

## SUPPLEMENTARY MATERIAL

### Association between residential proximity to agricultural crops and adaptive behaviors in children with autism spectrum disorder from the French ELENA cohort

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## I/ Interaction analyses

**Table S1.** *P-value* of interaction between total exposure score to agricultural crops within a 1000m and 500m radius around residential addresses and the intellectual quotient for developmental periods and each VABS-II subdomain score in children with autism spectrum disorder from the French ELENA cohort.

Buffer 1000m						
P <sub>interaction</sub>	Pregnancy period			First two years of life period		
	Communication	Daily living skills	Socialization	Communication	Daily living skills	Socialization
	<b>0.0006</b>	<b>&lt;.0001</b>	<b>0.0039</b>	<b>0.0008</b>	<b>&lt;.0001</b>	<b>0.0044</b>
Buffer 500m						
P <sub>interaction</sub>	Pregnancy period			First two years of life period		
	Communication	Daily living skills	Socialization	Communication	Daily living skills	Socialization
	<b>0.0004</b>	<b>&lt;.0001</b>	<b>0.0075</b>	<b>&lt;.0001</b>	<b>&lt;.0001</b>	<b>0.0042</b>

**Abbreviation:** VABS-II=Vineland Adaptive Behavior Scales 2<sup>nd</sup> edition

## II/ Supplementary descriptive analyses

**Table S2.** Comparison of main characteristics between the study population (n=183) and the “strictly urban”<sup>a</sup> subpopulation excluded for the pregnancy period (n=41) of exposure to agricultural crops in children with ASD from the ELENA cohort.

Characteristics	study population (n=183)	“Strictly urban” subpopulation excluded from analyses (n=41)	P value*
Children age at inclusion	6.1 (3.5)	6.3 (3.4)	<.0001
Children’s sex			0.950
Males	142 (78%)	32 (78%)	
Females	41 (22%)	9 (22%)	
Children intellectual quotient (IQ)			
IQ	76.9 (28.9)	75.5 (30.2)	<.0001
Intellectual disability (ID) Status			0.979
ID	71 (39%)	16 (39%)	
Non ID	112 (61%)	25 (61%)	
VABS-II subdomains scores			
Communication	73.0 (15.8)	70.9 (14.0)	<.0001
Daily living skills	74.8 (13.6)	73.2 (11.8)	<.0001
Socialization	71.8 (11.3)	69.6 (11.0)	<.0001
Total exposure score to agricultural crops during pregnancy	29% (27%)	0	-
Exposure score to “crops group 1”* during pregnancy	12% (21%)	0	-
Exposure score to “crops group 2”** during pregnancy	17% (21%)	0	-

a: The “strictly urban” status was defined by more than 99% of urbanized area within a 500-m radius around each address.

**Abbreviations:** ASD=autism spectrum disorder; ID=intellectual disability; **VABS-II**= Vineland Adaptive Behavior Scales 2<sup>nd</sup> edition

According to the Corine Land Cover classification (CLC; French Ministry of Environment, Statistics and Observation Department, scale 1:100 000), we defined crop groups as:

\* **Crops group 1**=*vineyards, fruit trees, and berry plantations*

\*\* **Crops group 2**= non-irrigated arable land (cereals, fodder crops, root crops and fallow land, flower and tree cultivation, and vegetables); annual crops associated with permanent crops (woody crops like shrubs, olives in combination with either non-permanent crops like fodder roots, fodder maize, forage kale, etc., or permanent grass surfaces) and land principally occupied by agriculture with significant areas of natural vegetation.

\*\*\* Wilcoxon or Student tests for quantitative variables, and Chi2 test for qualitative variables.

\* *Wilcoxon or Student tests for quantitative variables and Chi2 test for qualitative variables.*

### III/ Sensitivity analyses

#### 1. Additional adjustments and analyses by subgroup of crop exposure scores

**Table S3.** Associations [ $\beta$  (CI95%)], between each 20% increase in total exposure score to agricultural crops within a 1000m radius around maternal residential address during pregnancy and VABS-II subdomains scores<sup>a</sup> in children with autism spectrum disorder from the ELENA cohort (n=158).

