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WORKSHOP 1

ID 420. Language related brain areas and outcomes in extremely preterm children during childhood

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Introduction

Language disabilities are common among preterm children. Both positive and negative correlations between verbal IQ and grey and white matter volumes for very preterm children (<32 weeks) have been reported during childhood and adolescence. We reported altered patterns of brain asymmetry at term age in extremely preterm children with later diagnosis of autism. However, there is a lack of knowledge about the associations between language scores and brain volumetric data in extremely preterm children (<27 weeks) during childhood.

Methods

Brain volumetry was investigated in 50 EPT children (<27 weeks) and 37 controls at 10 years using atlas-based segmentation. Brain volumes of separate regions within the language network (inferior frontal gyrus (opercular and triangular), temporal gyri (superior, middle and inferior) supplementary motor areas, Heschl gyrus, supramarginal and angular cortices) and all regions summed together were compared between EPT children and controls. Results were adjusted for age at scan, intracranial volume, sex and handedness. We used the Bonferroni correction. An asymmetry index for the language network was calculated based on the formula: AI=(VL–VR)/(VL+VR). The brain volume of the volume and asymmetry score of the language network was correlated with language outcomes at 12 years (similarities scale, vocabulary scale and verbal IQ within WISC V and repetition of sentences within CELF 4) for n=40 EPT children and n=29 controls using Pearson's correlations for normally distributed data, correcting for age at scan, sex and handedness.

Results

All regions within the language network except for the Heschl'gyrus were significantly smaller for the EPT children compared to the controls, also after correcting for multiple comparisons (Table 1). Asymmetry indices were not different between extremely preterm children and controls. We found significant positive correlations between the volume of the language network and the vocabulary subscale within WISC V and repetitions of sentence scale within CELF 4, $p<0.05$. Asymmetry index of the language network did not correlate significantly with language scores.

Conclusion

These findings demonstrate abnormal development of language-related brain regions in EPT children with an impact on their functional outcome. However, brain asymmetry within the language network seems to be of less importance at this age.

Brain region	Extremely preterm children adjusted mean volumes, cm^3 (SD)	Controls adjusted mean volumes, cm^3 (SD)	Mean difference, (confidence interval), adjusted	3) *p*-value adjusted
Supplementary motor area, right	15.00 (0.47)	15.27 (0.53)	⍰0.27 (⍰0.40, ⍰0.14)	**<0.001**
Supplementary motor area, left	13.60 (0.53)	13.84 (0.56)	⍰0.25 (⍰0.37, ⍰0.13)	**<0.001**
Inferior frontal gyrus, triangular, right	13.64 (0.66)	13.89 (0.67)	⍰0.25 (⍰0.38, ⍰0.11)	**<0.001**
Inferior frontal gyrus, triangular, left	15.82 (0.37)	16.13 (0.51)	⍰0.31 (⍰0.47, ⍰0.15)	**<0.001**
Inferior frontal gyrus, opercular, right	9.04 (0.35)	9.18 (0.32)	⍰0.13 (⍰0.22, ⍰0.05)	**0.002**
Inferior frontal gyrus, opercular, left	6.39 (0.34)	6.49 (0.4)	⍰0.10 (⍰0.15, ⍰0.05)	**<0.001**
Heschel gyrus, right	1.53 (0.057)	1.55 (0.061)	⍰0.025 (⍰0.042, ⍰0.008)	0.005
Heschel gyrus, left	1.36 (0.028)	1.37 (0.052)	⍰0.015 (⍰0.032, ⍰0.003)	0.097
Angular gyrus, right	11.52 (0.49)	11.73 (0.49)	⍰0.20 (⍰0.30, ⍰0.11)	**<0.001**
Angular gyrus, left	6.98 (0.20)	7.10 (0.23)	⍰0.12 (⍰0.19, ⍰0.06)	**<0.001**
Supramarginal gyrus, right	12.3 (0.50)	12.6 (0.52)	⍰0.21 (⍰0.31, ⍰0.10)	**<0.001**
Supramarginal gyrus, left	7.24 (0.23)	7.36(0.24)	⍰0.13 (⍰0.18, ⍰0.07)	**<0.001**
Superior temporal gyrus, right	19.68 (0.71)	20.03 (0.79)	⍰0.35 (⍰0.52, ⍰0.17)	**<0.001**
Superior temporal gyrus, left	13.65 (0.37)	13.87 (0.44)	⍰0.21 (⍰0.33, ⍰0.09)	**0.001**
Middle temporal gyrus, right	27.56 (1.07)	28.00 (1.09)	⍰0.44 (⍰0.67, ⍰0.21)	**<0.001**
Middle temporal gyrus, left	28.99 (0.86)	29.47 (0.97)	⍰0.49 (⍰0.72, ⍰0.25)	**<0.001**
Inferior temporal gyrus, right	22.11 (0.78)	22.42 (0.85)	⍰0.32 (⍰0.51, ⍰0.14)	**0.001**
Inferior temporal gyrus, left	18.44 (0.47)	18.74 (0.57)	⍰0.31 (⍰0.46, ⍰0.15)	**<0.001**
Language network	244.85 (8.20)	248.96 (8.94)	⍰4.11 (⍰6.12, ⍰2.09)	**<0.001**

