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Magnetresonanztomographie beim Frühgeborenen

Möglichkeiten und Perspektiven

Pädiatrische Traunseeklausur 2024

Neonatologie und Notfallmedizin

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Pädiatrie II, Neonatologie

Medizinische Universität Innsbruck



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- Einleitung
- aktuelle Möglichkeiten: Routine-Sequenzen – und was sagen sie uns?
- Perspektiven

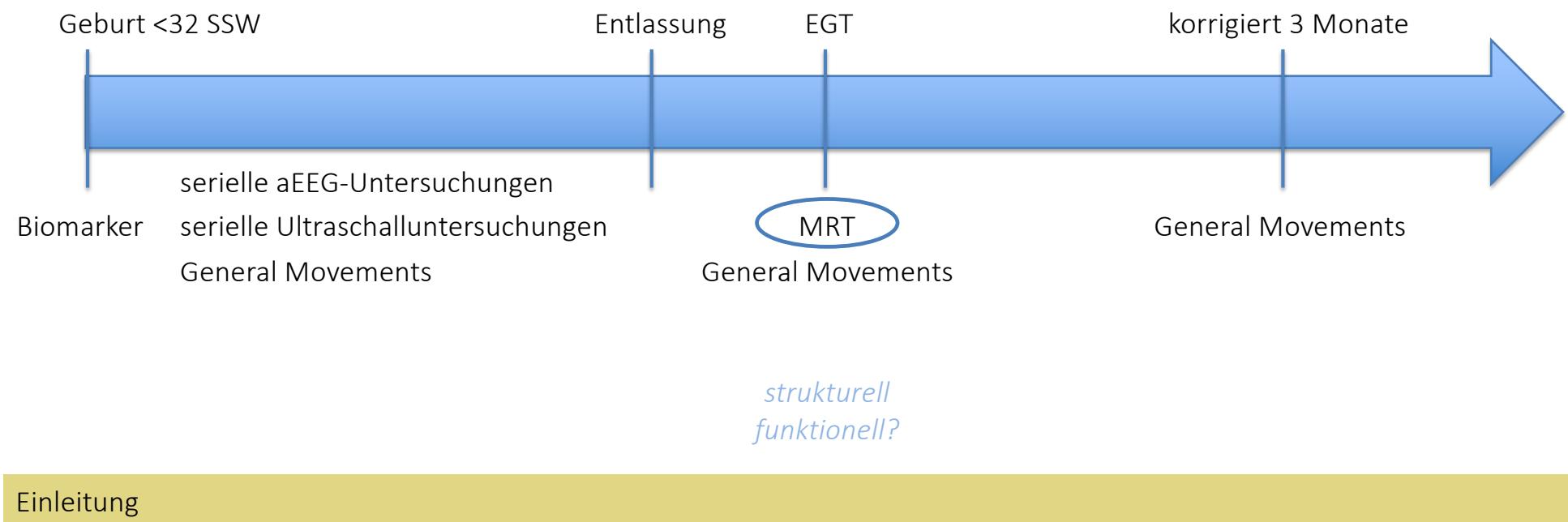


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Prognostische Tools





Magnetresonanztomographie



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- höhere Auflösung – auch in Bereichen, die für US nicht gut zugänglich sind
- genauere Detektion von Gehirnschädigung & Abbildung der Reife
- verschiedene Sequenzen je nach Fragestellung
- teuer & zeitaufwändig
- Durchführung beim kritisch-kranken Patienten schwierig
- Sedierung (?)

Einleitung



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REGULAR ARTICLE

Feasibility of cerebral MRI in non-sedated preterm-born infants at term-equivalent age: report of a single centre

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Keywords

Brain, MRI, Preterm, Sedation, Term-equivalent age

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*These authors equally contributed to this work.

ABSTRACT

Aim: MRI is gaining in importance as an imaging tool for brain development and injury in preterm infants. The aim of this study was to evaluate the feasibility of performing MRI in non-sedated preterm-born infants at term-equivalent age (TEA).

Methods: A total of 89 infants born before 32 gestational weeks were recruited. Infants were scanned without sedation. Duration of the entire examination including scan repetition and interruptions was registered.

Results: Of the 89 infants, 56 (63%) underwent MRI at TEA. Out-patients required significantly shorter total MR examination time than did in-patients (32 ± 12 vs. 54 ± 10 min, $p < 0.01$). Of the 56 infants, 39 (69.6%) were examined without interruption. Only four (7.2%) of the 56 scans were unusable because of motion artefacts. Mean duration of all scans was 36 ± 14 min. In cases with no interruptions, sessions were completed within 32 ± 12 min; MR sessions with interruption lasted 45 ± 13 min.

Conclusion: A well-trained team is indispensable in obtaining best-quality images as a prerequisite for good counselling. From our experience, we worked out a guideline to ensure that scans in stable non-sedated preterm-born infants at TEA run smoothly and provide high-quality images.

