Supplementary Materials

Neural correlates of theory of mind reasoning in congenitally blind children

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Analysis Decisions

This dataset was collected between 2010-2014 and study analyses were not pre-registered. FMRI analysis decisions follow the pre-registered analysis plan for a study using a subset of the non-blindfolded sighted children (n=76; https://osf.io/wzd8a, Project III; pre-registered December 8, 2017), with two exceptions. First, as described in the main text, we measured selectivity in individual functional ROIs defined as the top 80 voxels to the Mental > Physical contrast, rather than using the threshold-dependent definition procedure used in prior publications (Richardson, Koster-Hale, et al., 2020) and pre-registrations (https://osf.io/wzd8a). Results across the two individual-subject ROI definitions were the same: we did not observe robust group differences in selectivity of individual-subject ROIs between blind and sighted children under either definition (see *Selectivity analyses: threshold-dependent individual-subject ROIs* section, below). Results from group ROIs are included in the main text; group ROI definition matches that used in prior research (Richardson, Koster-Hale, et al., 2020; https://osf.io/wzd8a). Second, the referenced pre-registration proposed conducting primary ROI analyses in RTPJ and DMPFC, together. Here, we conducted analyses in RTPJ and, separately, in all ToM ROIs. This decision was based on recent evidence that response selectivity in RTPJ is reduced in children with delayed ToM development (Richardson, Koster-Hale, et al., 2020).

Selectivity Analyses: Blind vs. Blindfolded Children

We repeated ROI analyses to compare blind children to the subset of sighted children who were blindfolded (n=18), who were recruited for the same study and deliberately matched on age, handedness, and MRI head coil.

Among blindfolded sighted children, there was a significant effect of the Physical condition (relative to the Mental condition; all ToM ROIs: b=-.58, t=-5.1, p<.0001; RTPJ: b=-.91, t=-4.5, p<.001); the effect of the Social condition was not significant (all ToM ROIs: b=-.17, t=-1.5, p=.13; RTPJ: b=-.33, t=-1.6, p=.11; see Figure 3 in main text and Supplementary Figure 5). In a direct comparison of blind and blindfolded sighted children, there was a significant condition-by-group interaction such that the Mental > Physical condition difference was larger in blindfolded sighted children (all ToM ROIs: b=-.37, t=-2.4, p<.05; RTPJ: b=0.63, t=-2.7, p= <.01). The condition-by-group interaction for the Mental > Social difference was not significant (all ToM

ROIs: b=.002, t=.01, p=.99; RTPJ: b=-.15, t=-.64, p=.53). There was also a significant positive effect of age (all ToM ROIs: b=.31, t=2.8, p<.01; RTPJ: b=.50, t=2.8, p<.01) and a significant group-by-age interaction such that response magnitude (overall) increased less with age in blindfolded children (all ToM ROIs: -.56, t=-3.3, p<.005; RTPJ: b=-.74, t=-2.8, p<.01).

Response selectivity did not differ between blind and blindfolded children in individually defined regions of interest (RTPJ: b=-.06, t=-.18, CI=[-.67,.56], p=.86; all ToM ROIs: .26, t=1.0, CI=[-.24,.76], p=.32) or in group-defined regions of interest (RTPJ: b=-.32, t=-.93, CI=[-1.0,.38] p=.36; all ToM ROIs: b=-.24, t=-.72, CI=[-.90,.42], p=.47; Supplementary Figure 7); though note a group-by-ROI interaction, such that precuneus is more selective relative to RTPJ in blind children, relative to blindfolded children (b=.84, t=2.2, CI=[.07,1.6], p=.03; Supplementary Figure 7) and a ROI-by-age interaction such that there is more developmental change in selectivity in VMPFC relative to RTPJ across both groups (b=.42, t=2.2, CI=[.04,.81], p=.03).

Selectivity Analyses: Right-Handed Participants

Given that the lateralization of specialized responses can vary by handedness and relatively fewer blind children were right-handed as compared to sighted children (Fisher's exact test: odds ratio = .21, CI=[.04,1.2], p=.04), analyses of lateralized neural measures (i.e., RTPJ selectivity) were repeated in exclusively right-handed blind and sighted children (n=10 blind and n=92 sighted children). In individually-defined ROIs, RTPJ selectivity did not differ between right-handed blind and sighted children (b=-.17, t=-.80, CI=[-.58,.25], p=.43); this group difference was significant in group-defined RTPJ ROIs (b=-.54, t=-2.3, CI=[-1.0,.-.08], p=.02).

Selectivity Analyses: Threshold-dependent individual-subject ROIs

Following analysis protocols from prior research using the same fMRI experiment (https://osf.io/wzd8a), we initially analyzed responses in individual ROIs defined as contiguous (minimum k=10) suprathreshold (p<.001) voxels within a 9mm radius sphere of the peak voxels to the Mental > Physical contrast within previously defined region search spaces (described in the main text (Dufour et al., 2013)). The downside to this approach is that it excludes participants without identifiable ROIs from further analyses.

Individual-subject RTPJ ROIs were defined marginally less frequently in blind children, relative to sighted children (blind children: 10/17, all sighted: 93/114, blindfolded: 14/18; Fisher Exact test, blind vs. all sighted children: odds ratio=.33, 95% CI=[.10,1.1], p=.053; blind vs. blindfolded children: odds ratio=.42, 95% CI=[.07,2.2], p=.29). In all other ToM ROIs, individual-subject ROIs were defined with similar frequency across groups (all odds ratios >.4, ps>.1).

As in prior research, we calculated response selectivity within individual ROIs as the average beta estimate to (Mental – Social / Mental – Physical)*100 (Gweon et al., 2012; Richardson, Koster-Hale, et al., 2020). Response selectivity did not vary by group across all ToM ROIs (blind vs. all sighted: b=.08, t=.26, CI=[-.54,.72], p=.08; blind vs. blindfolded: b=.31, t=1.1, CI=[-.26,.88], p=.29). In analyses with all sighted children, there was a ROI (MMPFC)-by-age interaction: b=-.42, t=-3.4, CI=[-.68,-.18], p=.0008, such that MMPFC changed less with age, relative to RTPJ, across all children, and group-by-ROI-by-age interactions such that selectivity in LTPJ (b=.65, t=2.6, CI=[.15,1.1], p=.009) and MMPFC (b=.84, t=3.2, CI=[.31,1.3], p=.002) changed more with age (compared to RTPJ) in blind children, relative to sighted children; these interactions were not significant in analyses with blind and blindfolded children only. In RTPJ specifically, there were no group differences in response selectivity (blind vs. all sighted: b=.28, t=.26, CI=[-.54,.72], p=.79, group-by-age interaction: b=-.33, t=-2.6, CI=[-.58,-.08], p=.01; blind vs. blindfolded: b=.45, t=1.1, CI=[-.45,1.4], p=.31).