** All analyses are corrected for sex, age at scan, intracranial volume and handedness. Bold values remained significant after correcting for multiple comparisons.

Brain volumetric differences between extremely preterm children and control children corrected for sex, age at scan, handedness and intracranial volume.

Brain volumetric differences between extremely preterm children and control children corrected for sex, age at scan, handedness and intracranial volume.

None declared

ID 478. Morphine exposure and neurodevelopmental outcome in extremely preterm infants

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Background: Opioids are the most common drugs used to treat pain and stress in infants receiving mechanical ventilation in the NICU. However, controversial data regarding their effects on long-term neurological outcome have been reported.
Methods: We conducted a retrospective study in extremely preterm infants (gestational age (GA) <28 weeks), admitted to the Wilhelmina Children's Hospital NICU, Utrecht, between 2008 and 2011 with the aim to investigate the association between morphine exposure up to term age and neurodevelopmental outcome at 2 and 5 years. Morphine administration was expressed as cumulative dose (mg/kg) until term-equivalent age (TEA). Neurodevelopmental outcome was assessed at 2 years with the Bayley Scales of Infant and Toddler Development (BSID-III-NL) and at 5 years with the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III-NL). Multivariable linear regression analysis was used to assess the association between morphine exposure and outcome. Analyses were adjusted for confounders: GA, patent ductus arteriosus, long-term mechanical ventilation (> 7 days), postnatal corticosteroids, number of painful procedures, intraventricular hemorrhage (IVH), white matter injury (WMI), cerebellar hemorrhage and maternal education.
Results: 106 extremely preterm infants were included in the study, sixty-four received morphine (60.4%) at a mean dose 2.03 +- 2.09 mg/kg during their NICU admission. Infants exposed to morphine were more frequently male, had a lower GA and birth weight, longer mechanical ventilation, a higher incidence of IVH, bronchopulmonary dysplasia and WMI at TEA compared to not-exposed infants. Moreover, exposed subjects revealed a significantly worse motor performance at 2 years ($p<0.005$), whereas no differences were observed in cognitive and language of Bayley-III-NL and in WPSSI-III-NL score, respectively. At regression analysis morphine exposure did not represent a risk factor for a worse Bayley-III-NL scores at 2 years. Nevertheless, morphine-exposure resulted a risk factor for a lower Fullscale-IQ scores ($p=0.008$, B=-9.3, CI -15.6 -3.1) and Performance-IQ scores ($p=0.005$, B=-17.5, CI -27.9 -7) at 5 years of age.
Conclusion: Morphine exposure in extremely preterm infants is not associated with neurological outcome at 2 years. However, an association is found with poorer Fullscale -IQ and Performance IQ at 5 years. Future, prospective studies with larger sample sizes are needed to confirm these findings.
None declared