Einleitung



Ablauf



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- Routine-Untersuchung für alle Frühgeborenen <32 Schwangerschaftswochen
- am errechneten Geburtstermin
- meist nach Entlassung – i.R.d. Kontrolle an der Nachsorgeambulanz
- Zeit zum Füttern eingeplant
- ärztliche Begleitung – Sicherstellung Bildqualität, Überwachung

Einleitung



Ablauf



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- Feed and Wrap – postprandialer Schlaf
- Vakuummatratze (*VacFix®*, Par Scientific A/S, Odense S, Denmark)
- Überwachung mittels Pulsoxymetrie
- 3-Tesla-MRT – 60 Minuten Timeslot eingebucht
- Kontrolle Bild-
qualität nach
jeder Sequenz
– ggf. WH



Einleitung



Sequenzen im Routine-MRT



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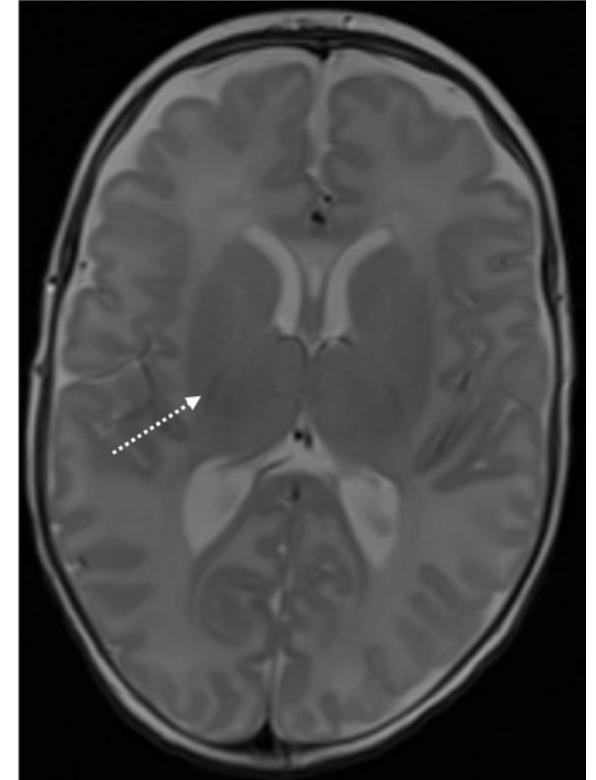
- T2-weighted images
- T1-MPRage
- Susceptibility weighted images
- Diffusion Tensor Imaging

Sequenzen



T2-weighted images

- Kontrast durch Zeit in der MR-Signal abnimmt
- Liquor hell, Hirnparenchym ebenfalls hell (erhöhter Wasseranteil, geringe Myelinisierung)
- PLIC wird mit zunehmender Reifung dunkler



Sequenzen

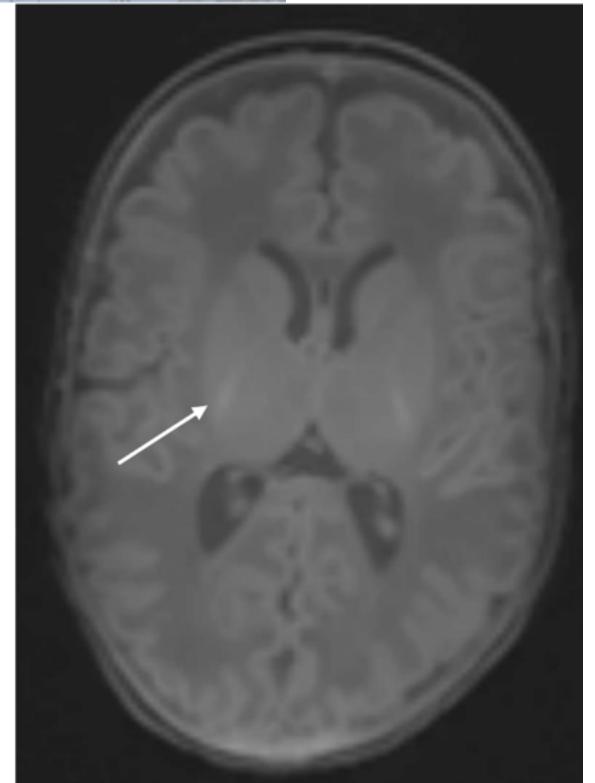


T1-MPRage



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- Kontrast durch Zeit in der sich die Spins erholen
- Liquor dunkel, Fett hell
- PLIC wird mit zunehmender Reifung heller



Sequenzen



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Neonatology

Neonatology 2015;107:179–184
DOI: [10.1159/000369199](https://doi.org/10.1159/000369199)

T2WI & T1-MPRage

Bronchopulmonary Dysplasia Is Associated with Delayed Structural Brain Maturation in Preterm Infants

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Myelinisierung
Kortikale Faltung
Germinale Matrix
Zellmigration