Number of suprathreshold voxels to Mental > Physical in Group ToM ROIs

In analyses reported in the main text, blind children showed a smaller effect of condition on responses in ToM ROIs, relative to sighted children. One possibility is that there are fewer mental-state selective voxels within group-defined ToM ROIs in blind children, relative to sighted children. To test this, we calculated the number of suprathreshold voxels (p<.001, T=3.10) to the Mental > Physical contrast within the group-defined ToM ROIs. Blind children had fewer suprathreshold voxels in RTPJ (b=-.55, t=-2.6, CI=[-.98,-.13], p=.01) and across all ToM ROIs (b=-.71, t=-2.99, CI=[-1.3,.-.27], p=.003), relative to sighted children (see Supplementary Figure 8). When comparing blind children to blindfolded sighted children, this group difference was significant across all ToM ROIs (-.77, t=-3.0, CI=[-1.6,-.35], p=.004) but not in RTPJ (b=-.40, t=-1.3, CI=[-1.0,.23], p=.21).

Inter-Region Correlation Analyses: Blind vs. Blindfolded Children

Among blindfolded children, ToM and language networks were functionally distinct: brain regions within each network were more correlated with other within-network brain regions than with brain regions in the other functional network (within-ToM [M(SE)=.30(.03)] vs. across-ToM-Language [M(SE)=.22(.02)]: t(17)=4.4, CI=[.05,Inf], p=.0002; within-Language [M(SE)=.29(.02)] vs. across-ToM-language: t(17)=7.6, CI=[.05,Inf], $p=3.7x10^{-7}$; Figure 5).

Inter-region correlations within and across the ToM and language networks did not differ between blind and blindfolded children (within-ToM: b=-.43, t=-1.4, CI=[-1.1,.18], p=.16; within-language: b=-.03, t=-.10, CI=[-.74,.67], p=.92; across-ToM-language: b=-.42, t=-1.1, CI= [-1.2,.38], p=.29, group-by-age interaction: b=.90, t=2.7, CI=[.20,1.6], p=.01). Given the small sample size and lack of replication in the large sighted control group (main text), we advise interpreting the group-by-age interaction with caution.

Condition Model Fit to Neural Response Dissimilarity Matrices: Methods & Results

We examined the extent to which a "condition model" – i.e., a model of how similar individual story stimuli were in terms of their social content (as proxied by Mental, Social, Physical condition labels) – correlated with how similar story stimuli were in terms of the response patterns they evoked in ToM brain regions. This procedure was pre-registered (https://osf.io/wzd8a) and described in detail in a prior publication, which found that the condition model fit was atypical in autistic children relative to neurotypical children, specifically in RTPJ (Richardson, Gweon, et al., 2020). As in this prior paper, ROIs were defined as the 80 voxels with the highest T-value to an all stories (MSP) > rest contrast, within 10mm sphere hypothesis spaces drawn around peaks of large search spaces (Dufour et al., 2013). We calculated similarity in neural response patterns across stories as the Euclidean distance between the T-values of each pair of stories, across all voxels, and used Kendall's tau correlations to calculate the similarity between neural response pattern similarity matrices and the condition model ("condition model fit"). One-sided Wilcoxon signed rank tests were used to compare Kendall tau correlation values to chance (mu=0) and robust regressions were used to compare values across groups, as values were non-normally distributed

(Shapiro-Wilk normality test: W=.91, p=4.0x10^{-7}). Variance was similar across groups (blind vs. all sighted: F(1,126)=2.4, p=.13; blind vs. blindfolded: F(1,33)=2.2, p=.15).

The condition model fit to RTPJ neural RDMs outperformed chance in sighted children only (all sighted: W=4793, p=3.6x10^{-7}; blindfolded: W=138, p=.01; blind: W=95, p=.20; one-sided Wilcoxon tests against zero). However, condition model fit values did not differ across blind and sighted children in RTPJ (blind vs. all sighted: b=-.26, t=-1.2, CI=[-.69,.16], p=.22; blind vs. blindfolded: b=-.48, t=-1.4, CI=[-1.2,.20], p=.16), though there was a significant group-by-age interaction such that values increased more with age in blind children relative to blindfolded sighted children (b=.52, t=2.1, CI=[.008,1.02], p=.047). Condition model fit values did not differ across groups in analyses of all ToM ROIs (blind vs. all sighted: b=-.21, t=-1.3, CI=[-.53,.10], p=.19; blind vs. blindfolded: b=-.21, t=-.91, CI=[-.66,.24], p=.37; Supplementary Figure 9).

Condition model fit in RTPJ correlated with performance on the behavioral ToM task, controlling for age and motion (b=.38, t=3.9, CI=[.18,.59], p=.0008; effect of age: b=.69, t=7.3, CI=[.49,.88], p=2.0x10^{-7}). This brain-behavior correlation remained significant in a regression that additionally included group as a main effect (b=.31, t=2.1, CI=[.01,.62], p=.046). The correlation between condition model fit and ToM task performance did not differ by group (group-by-model fit interaction: b=.24, t=.83, CI=[-.36,.85], p=.41). Exploratory analyses with other ToM regions revealed a similar brain-behavior correlation in precuneus (b=.37, t=3.5, CI=[.15,.60], p=.002; with group effect added: b=.40, t=3.2, CI=[.14,.65], p=.004; Supplementary Figure 10).

References

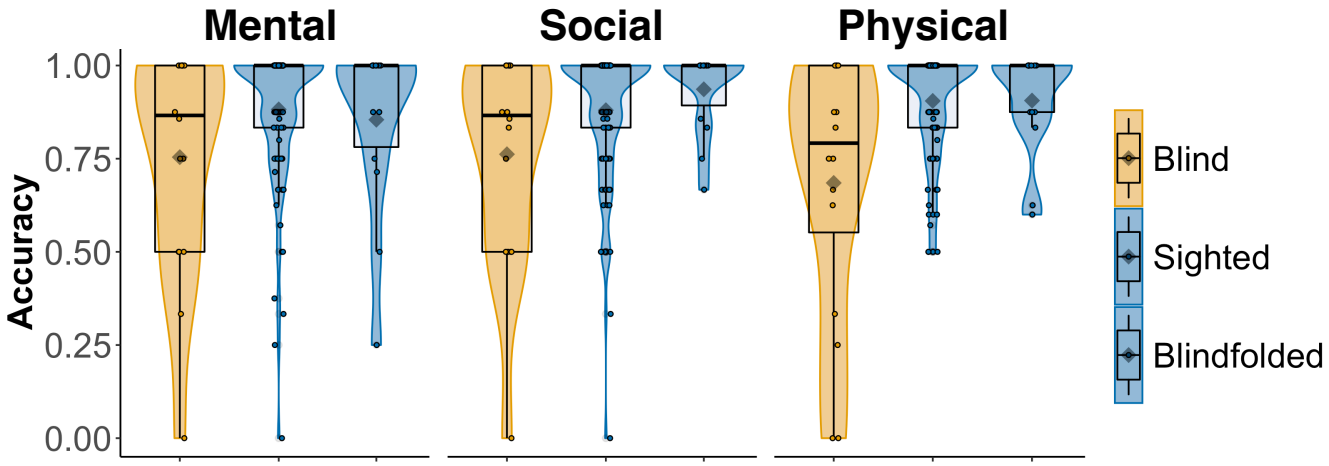
Dufour, N., Redcay, E., Young, L., Mavros, P. L., Moran, J. M., Triantafyllou, C., Gabrieli, J. D., & Saxe, R. (2013). Similar brain activation during false belief tasks in a large sample of adults with and without autism. *PLoS ONE*, *8*(9), e75468.

