical Development No. (%)	OR ^b (95% CI)	Expected Joint OR: Additive Model	Expected Joint OR: Multiplicative Model
<i>TCN2</i>	Child	Yes	CC ^c	23 (18)	32 (30)	1.0		
			CG+GG	61 (48)	49 (45)	2.0 (0.92–4.5)		
		No	CC	8 (6)	8 (7)	1.6 (0.46–5.5)		
			CG+GG	36 (28)	19 (18)	3.2 (1.3–8.1)	2.6	3.3

Abbreviations: CI, confidence interval; OR, odds ratio.

^a Any reported for the three months before pregnancy and the first month of pregnancy.

^b ORs adjusted for maternal education and child's birth year. ORs for maternal *COMT* 472 adjusted for child genotype. Maternal and child *CBS* adjusted for one another. Maternal and child *BHMT* adjusted for one another. Maternal and child *TCN2* adjusted for one another.

^c Reference category.

eAPPENDIX. Interview questions for ascertaining vitamin intake before and during pregnancy

The next questions are about prenatal vitamins and other supplements you may have taken.

40. a. During the index time [and through the end of breast feeding], did you take any....	b. What was the brand name you took?
Prenatal vitamins	Y N RF DK
Multivitamins	Y N RF DK
Vitamin A	Y N RF DK
Vitamin B6	Y N RF DK
Vitamin B12	Y N RF DK
Folic acid	Y N RF DK
Vitamin C	Y N RF DK
Vitamin D	Y N RF DK
Vitamin E	Y N RF DK
Iron	Y N RF DK
Calcium	Y N RF DK
Zinc	Y N RF DK
Cereals	Y N RF DK
Other supplements e.g. Slim Fast, Instant Breakfast, protein powder, brewer's yeast	
ST John's worts	Y N RF DK
Ginseng	Y N RF DK

For each 'yes' response in 40:

41. During which months [including breastfeeding] did you take (VITAMIN/ SUPPLEMENT NAME)?

_____ -3 -2 -1 1 2 3 4 5 6 7 8 9 BF RF DK

_____ -3 -2 -1 1 2 3 4 5 6 7 8 9 BF RF DK

_____ -3 -2 -1 1 2 3 4 5 6 7 8 9 BF RF DK

42. How many pills/servings per day of (VITAMIN/ SUPPLEMENT NAME) did you take? And, what was the frequency for each dose/serving?

NAME	#PILLS/SERVINGS	FREQUENCY
_____	_____ RF DK	_____ RF DK
_____	_____ RF DK	_____ RF DK
_____	_____ RF DK	_____ RF DK