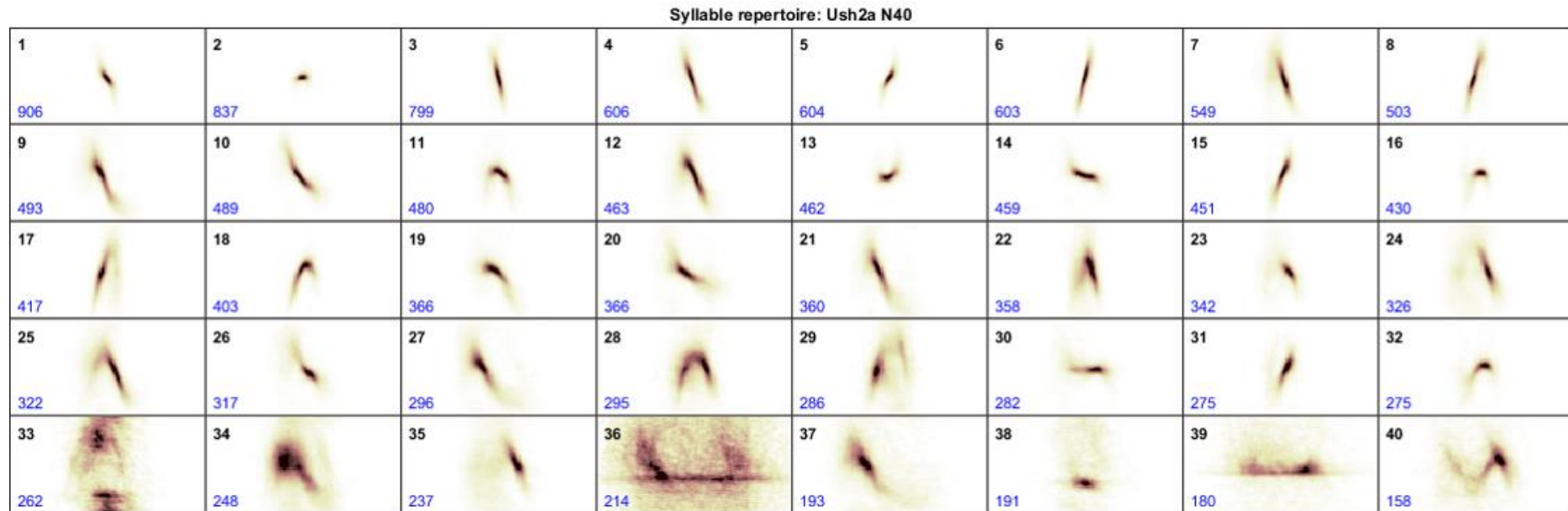


Online Supplement for *Multi-level evidence of an allelic hierarchy of USH2A variants in hearing, auditory processing and speech/language outcomes*

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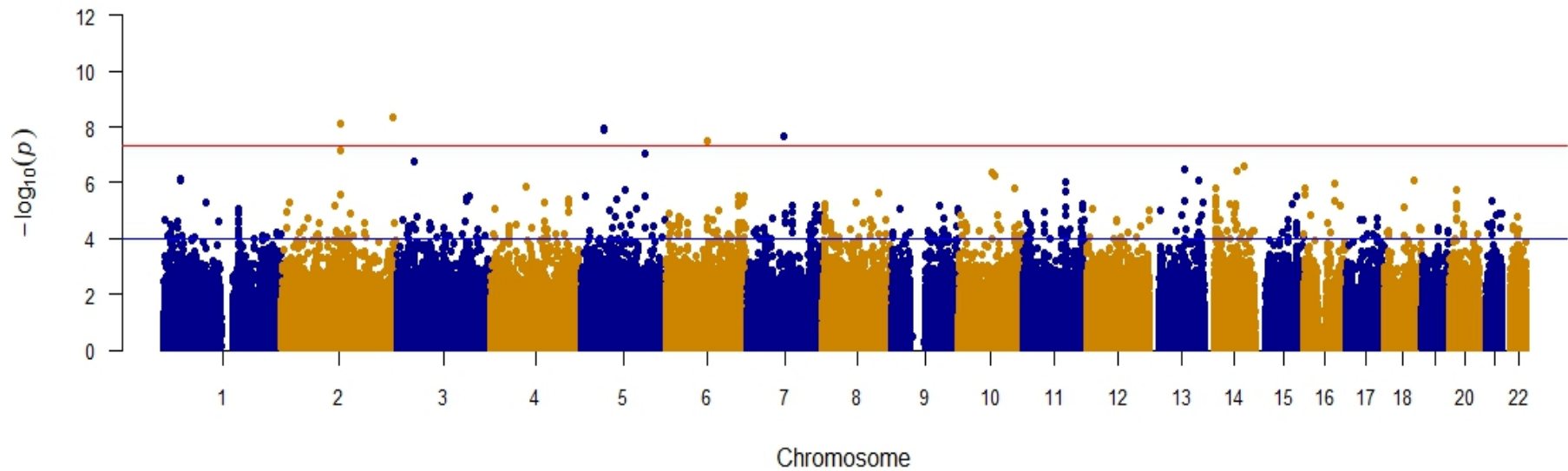
Supplementary Figures