Gweon, H., Dodell-Feder, D., Bedny, M., & Saxe, R. (2012). Theory of mind performance in children correlates with functional specialization of a brain region for thinking about thoughts. *Child Development*, *83*(6), 1853–1868.

Richardson, H., Gweon, H., Dodell-Feder, D., Malloy, C., Pelton, H., Keil, B., Kanwisher, N., & Saxe, R. (2020). Response patterns in the developing social brain are organized by social and emotion features and disrupted in children diagnosed with autism spectrum disorder. *Cortex*, *125*, 12–29. https://doi.org/10.1016/j.cortex.2019.11.021

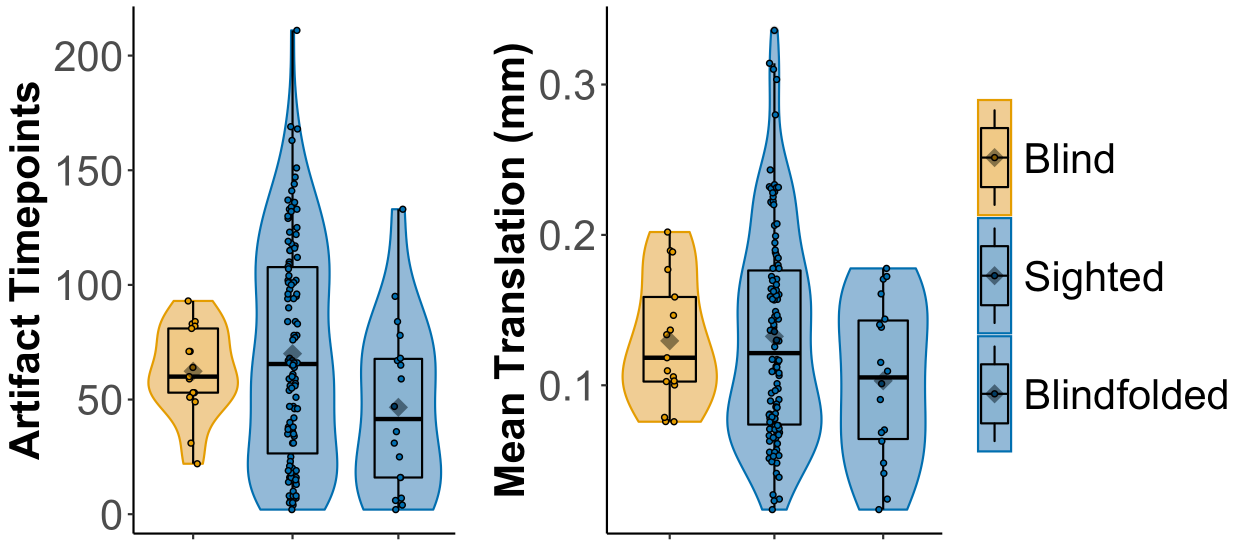
Richardson, H., Koster-Hale, J., Caselli, N., Magid, R., Benedict, R., Olson, H., Pyers, J., & Saxe, R. (2020). Reduced neural selectivity for mental states in deaf children with delayed exposure to sign language. *Nature Communications*, *11*(1), 1–13.

Supplementary Figure 1



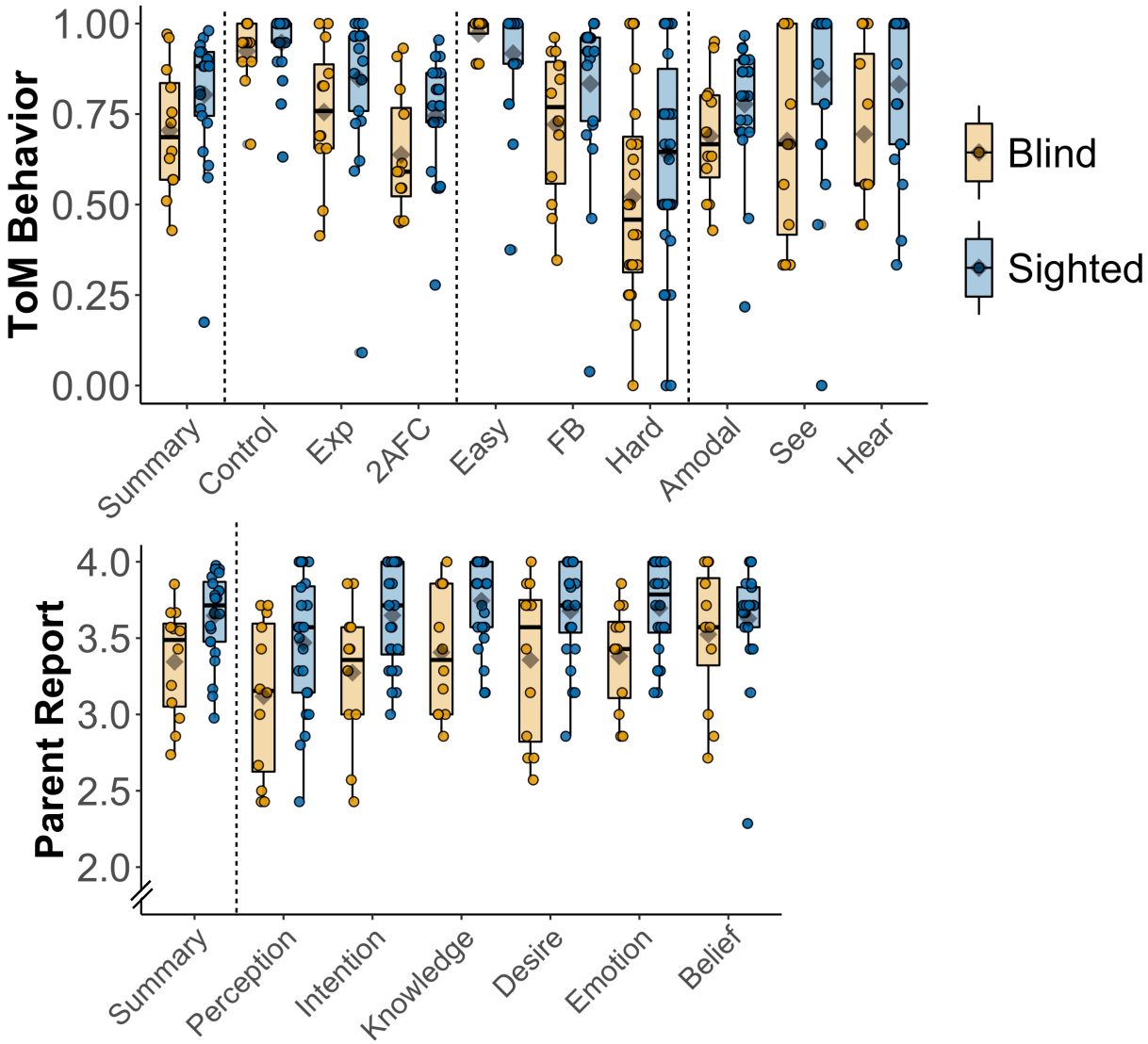
SM Figure 1. Behavioural performance on fMRI task. Box and violin plots show accuracy on the "Does this come next?" task (y-axis) by story condition (Mental, Social, Physical) and by group (blind in orange [n=16], sighted (including blindfolded) in blue [n=108], blindfolded in blue [n=14]). Center line indicates median, box reflects interquartile range, whiskers show first quartile/third quartile -/+ 1.5*IQR, transparent black diamonds indicate group average. Accuracy (proportion of answered questions that were answered correctly) was high across groups and conditions, indicating attention to the story task.