Total exposure score to crops		VABS-II subdomains scores		
		ASD without ID		
		Communication $\beta$ (CI95%)	Daily living skills $\beta$ (CI95%)	Socialization $\beta$ (CI95%)
Model*		-2.90 (-5.06 to -0.74)	-1.88 (-3.74 to -0.01)	-1.34 (-3.13 to 0.44)
		ASD with ID		
		Communication $\beta$ (CI95%)	Daily living skills $\beta$ (CI95%)	Socialization $\beta$ (CI95%)
Model*		1.18 (-1.69 to 4.06)	0.86 (-1.70 to 3.43)	0.04 (-1.84 to 1.92)

\*Sensitivity analysis, Model\*= final model [adjusted on Child's sex (female, male), age at the inclusion in the ELENA cohort ( $\leq$ median,  $>$ median), higher level of parental education in the household ( $\leq$  high school, university)] additionally adjusted on + maternal folic acid intake (yes/no), alcohol consumption (yes/no), smoking during pregnancy (yes/no), child's birth season (Spring, Summer, Autumn, Winter), recruiting center (*Occitanie, Auvergne-Rhône-Alpes, Ile-de-France, Provence-Alpes-Côte d'Azur, Nouvelle Aquitaine, Grand Est*)

*a*: negative Beta indicating alteration in adaptive functioning

**VABS-II:** Vineland Adaptive Behavior Scales 2<sup>nd</sup> edition

**Table S4.** Associations [ $\beta$  (CI95%)] between each 20% increase in total exposure score to agricultural crops within a 1000m radius around residential address during the first two years of life and VABS-II subdomains scores<sup>a</sup> in children with autism spectrum disorder from the ELENA cohort (n=168).

Total exposure score to crops		VABS-II subdomains scores		
		ASD without ID		
		Communication $\beta$ (CI95%)	Daily living skills $\beta$ (CI95%)	Socialization $\beta$ (CI95%)
Model*		-2.36 (-4.33 to -0.38)	-1.49 (-3.17 to 0.18)	-1.30 (-2.88 to 0.29)
		ASD with ID		
		Communication $\beta$ (CI95%)	Daily living skills $\beta$ (CI95%)	Socialization $\beta$ (CI95%)
Model*		2.25 (-0.63 to 5.13)	2.03 (-0.32 to 4.39)	0.21 (-1.57 to 1.98)

\*Sensitivity analysis, Model\*= final model [adjusted on Child's sex (female, male), age at the inclusion in the ELENA cohort ( $\leq$ median,  $>$ median), higher level of parental education in the household ( $\leq$  high school, university)] additionally adjusted on + maternal folic acid intake (yes/no), alcohol consumption (yes/no), smoking during pregnancy (yes/no), child's birth season (Spring, Summer, Autumn, Winter), recruiting center (*Occitanie, Auvergne-Rhône-Alpes, Ile-de-France, Provence-Alpes-Côte d'Azur, Nouvelle Aquitaine, Grand Est*)

*a*: negative Beta indicating alteration in adaptive functioning

**VABS-II:** Vineland Adaptive Behavior Scales 2<sup>nd</sup> edition

**Table S5.** Associations [ $\beta$  (CI95%)] between each 20% increase in exposure score to crops group 1\* within a 1000m radius around maternal residential address during pregnancy and VABS-II subdomains scores<sup>a</sup> in children with autism spectrum disorder from the ELENA cohort (n=183).

Exposure score to crops group 1*	VABS-II subdomains scores		
	ASD without ID		
	Communication $\beta$ (CI95%)	Daily living skills $\beta$ (CI95%)	Socialization $\beta$ (CI95%)
<b>Crude model</b>			
Exposure score $\leq$ median	Ref	Ref	Ref
Exposure score $>$ median	-0.60 (-5.99 to 4.78)	-0.22 (-4.77 to 4.33)	-1.14 (-5.12 to 2.84)
<b>Adjusted model</b>			
Exposure score $\leq$ median	Ref	Ref	Ref
Exposure score $>$ median	-0.46 (-5.70 to 4.79)	-0.98 (-5.70 to 3.75)	-0.97 (-5.05 to 3.12)
	ASD with ID		
	Communication $\beta$ (CI95%)	Daily living skills $\beta$ (CI95%)	Socialization $\beta$ (CI95%)
<b>Crude model</b>			
Exposure score $\leq$ median	Ref	Ref	Ref
Exposure score $>$ median	4.53 (-1.47 to 10.52)	1.16 (-4.83 to 7.16)	2.15 (-2.99 to 7.29)
<b>Adjusted model</b>			
Exposure score $\leq$ median	Ref	Ref	Ref
Exposure score $>$ median	5.81 (-0.23 to 11.85)	2.03 (-4.07 to 8.12)	3.76 (-1.10 to 8.61)