Supplementary Figure 1: Ush2a ultrasonic vocalization syllable repertoire generated from MUPET



40 unique syllables were generated via MUPET USV analysis (collapsed across all subjects). Each syllable was assigned to one of eight call types⁸⁰. Number in bottom left corner indicates number of utterances seen across all subjects.

Supplementary Figure 2: Manhattan Plot of genomewide interaction study



Four hundred and fifty SNPs had P -values $\leq 10^{-5}$ and were entered into pathway analyses to identify gene pathways modulated by low frequency hearing.

Supplementary Tables

Supplementary Table 1: Language and hearing candidate genes

Hearing-related Genes							Language-related Genes	
<i>AAK1</i>	<i>COL11A1</i>	<i>EPS8L2</i>	<i>IFNLR1</i>	<i>MYO6</i>	<i>PPIP5K2</i>	<i>TJP2</i>	<i>ARID1A</i>	<i>STARD9</i>
<i>ACSL4</i>	<i>COL11A2</i>	<i>ERAL1</i>	<i>IKZF5</i>	<i>MYO7A</i>	<i>PPM1A</i>	<i>TMC1</i>	<i>ATP2C2</i>	<i>SYNPR</i>
<i>ACTG1</i>	<i>COL2A1</i>	<i>ESPN</i>	<i>IL1R2</i>	<i>NARS2</i>	<i>PRPS1</i>	<i>TMEM132E</i>	<i>AUTS2</i>	<i>TM4SF20</i>
<i>ACVR2A</i>	<i>COL4A3</i>	<i>ESRP1</i>	<i>ILDR1</i>	<i>NDP</i>	<i>PTPRQ</i>	<i>TMEM30B</i>	<i>BCL11A</i>	<i>TNRC6B</i>
<i>ADCY1</i>	<i>COL4A4</i>	<i>ESRRB</i>	<i>KARS</i>	<i>NEDD4L</i>	<i>RDX</i>	<i>TMIE</i>	<i>CHD3</i>	<i>TRIO</i>
<i>AHSG</i>	<i>COL4A5</i>	<i>EWSR1</i>	<i>KCNJ10</i>	<i>NFATC3</i>	<i>ROR1</i>	<i>TMPRSS3</i>	<i>CMIP</i>	<i>WDR5</i>
<i>AIFM1</i>	<i>COL4A6</i>	<i>EYA1</i>	<i>KCNQ1</i>	<i>NIN</i>	<i>RP11-166N6.3</i>	<i>TMTC4</i>	<i>CNTNAP2</i>	<i>ZFHX4</i>
<i>ANKRD11</i>	<i>COL9A1</i>	<i>EYA4</i>	<i>KCNQ4</i>	<i>NISCH</i>	<i>RP11-20I23.1</i>	<i>TNC</i>	<i>CNTNAP5</i>	
<i>AP3M2</i>	<i>COL9A2</i>	<i>FAM65B</i>	<i>KIAA1024L</i>	<i>NLRP3</i>	<i>S1PR2</i>	<i>TOX</i>	<i>CTNND2</i>	
<i>AP3S1</i>	<i>COL9A3</i>	<i>FOXI1</i>	<i>KITLG</i>	<i>NM_001702</i>	<i>SEMA3E</i>	<i>TPRN</i>	<i>DCDC2</i>	
<i>ATP2B1</i>	<i>CRYM</i>	<i>GATA2</i>	<i>KLC2</i>	<i>NM_032119</i>	<i>SEMA3F</i>	<i>TRAM2</i>	<i>DOCK4</i>	
<i>BAIAP2L2</i>	<i>CTC-454I21.3</i>	<i>GGA1</i>	<i>KLHL18</i>	<i>NPTN</i>	<i>SERPINB6</i>	<i>TRIOBP</i>	<i>DYX1C1</i>	