Supplementary Figure 2



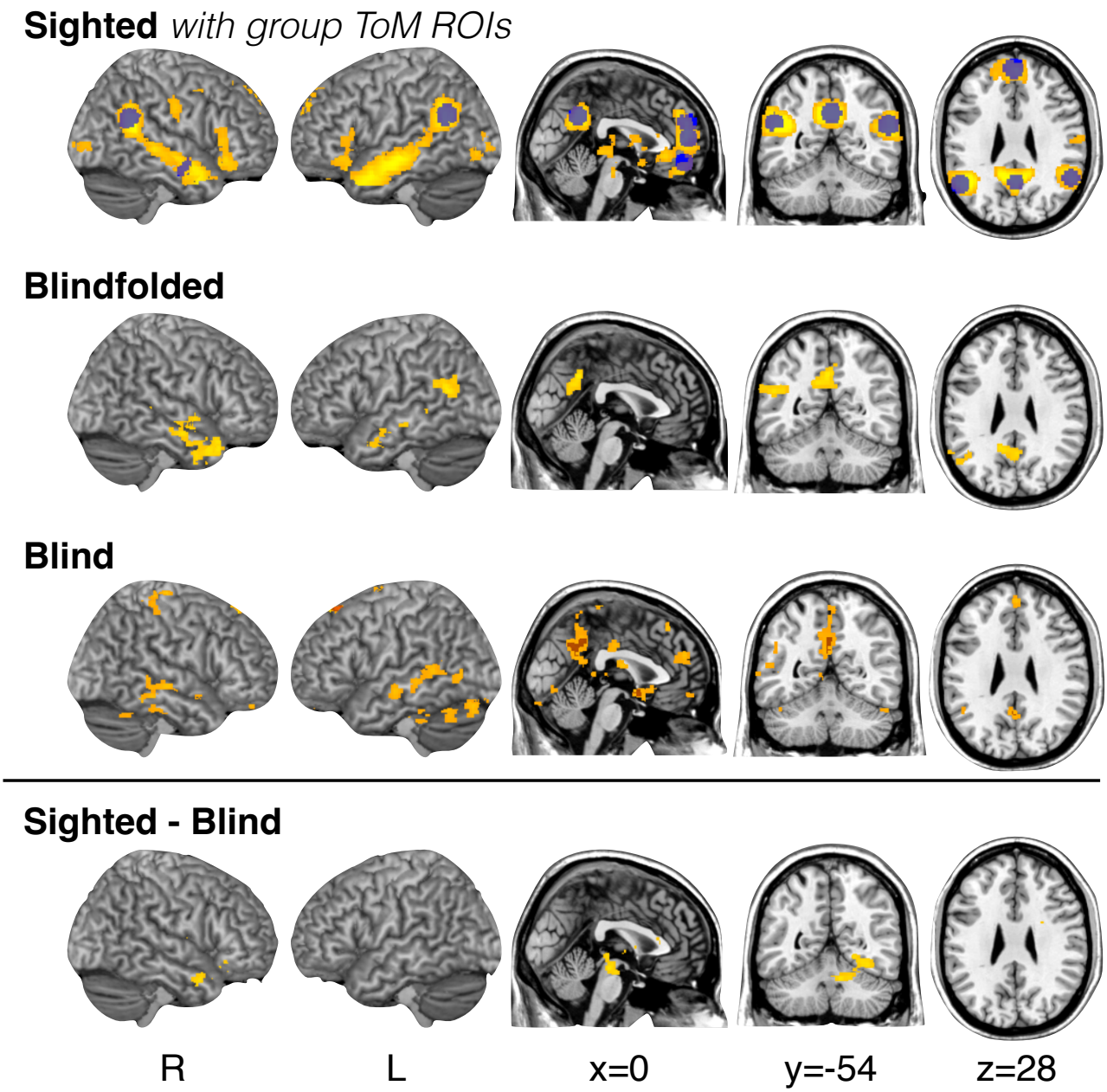
SM Figure 2. Motion during the fMRI experiment. Box and violin plots show the number of artifact timepoints (left; y-axis) and mean translation (i.e., motion between frames in x, y, and z directions prior to removal of artifact timepoints, in millimeters, right; y-axis) in blind children (n=17, orange), sighted children (including blindfolded children, n=114; blue), and blindfolded children only (n=18, blue). Center line indicates median, box reflects interquartile range, whiskers show first quartile/third quartile -/+ 1.5*IQR, transparent black diamonds indicate group average.