**Model 2:** Adjusted model on Child's sex (female, male), age at the inclusion in the ELENA cohort ( $\leq$ median,  $>$ median), higher level of parental education in the household ( $\leq$  high school, university)

According to the Corine Land Cover classification (CLC; French Ministry of Environment, Statistics and Observation Department, scale 1:100 000), **Crops group**

**1\***=vineyards, fruit trees, and berry plantations

***a***: negative Beta indicating alteration in adaptive functioning

**VABS-II**: Vineland Adaptive Behavior Scales 2<sup>nd</sup> edition



**Table S6.** Associations [ $\beta$  (CI95%)] between each 20% increase in exposure score to crops group 2\* within a 1000m radius around maternal residential address during pregnancy and VABS-II subdomains scores<sup>a</sup> in children with autism spectrum disorder from the ELENA cohort (n=183).

Exposure score to crops group 2*	VABS-II subdomains scores		
	ASD without ID		
	Communication $\beta$ (CI95%)	Daily living skills $\beta$ (CI95%)	Socialization $\beta$ (CI95%)
<b>Crude model</b>			
Exposure score $\leq$ median	Ref	Ref	Ref
Exposure score $>$ median	-3.08 (-8.29 to 2.13)	-0.21 (-4.64 to 4.22)	0.46 (-3.42 to 4.35)
<b>Adjusted model</b>			
Exposure score $\leq$ median	Ref	Ref	Ref
Exposure score $>$ median	-2.43 (-7.51 to 2.64)	-0.71 (-5.30 to 3.87)	1.27 (-2.68 to 5.23)
	ASD with ID		
	Communication $\beta$ (CI95%)	Daily living skills $\beta$ (CI95%)	Socialization $\beta$ (CI95%)
<b>Crude model</b>			
Exposure score $\leq$ median	Ref	Ref	Ref
Exposure score $>$ median	0.12 (-6.04 to 6.29)	4.51 (-1.47 to 10.49)	0.33 (-4.90 to 5.56)
<b>Adjusted model</b>			
Exposure score $\leq$ median	Ref	Ref	Ref
Exposure score $>$ median	-1.62 (-7.93 to 4.68)	3.98 (-2.16 to 10.13)	-1.26 (-6.29 to 3.76)

**Model 2:** Adjusted model on Child's sex (female, male), age at the inclusion in the ELENA cohort ( $\leq$ median,  $>$ median), higher level of parental education in the household ( $\leq$  high school, university)

According to the Corine Land Cover classification (CLC; French Ministry of Environment, Statistics and Observation Department, scale 1:100 000), **crops group 2\*\***= non-irrigated arable land (cereals, fodder crops, root crops and fallow land, flower and tree cultivation, and vegetables); annual crops associated with permanent crops (woody crops like shrubs, olives in combination with either non-permanent crops like fodder roots, fodder maize, forage kale, etc., or permanent grass surfaces) and land principally occupied by agriculture with significant areas of natural vegetation.

*$\alpha$ : negative Beta indicating alteration in adaptive functioning*

**VABS-II:** Vineland Adaptive Behavior Scales 2<sup>nd</sup> edition

**Table S7.** Associations [ $\beta$  (CI95%)] between each 20% increase in exposure score to crops group 1\* within a 1000m radius around residential address during the first two years of life and VABS-II subdomains scores<sup>a</sup> in children with autism spectrum disorder from the ELENA cohort (n=193).

Exposure score to crops group 1*	VABS-II subdomains scores		
	ASD without ID		
	Communication $\beta$ (CI95%)	Daily living skills $\beta$ (CI95%)	Socialization $\beta$ (CI95%)
<b>Crude model</b>			
Exposure score $\leq$ median	Ref	Ref	Ref
Exposure score $>$ median	-1.63 (-6.86 to 3.61)	-0.27 (-4.70 to 4.17)	-0.52 (-4.38 to 3.34)
<b>Adjusted model</b>			
Exposure score $\leq$ median	Ref	Ref	Ref
Exposure score $>$ median	-1.68 (-6.78 to 3.42)	-0.68 (-5.22 to 3.86)	-0.39 (-4.29 to 3.50)
	ASD with ID		
	Communication $\beta$ (CI95%)	Daily living skills $\beta$ (CI95%)	Socialization $\beta$ (CI95%)
<b>Crude model</b>			
Exposure score $\leq$ median	Ref	Ref	Ref
Exposure score $>$ median	6.10 (0.10 to 12.10)	4.13 (-1.57 to 9.83)	1.69 (-3.13 to 6.50)
<b>Adjusted model</b>			
Exposure score $\leq$ median	Ref	Ref	Ref
Exposure score $>$ median	6.86 (0.95 to 12.77)	4.93 (-0.63 to 10.49)	2.57 (-1.91 to 7.04)

