

## Appendix. Participant Characteristics

## Supplement Table A. Demographics and Health History

Participant	Sex	Age at Scan (Yrs)	Family History (self-reported)		
			Autism or Autism Spectrum Disorder	Language Impairment or Speech Delay	Learning Disability or Cognitive Delay
<b>Case 1</b>	<b>F</b>	<b>15.4</b>	<b>No</b>	<b>No</b>	<b>Yes</b>
Control 1	F	15.6	No	No	No
<b>Case 2</b>	<b>M</b>	<b>7.7, 8.0</b>	<b>No</b>	<b>Yes</b>	<b>No</b>
Control 2	M	8.8	No	No	No
<b>Case 3</b>	<b>M</b>	<b>6.5</b>	<b>Yes</b>	<b>No</b>	<b>No</b>
Control 3	M	7.8	No	Yes	No
<b>Case 4</b>	<b>M</b>	<b>12.7</b>	<b>Yes</b>	<b>Yes</b>	<b>Yes</b>
Control 4	M	13.0	No	No	No
<b>Case 5</b>	<b>F</b>	<b>12.9</b>	<b>Yes</b>	<b>Yes</b>	<b>Yes</b>
Control 5	F	13.8	No	No	No
<b>Case 6</b>	<b>M</b>	<b>18.4</b>	<b>Yes</b>	<b>Yes</b>	<b>Yes</b>
Control 6	M	18.3	No	No	No

## Supplement Table B. Mitochondrial Phenotype and Diagnosis

Participant	Characteristics and Workup That Suggest Mitochondrial Concerns	Final Mitochondrial Diagnosis
<b>Case 1</b>	Myopathy, subsequently confirmed complex IV deficiency	Definite
<b>Case 2</b>	Lactic acidemia, abnormal organic acids, and abnormal polarography	Definite
<b>Case 3</b>	Hypotonia. (Subsequently confirmed mitochondrial proliferation on biopsy, elevated plasma alanine)	Probable
<b>Case 4</b>	Hypotonia. (Subsequently confirmed mitochondrial proliferation on biopsy, abnormal urine organic acids)	Possible
<b>Case 5</b>	History of developmental regression and autism in younger brother	Possible
<b>Case 6</b>	Myopathy, elevated CPK and +FH in a maternal uncle	Possible

**Supplement Table C. Participant Autism Diagnostic Observation Scales<sup>1</sup>**

Participant	Module	COM	SOC	COM+ SOC	IC	SBRI	Overall Diagnosis
<b>Case 1</b>	<b>3</b>	<b>5</b>	<b>14</b>	<b>19</b>	<b>2</b>	<b>2</b>	<b>Autism; GAD /SAD</b>
Control 1	3	1	0	0	1	0	No Diagnosis
<b>Case 2</b>	<b>2</b>	<b>4</b>	<b>9</b>	<b>13</b>	<b>1</b>	<b>3</b>	<b>Autism; SAD</b>
Control 2	3	2	2	4	1	0	No Diagnosis
<b>Case 3</b>	<b>3</b>	<b>3</b>	<b>7</b>	<b>10</b>	<b>1</b>	<b>5</b>	<b>Autism</b>
Control 3	3	0	1	1	0	0	No Diagnosis
<b>Case 4</b>	<b>3</b>	<b>1</b>	<b>10</b>	<b>11</b>	<b>0</b>	<b>0</b>	<b>Autism</b>
Control 4	3	0	2	2	0	0	No Diagnosis
<b>Case 5</b>	<b>3</b>	<b>2</b>	<b>8</b>	<b>10</b>	<b>0</b>	<b>1</b>	<b>Autism</b>
Control 5	3	1	1	2	0	0	No Diagnosis
<b>Case 6</b>	<b>4</b>	<b>3</b>	<b>4</b>	<b>7</b>	<b>0</b>	<b>2</b>	<b>ASD; Asperger's Syndrome</b>
Control 6	4	3	1	4	1	0	No Diagnosis

COM - Communication Domain. SOC - Social Interaction Domain. IC - Imagination/ Creativity Domain. SBRI - Stereotyped Behaviors and Restricted Interests Domain. GAD - Generalized Anxiety Disorder. SAD - Social Anxiety Disorder.

*Module 2* Autism/Autism Spectrum cut-offs for Communication (scores 0-10), Social Interaction (scores 0-14), and Communication + Social Interaction (scores 0-24) domains are 5/3, 6/4, and 12/8, respectively. Imagination/ Creativity Domain (scores 0-2); Stereotyped Behaviors and Restricted Interests Domain (scores 0-6).

*Module 3, 4* Autism/Autism Spectrum cut-offs for Communication (scores 0-8), Social Interaction (scores 0-14), and Communication + Social Interaction (scores 0-22) domains are 3/2, 6/4, and 10/7, respectively. Imagination/ Creativity Domain (scores 0-2); Stereotyped Behaviors and Restricted Interests Domain (scores 0-8).

**Supplement Table D. Participant Autism Diagnostic Interview-Revised<sup>2</sup> Scores (Version 4 Years, 0 Months or More)**

Participant	Autism Diagnostic Interview-Revised				D Total (1)
	Social Interaction Total Scores 0-30 (10)	Communication Verbal Total Scores 0-26 (8)	Communication Non-Verbal Total Scores 0-14 (7)	Stereotyped Behaviors Total Scores 0-12 (3)	
<b>Case 1</b>	<b>17</b>	<b>N/A</b>	<b>8</b>	<b>2</b>	<b>3</b>
Control 1	1	1	1	0	0
<b>Case 2</b>	<b>20</b>	<b>14</b>	<b>8</b>	<b>6</b>	<b>4</b>
Control 2	2	4	3	0	0
<b>Case 3</b>	<b>17</b>	<b>19</b>	<b>11</b>	<b>6</b>	<b>5</b>
Control 3	2	1	1	2	0
<b>Case 4</b>	<b>18</b>	<b>22</b>	<b>11</b>	<b>7</b>	<b>5</b>
Control 4	1	1	1	0	0
<b>Case 5</b>	<b>14</b>	<b>6</b>	<b>2</b>	<b>4</b>	<b>3</b>
Control 5	0	0	0	0	2
<b>Case 6</b>	<b>17</b>	<b>9</b>	<b>4</b>	<b>7</b>	<b>3</b>
Control 6	0	2	2	0	0

D= Abnormality of Development Evident at or Before 36 Months (Autism cut-off)

## References

1. Lord C, Risi S, Lambrecht L, et al. The autism diagnostic observation schedule-generic: a standard measure of social and communication deficits associated with the spectrum of autism. *J Autism Dev Disord.* Jun 2000;30(3):205-223.
2. Lord C, Rutter M, Le Couteur A. Autism Diagnostic Interview-Revised: a revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *J Autism Dev Disord.* Oct 1994;24(5):659-685.