<i>BDP1</i>	<i>CYB5R2</i>	<i>GIPC3</i>	<i>LARS2</i>	<i>OCM2</i>	<i>SIX1</i>	<i>TSPEAR</i>	<i>ERC1</i>	
<i>BSND</i>	<i>DCDC2</i>	<i>GJB2</i>	<i>LHFPL5</i>	<i>ODF3L2</i>	<i>SIX5</i>	<i>UBE2B</i>	<i>FOXP1</i>	
<i>CABP2</i>	<i>DFNB31</i>	<i>GJB3</i>	<i>LOXHD1</i>	<i>OSBPL2</i>	<i>SLC17A8</i>	<i>UBE2G1</i>	<i>FOXP2</i>	
<i>CCDC50</i>	<i>DFNB59</i>	<i>GJB6</i>	<i>LRTOMT</i>	<i>OTOA</i>	<i>SLC22A4</i>	<i>USH1C</i>	<i>GRIN2A</i>	
<i>CCDC88C</i>	<i>DIABLO</i>	<i>GPR152</i>	<i>MARVELD2</i>	<i>OTOF</i>	<i>SLC26A4</i>	<i>USH1G</i>	<i>GRIN2B</i>	
<i>CCDC92</i>	<i>DIAPH1</i>	<i>GPR50</i>	<i>MCM2</i>	<i>OTOG</i>	<i>SLC26A5</i>	<i>USH2A</i>	<i>KAT6A</i>	
<i>CD164</i>	<i>DIAPH3</i>	<i>GPR98</i>	<i>MED28</i>	<i>OTOGL</i>	<i>SLC4A10</i>	<i>VTI1A</i>	<i>KIAA0319</i>	
<i>CDC14A</i>	<i>DMXL2</i>	<i>GPSM2</i>	<i>MET</i>	<i>P2RX2</i>	<i>SLC5A5</i>	<i>WBP2</i>	<i>KMT2D</i>	
<i>CDH23</i>	<i>DNASE1</i>	<i>GRHL2</i>	<i>MIR96</i>	<i>PAX3</i>	<i>SMPX</i>	<i>WDTC1</i>	<i>MACROD2</i>	
<i>CEACAM16</i>	<i>DUOXA2</i>	<i>GRXCR1</i>	<i>MITF</i>	<i>PCDH15</i>	<i>SNAI2</i>	<i>WFS1</i>	<i>MKL2</i>	
<i>CH507-396I9.6</i>	<i>EDN3</i>	<i>GRXCR2</i>	<i>MPDZ</i>	<i>PDZD7</i>	<i>SOX10</i>	<i>ZCCHC14</i>	<i>NFXL1</i>	
<i>CHD7</i>	<i>EDNRB</i>	<i>GSDME</i>	<i>MSRB3</i>	<i>PHF6</i>	<i>SPNS2</i>		<i>OXR1</i>	
<i>CIB2</i>	<i>ELMOD1</i>	<i>HARS</i>	<i>MYH1</i>	<i>PNPT1</i>	<i>SRRM4</i>		<i>ROBO1</i>	
<i>CLDN14</i>	<i>ELMOD3</i>	<i>HARS2</i>	<i>MYH14</i>	<i>POLR1C</i>	<i>STRC</i>		<i>SCN9A</i>	
<i>CLIC5</i>	<i>EMB</i>	<i>HGF</i>	<i>MYH9</i>	<i>POLR1D</i>	<i>SYNE4</i>		<i>SEMA6D</i>	
<i>CLPP</i>	<i>EPS8</i>	<i>HOMER2</i>	<i>MYO15A</i>	<i>POU3F4</i>	<i>TCOF1</i>		<i>SETBP1</i>	
<i>COCH</i>	<i>EPS8L1</i>	<i>HSD17B4</i>	<i>MYO3A</i>	<i>POU4F3</i>	<i>TECTA</i>		<i>SRPX2</i>	

Hearing-related (N=197) and language-related (N=37) genes from literature. Genes highlighted in grey and bold had SNP hits with P-values <10⁻⁵ in the GWIs

Supplementary Notes, Discussion, Methods

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