**Model 2:** Adjusted model on Child's sex (female, male), age at the inclusion in the ELENA cohort ( $\leq$ median,  $>$ median), higher level of parental education in the household ( $\leq$  high school, university)

According to the Corine Land Cover classification (CLC; French Ministry of Environment, Statistics and Observation Department, scale 1:100 000), **Crops group**

**1\***=vineyards, fruit trees, and berry plantations

***a***: negative Beta indicating alteration in adaptive functioning

**VABS-II**: Vineland Adaptive Behavior Scales 2<sup>nd</sup> edition

**Table S8.** Associations [ $\beta$  (CI95%)] between each 20% increase in exposure score to crops group 2\* within a 1000m radius around residential address during the first two years of life and VABS-II subdomains scores<sup>a</sup> in children with autism spectrum disorder from the ELENA cohort (n=193).

Exposure score to crops group 2*	VABS-II subdomains scores		
	ASD without ID		
	Communication $\beta$ (CI95%)	Daily living skills $\beta$ (CI95%)	Socialization $\beta$ (CI95%)
Crude model			
Exposure score $\leq$ median	Ref	Ref	Ref
Exposure score $>$ median	-2.93 (-8.01 to 2.15)	-1.09 (-5.41 to 3.23)	-0.07 (-3.84 to 3.69)
Adjusted model			
Exposure score $\leq$ median	Ref	Ref	Ref
Exposure score $>$ median	-2.04 (-7.02 to 2.94)	-1.31 (-5.75 to 3.13)	0.68 (-3.12 to 4.49)
	ASD with ID		
	Communication $\beta$ (CI95%)	Daily living skills $\beta$ (CI95%)	Socialization $\beta$ (CI95%)
Crude model			
Exposure score $\leq$ median	Ref	Ref	Ref
Exposure score $>$ median	0.48 (-5.68 to 6.64)	1.51 (-4.25 to 7.28)	-1.01 (-5.84 to 3.82)
Adjusted model			
Exposure score $\leq$ median	Ref	Ref	Ref
Exposure score $>$ median	-0.60 (-6.77 to 5.56)	0.70 (-5.01 to 6.42)	-2.06 (-6.58 to 2.46)

**Model 2:** Adjusted model on Child's sex (female, male), age at the inclusion in the ELENA cohort ( $\leq$ median,  $>$ median), higher level of parental education in the household ( $\leq$  high school, university)

According to the Corine Land Cover classification (CLC; French Ministry of Environment, Statistics and Observation Department, scale 1:100 000), **crops group 2\***= non-irrigated arable land (cereals, fodder crops, root crops and fallow land, flower and tree cultivation, and vegetables); annual crops associated with permanent crops (woody crops like shrubs, olives in combination with either non-permanent crops like fodder roots, fodder maize, forage kale, etc., or permanent grass surfaces) and land principally occupied by agriculture with significant areas of natural vegetation.

*$\alpha$ : negative Beta indicating alteration in adaptive functioning*

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**2. Associations between cumulative (from pregnancy to the first two years of life) total exposure score to agricultural crops within a 1000m radius around residential addresses and VABS-II subdomains scores.**

**Table S9.** Associations [ $\beta$  (CI95%)], between each 20% increase in the cumulative total exposure score (from pregnancy to the first two years of children's life) to agricultural crops within a 1000m radius around residential address and VABS-II subdomains scores<sup>a</sup> in children with autism spectrum disorder from the ELENA cohort (n=177, 108 without ID and 69 with ID).