Supplementary Figure 3



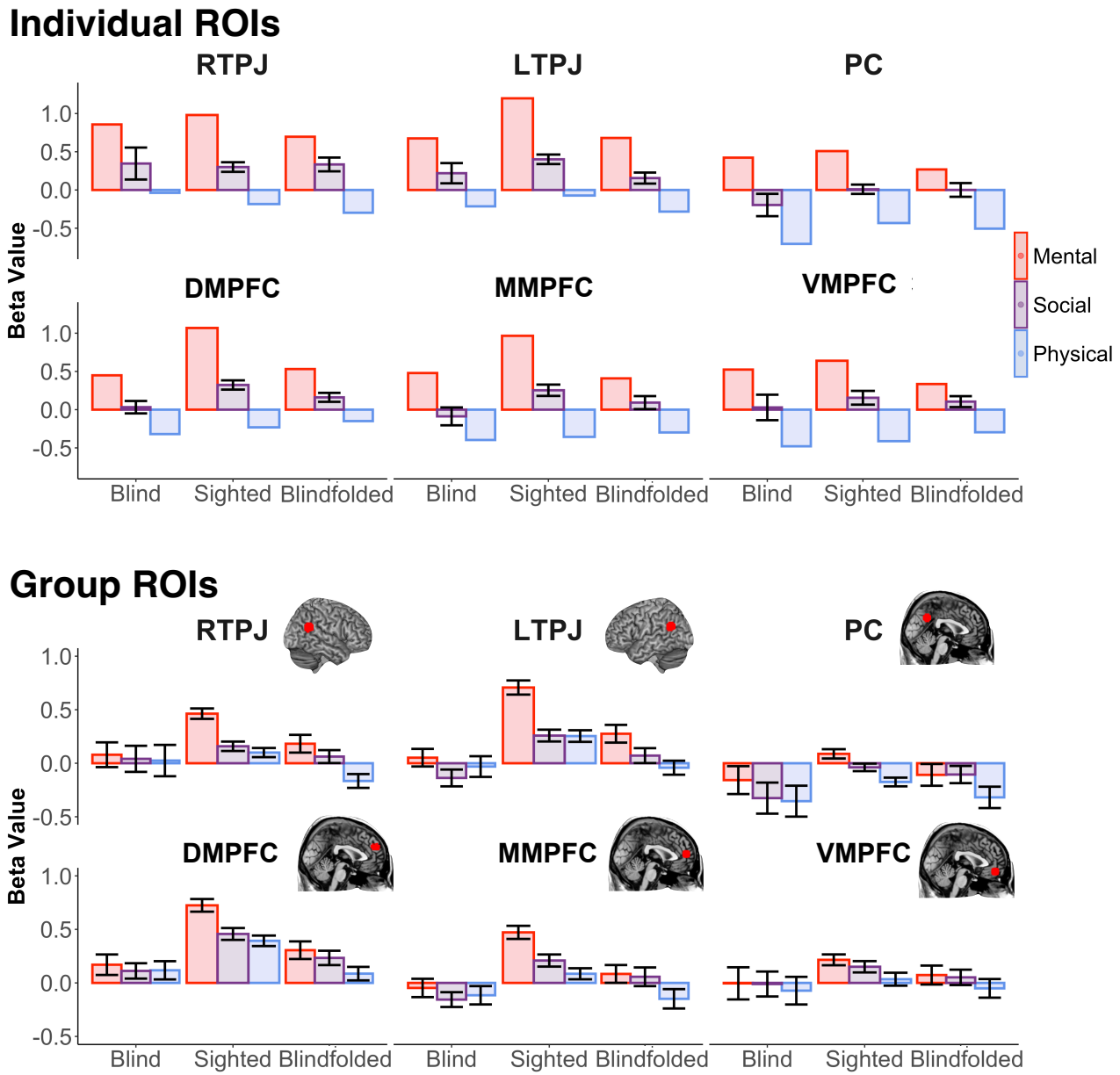
SM Figure 3. ToM Behavior and Parent Report. **Top:** Box plots show the distribution of proportion correct values on the ToM behavioral task (y-axis), calculated for the overall summary score (left), and for items by question type (Control, Explanation ("Exp"), 2-alternative forced choice ("2AFC"), ToM concept category (Easy, False Belief ("FB"), Hard), and by source modality (Amodal, Visual ("See"), or Aural ("Hear")) for blind (n=12, orange) and sighted (n=21, blue). **Bottom:** Box plots show the distribution of mean values on the Children's Social Understanding Scale (y-axis), calculated across all items ("Summary", left), and across items by concept category for blind (n=16, orange) and sighted (n=24, blue) children. The full range of values was 0-4. For all box plots, center line indicates median, box reflects interquartile range, whiskers show first quartile/third quartile -/+ 1.5*IQR, transparent black diamonds indicate group average score.

Supplementary Figure 4



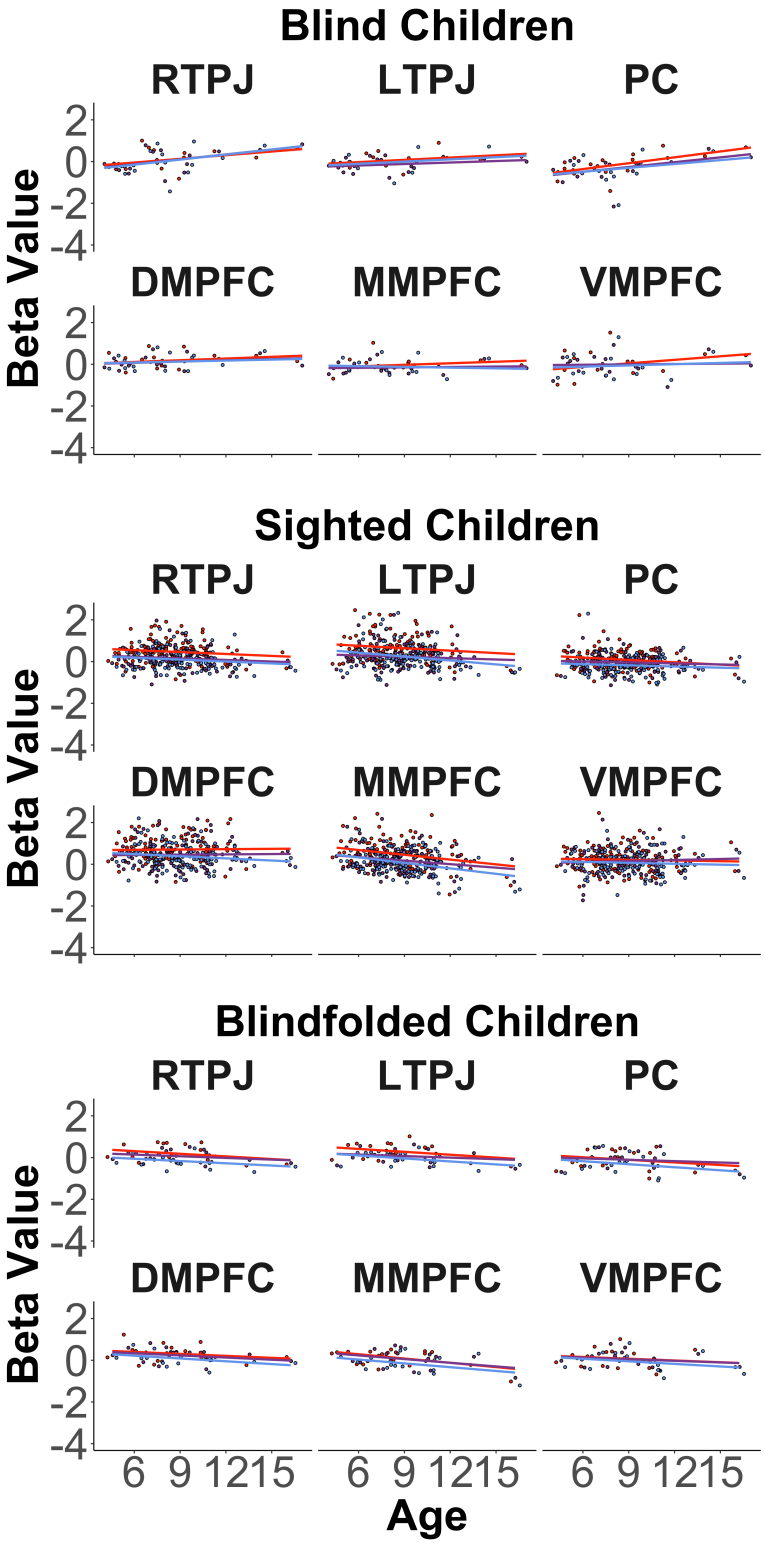
SM Figure 4. Whole-brain random effects analysis of the Mental > Physical contrast. Sighted row shows results from all sighted children (n=114, including n=18 blindfolded); group ROIs for ToM regions are shown in blue (see Richardson et al., 2020 for details and https://osf.io/pavdg/ to download). Blindfolded row shows results from blindfolded children only (n=18). All results were corrected for multiple comparisons at p<.05, except for the results in blind children (n=17), which are shown at uncorrected thresholds (yellow: p<.05, k=10; red: p<.01, k=50). Subtraction analysis shows clusters that were significantly more active in sighted children (including blindfolded children) relative to blind children, corrected for multiple comparisons at p<.05.

Supplementary Figure 5



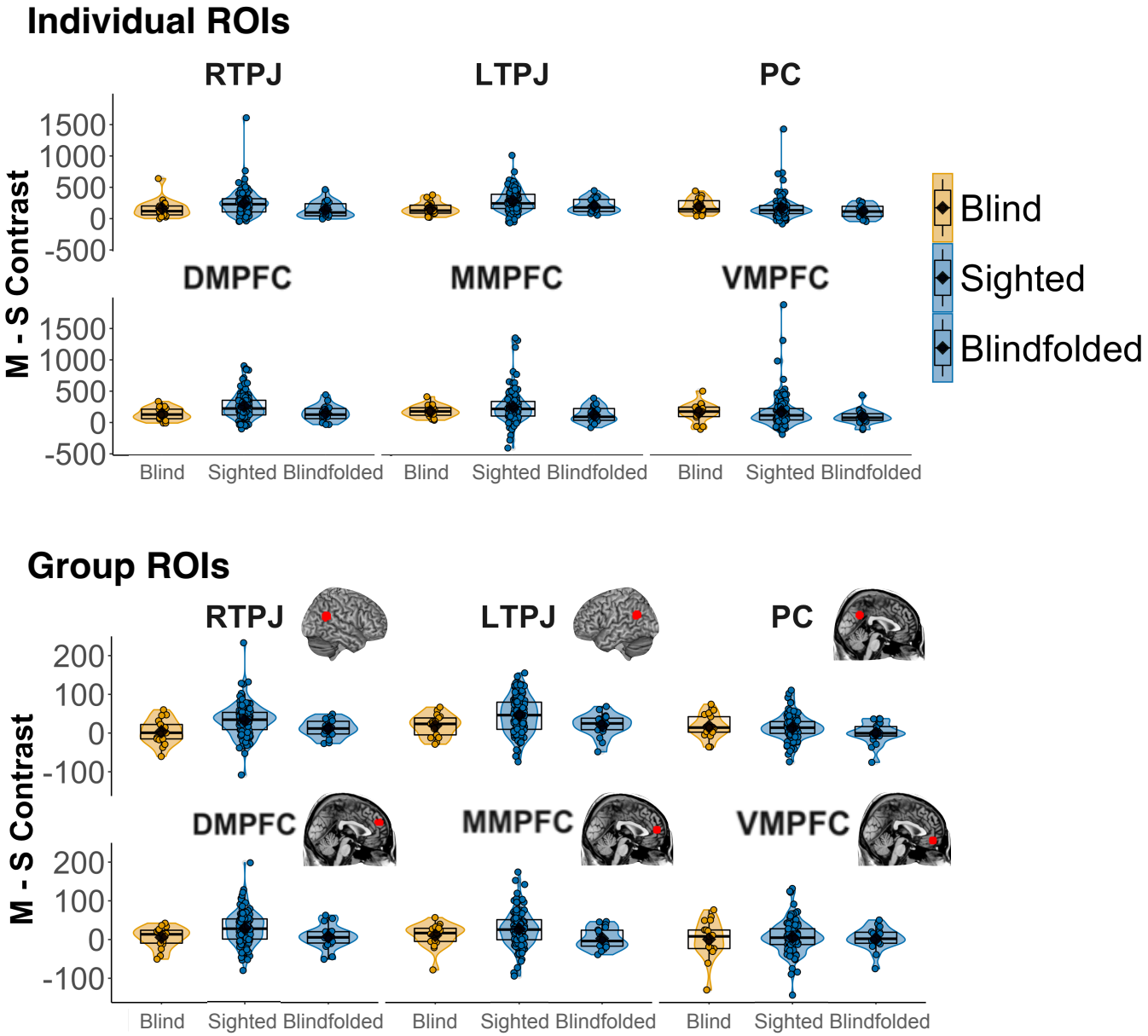
SM Figure 5. Beta values per region of interest definition, region of interest, group, and condition. Bar charts show the beta value per story condition (Mental, Social, Physical) extracted from individual-subject (top) and group-defined (bottom) ToM ROIs in blind (n=17), all sighted (n=114), and blindfolded sighted (n=18) children. Error bars indicate standard error from the mean. Error bars are omitted for Mental and Physical conditions in the individual-subject ROI plots because these conditions were used for individual ROI definition.