Cumulative total exposure score to crops	VABS-II subdomains scores		
	ASD without ID		
	Communication $\beta$ (CI95%)	Daily living skills $\beta$ (CI95%)	Socialization $\beta$ (CI95%)
Crude model	-2.32 (-4.28 to -0.37)	-1.10 (-2.78 to 0.59)	-1.74 (-3.18 to -0.29)
Adjusted model	-2.33 (-4.25 to -0.40)	-1.46 (-3.21 to 0.29)	-1.60 (-3.10 to -0.10)
	ASD with ID		
	Communication $\beta$ (CI95%)	Daily living skills $\beta$ (CI95%)	Socialization $\beta$ (CI95%)
Crude model	0.53 (-1.84 to 2.89)	0.78 (-1.52 to 3.09)	0.58 (-1.43 to 2.58)
Adjusted model	0.42 (-1.95 to 2.79)	0.62 (-1.68 to 2.93)	0.39 (-1.50 to 2.28)

Adjusted model on Child's sex (female, male), age at the inclusion in the ELENA cohort ( $\leq$ median,  $>$ median), higher level of parental education in the household ( $\leq$  high school, university)

*$\alpha$ : negative Beta indicating alteration in adaptive functioning*

**VABS-II:** Vineland Adaptive Behavior Scales 2<sup>nd</sup> edition

### 3. Associations between total exposure scores to agricultural crops within a 500m radius around residential addresses and VABS-II subdomains scores.

#### 3.1. Pregnancy period

**Table S10.** Associations [ $\beta$  (CI95%)] between each 20% increase in total exposure score to agricultural crops within a 500m radius around maternal residential address during pregnancy and VABS-II subdomains scores<sup>a</sup> in children with autism spectrum disorder from the ELENA cohort (n=183).

Total exposure score to crops		VABS-II subdomains scores		
		ASD without ID		
		Communication $\beta$ (CI95%)	Daily living skills $\beta$ (CI95%)	Socialization $\beta$ (CI95%)
	Crude model	-2.73 (-4.89 to -0.58)	-0.81 (-2.69 to 1.07)	-1.65 (-3.28 to -0.02)
	Adjusted model	-2.38 (-4.47 to -0.29)	-0.97 (-2.90 to 0.97)	-1.41 (-3.07 to 0.26)
		ASD with ID		
		Communication $\beta$ (CI95%)	Daily living skills $\beta$ (CI95%)	Socialization $\beta$ (CI95%)
	Crude model	0.27 (-2.04 to 2.59)	0.83 (-1.45 to 3.10)	0.96 (-0.99 to 2.91)
	Adjusted model	0.06 (-2.25 to 2.36)	0.65 (-1.61 to 2.91)	0.67 (-1.16 to 2.49)

Adjusted model on Child's sex (female, male), age at the inclusion in the ELENA cohort ( $\leq$ median,  $>$ median), higher level of parental education in the household ( $\leq$  high school, university)

$\alpha$ : negative Beta indicating alteration in adaptive functioning

**VABS-II:** Vineland Adaptive Behavior Scales 2<sup>nd</sup> edition



### 3.2. First two years of life period

**Table S11.** Associations [ $\beta$  (CI95%)] between each 20% increase in total exposure score to agricultural crops within a 500m radius around residential address during the first two years of life and VABS-II subdomains scores<sup>a</sup> in children with autism spectrum disorder from the ELENA cohort (n=193).

Total exposure score to crops		VABS-II subdomains scores		
		ASD without ID		
		Communication $\beta$ (CI95%)	Daily living skills $\beta$ (CI95%)	Socialization $\beta$ (CI95%)
	Crude model	-1.40 (-3.29 to 0.48)	-0.47 (-2.07 to 1.14)	-1.55 (-2.92 to -0.18)
	Adjusted model	-1.41 (-3.23 to 0.42)	-0.59 (-2.23 to 1.05)	-1.39 (-2.78 to -0.01)
		ASD with ID		
		Communication $\beta$ (CI95%)	Daily living skills $\beta$ (CI95%)	Socialization $\beta$ (CI95%)
	Crude model	0.29 (-2.14 to 2.72)	0.98 (-1.29 to 3.25)	0.80 (-1.10 to 2.70)
	Adjusted model	-0.04 (-2.47 to 2.39)	0.79 (-1.46 to 3.03)	0.57 (-1.22 to 2.36)

Adjusted model on Child's sex (female, male), age at the inclusion in the ELENA cohort ( $\leq$ median,  $>$ median), higher level of parental education in the household ( $\leq$  high school, university)

*a*: negative Beta indicating alteration in adaptive functioning

**VABS-II:** Vineland Adaptive Behavior Scales 2<sup>nd</sup> edition