Supplementary Figure 6



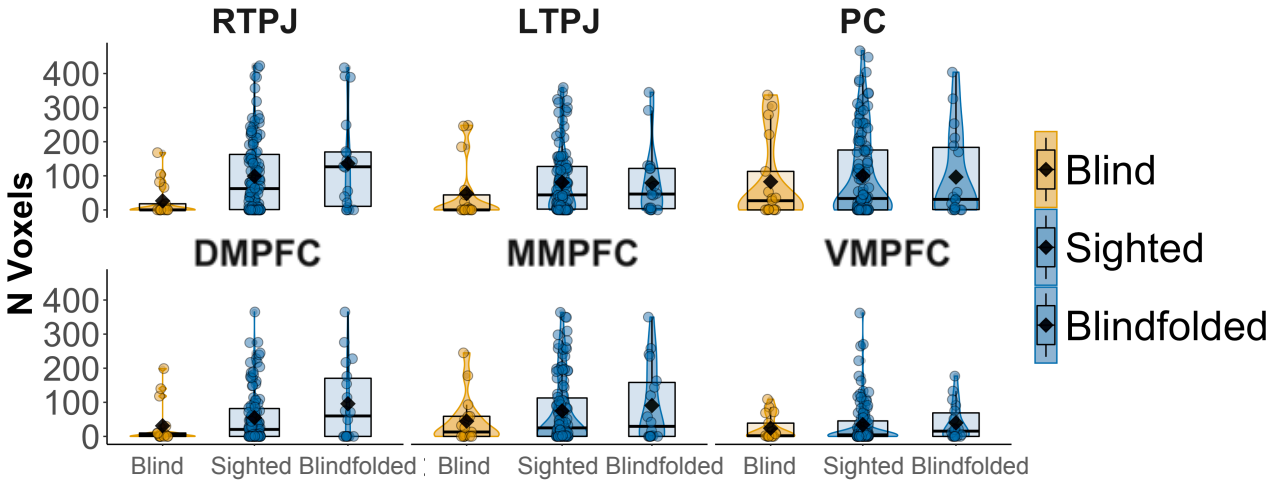
SM Figure 6. Beta values per group, region of interest, condition, and age. Scatter plots show the beta value (y-axis) per story condition (Mental, Social, Physical) extracted from group-defined ToM ROIs in blind (n=17), all sighted (n=114), and blindfolded sighted (n=18) children, by age (x-axis).

Supplementary Figure 7



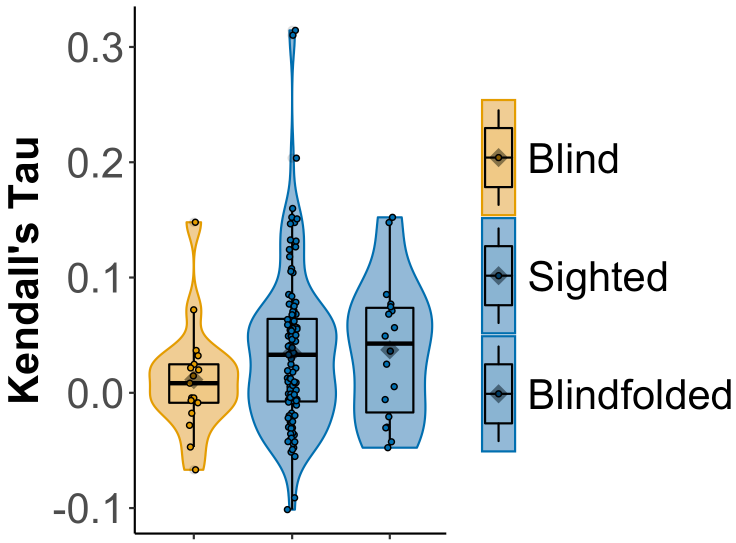
SM Figure 7. Selectivity values per region of interest definition, region of interest, and group. Box and violin plots show response selectivity (Mental - Social contrast value; y-axis) in blind children (n=17, orange), sighted children (including blindfolded children, n=114; blue), and blindfolded children only (n=18, blue). Center line indicates median, box reflects interquartile range, whiskers show first quartile/third quartile -/+ 1.5*IQR, transparent black diamonds indicate group average.

Supplementary Figure 8



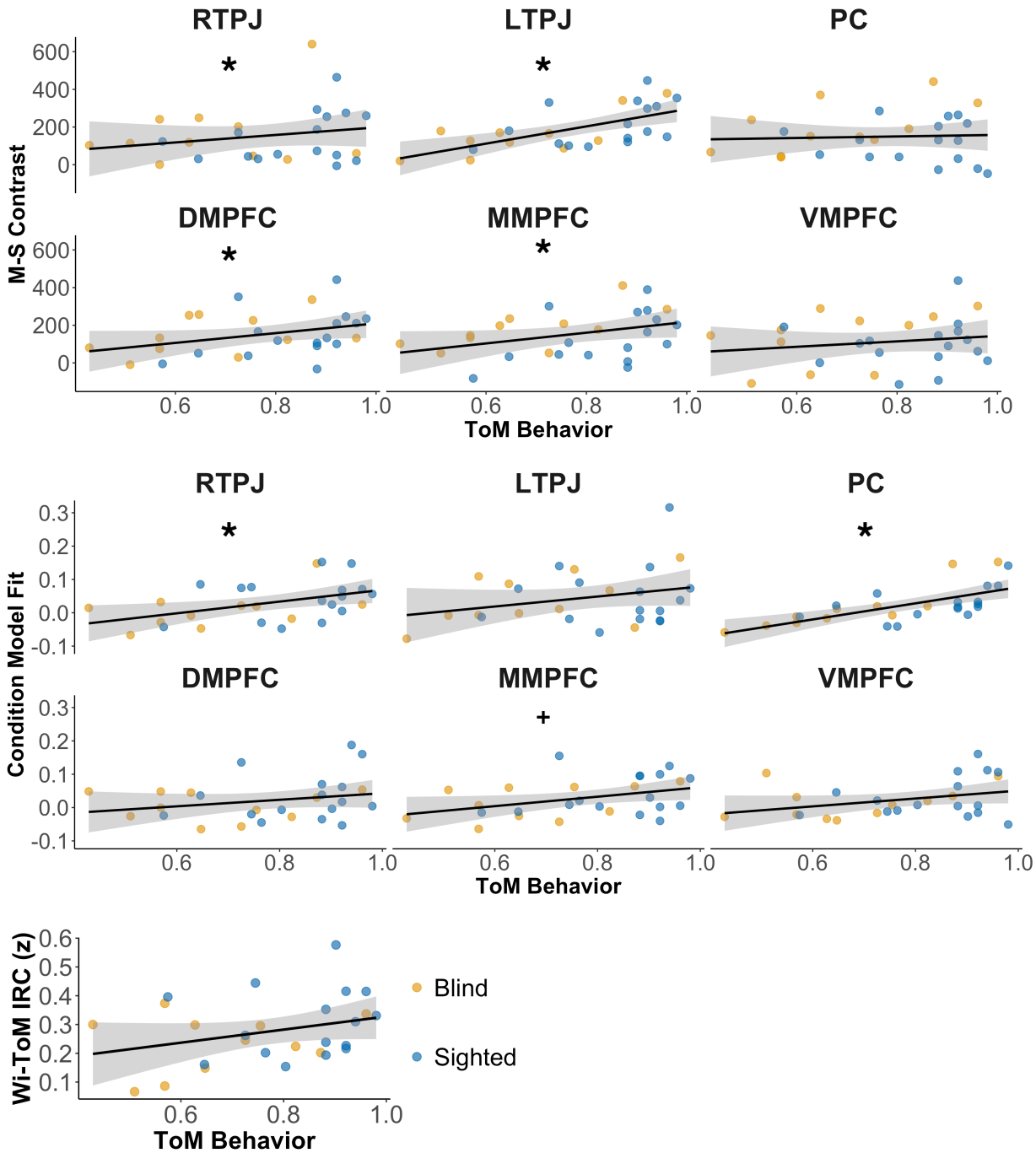
SM Figure 8. Suprathreshold voxels within group-defined ToM ROIs. Violin and box plots show the number of suprathreshold voxels (p<.001, T=3.10) to the Mental > Physical contrast within each group-defined ToM ROI (y-axis). Values are shown per group (blind in orange [n=17], sighted (including blindfolded) in blue [n=114], blindfolded also in blue [n=18]). Center line indicates median, box reflects interquartile range, whiskers show first quartile/third quartile -/+ 1.5*IQR, transparent black diamonds indicate group average.

Supplementary Figure 9



SM Figure 9. RTPJ Condition Model Fit. Violin and box plots show Kendall's tau correlation value (y-axis), which indicates the extent to which a model that described story stimuli similarity in terms of their condition label ("Condition model") correlated with a neural model of story stimuli similarity in terms of the pattern of response that they evoked in RTPJ. Values are shown per group (blind in orange [n=17], sighted (including blindfolded) in blue [n=114], blindfolded also in blue [n=18]). Center line indicates median, box reflects interquartile range, whiskers show first quartile/third quartile -/+ 1.5*IQR, transparent black diamonds indicate group average. Condition model fit in RTPJ did not differ significantly between blind and sighted children.

Supplementary Figure 10



SM Figure 10. Brain-Behavior Correlations. Scatter plots show proportion correct on the non-visual story-based behavioral ToM task, administered outside of the scanner (x-axis), by response selectivity (Mental > Social contrast value, top), condition model fit (Kendall tau correlation, middle), and within-ToM inter-region correlation value (z-scored correlation, bottom) on the y-axis in blind children (orange, n=11) and sighted children (blue, n=16). Asterisks indicate significant brain-behavior correlations, controlling for age and motion ($p<.05$, robust regression); plus sign indicates marginal effect ($p<.1$, robust regression).

Supplementary Table 1

Participant	Gender	Age-fMRI	Age-Behavior	Handedness	Age when learned English	Mono/MultiLingual	Age of Blindness	Cause of Blindness	Residual Vision	Included in fMRI	NVToM	CSUS
BC1	M	8.05	9.59	Left	Birth	Multilingual	Birth	Premature birth/ROP	Minimal LP	Y	NA	3.52
BC2	M	5.7	7.17	Ambi	28.5 mo	Multilingual	Birth	Microphthalmia, Retinal Dysplasia, CM, PA	None	Y	0.51	2.98
BC3	F	4.03	5.42	Right	24 mo	Multilingual	Birth	Premature birth/ROP Stage V	None	Y	NA	3.36
BC4	F	17	18.55	Right	Birth	Monolingual	Birth	Optic Nerve Hypoplasia	None	Y	NA	3.71
BC5	F	7.53	7.53	Right	Birth	Monolingual	2-5 yrs	Uveitis	Minimal LP	Y	NA	NA
BC6	F	9.5	9.5	Ambi-Right	Birth	Monolingual	Birth	Familial Exudative Vitreoretinopathy (FEVR)	None	Y	NA	NA
BC7	M	14.24	15.54	Ambi	Birth	Monolingual	Birth	Bilateral detached retinas at birth	None	Y	NA	3.93
BC8	M	8.37	8.37	Right	Birth	Monolingual	Birth	Leber's Congenital Amaurosis	None	N	0.97	3.56
BC9	M	9.62	9.62	Ambi-Right	Birth	Monolingual	Birth	Leber's Congenital Amaurosis	Light/Some form P	Y	0.75	2.74
BC10	F	7.22	7.22	Ambi-Right	Birth	Monolingual	2 mo	Leber's Congenital Amaurosis	LP	Y	0.87	3.67
BC11	M	4.64	4.64	Right	Birth	Multilingual	Birth	Leber's Congenital Amaurosis	None	Y	0.65	3.19
BC12	F	11.55	11.55	Left	Birth	Monolingual	Birth	Leber's Congenital Amaurosis	None	Y	0.96	3.85
BC13	M	5.13	5.13	Right	Birth	Multilingual	Birth	Microphthalmia with sclerocornea	LP, some color	Y	0.43	3.08
BC14	F	5.05	5.05	Right	Birth	Monolingual	Birth	Leber's Congenital Amaurosis	LP	Y	0.63	3.55
BC15	M	6.76	6.76	Right	Birth	Monolingual	Birth	Leber's Congenital Amaurosis	None	Y	0.73	3.43
BC16	M	7.78	7.78	Right	Birth	Monolingual	Birth	Leber's Congenital Amaurosis	LP	Y	0.57	3.67
BC17	F	5.69	5.69	Right	Birth	Monolingual	Birth	Microphthalmia	None	Y	0.57	3.57
BC18	M	9.24	9.24	Right	Birth	Monolingual	Birth	Leber's Congenital Amaurosis Type 1	LP	Y	0.82	2.86

Blind children (fMRI: n=17, 4-17 years old, M(SD)=8.16(3.5); 8 girls; 11 right-handed, 5 ambidextrous (3 right-hand dominant), 2 left-handed; 12 monolingual, 5 multilingual; behavioral ToM: n=12, 4-11 years, M(SD)=7.4(2.1), 4 girls)
Blindfolded children (fMRI: n=18, 4.5-16 years old, M(SD)=8.99(2.9); 12 girls; 13 right-handed, 5 left-handed; 10 monolingual, 8 multilingual; behavioral ToM: n=21, 4-11 years, M(SD)=7.9(2.0), 14 girls)
All sighted children (fMRI: n=114, 4.5-16 years old, M(SD)=8.77(2.2); 39 girls; 92 right-handed, 1 ambidextrous, 10 left-handed, 11 handedness unknown; 58 monolingual, 14 multilingual, 42 unknown)

SM Table 1. Participant demographics. Age of blindness describes onset of blindness, which is defined as absence of vision with at most minimal light perception (LP). NVToM shows proportion correct on the NV ToM behavioral task (administered outside of the scanner); CSUS shows average score on the CSUS Parent Report measure. BC: Blind child; ROP: retinopathy of prematurity; CM: coloboma microcornea; PA: Peter's anomaly.