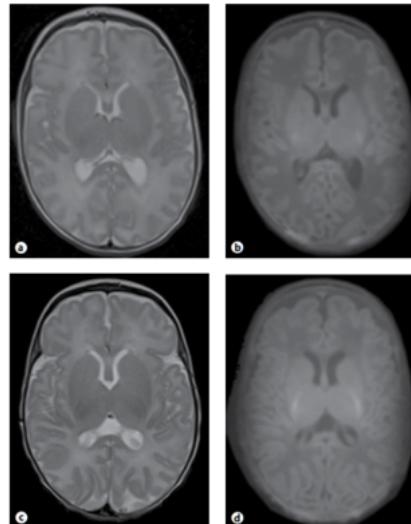


Fig. 2. Representative T2-weighted (**a, c**) and T1-weighted (**b, d**) MRI at TEA. **a, b** Infant 1, GA at birth 30 0/7 weeks, scanned at 40 3/7 weeks. TMS: 11.5 (myelination: 2.5, cortical folding: 3, germinal matrix: 3, bands of migrating cells: 3). **c, d** Infant 2, GA at birth 30 1/7 weeks, scanned at 40 4/7 weeks. TMS: 17.0 (myelination: 5, cortical folding: 4, germinal matrix: 4, bands of migrating cells: 4).

Abstract

Background: In recent years, cerebral magnetic resonance imaging (MRI) has been increasingly used to depict the wide spectrum of preterm brain injury. Furthermore, it has already been demonstrated by MRI at term-equivalent age (TEA) that preterm infants show delayed brain maturation as compared to term infants, and this delay has been related to neurobehavioral outcome. **Objectives:** The aim of the current study was to investigate the influence of prevalent neonatal risk factors for adverse outcome on structural brain maturation in very preterm infants at TEA. **Methods:** One hundred and thirty very preterm infants born at a mean gestational age of 29.7 weeks were included. MRI was performed at TEA and given a validated 'total maturation score'. Brain maturation scores were compared with neonatal data. **Results:** In univariate analysis, bronchopulmonary dysplasia (BPD), late-onset sepsis and retinopathy of prematurity were significantly associated with delayed brain maturation. Furthermore, infants with delayed maturation had been ventilated significantly longer and more often suffered from severe arterial hypotension. In multivariate analysis, BPD remained significant as predictor of delayed brain maturation. **Conclusions:** This study is the first to show that delayed structural brain maturation as evaluated by MRI at TEA is preceded by BPD, which is known to be a predictor of adverse outcome in preterm infants. This finding adds further evidence to show that adverse outcome in preterm infants may have additional neural correlates that exceed common brain injury.

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Sequenzen – und was sagen sie uns?

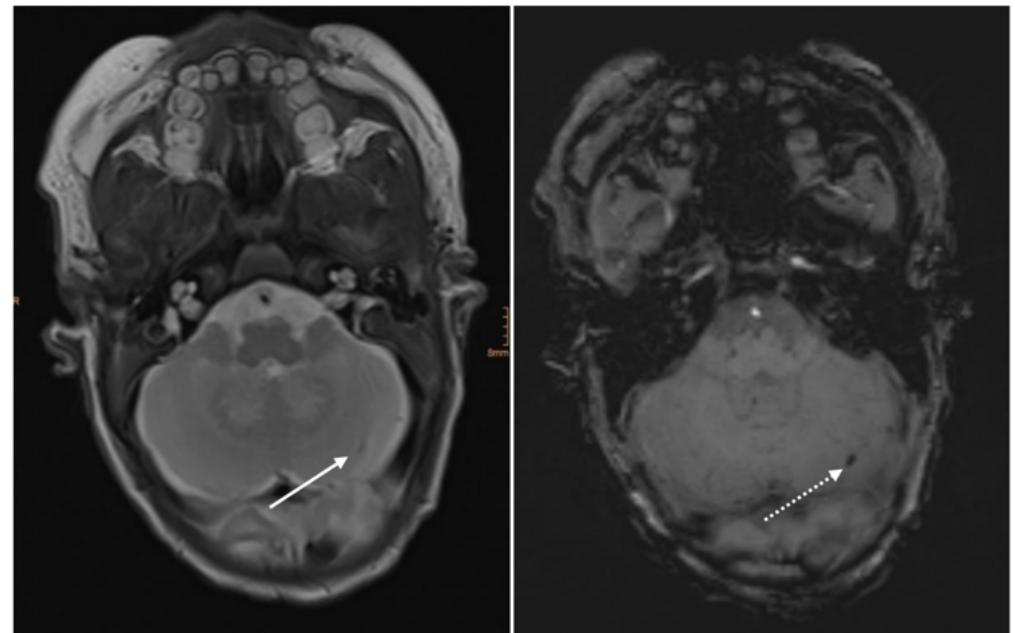


Susceptibility-weighted images



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- empfindlich gegenüber Stoffen, die Magnetfeld verzerren (Signalverlust)
- Erkennen von Hämosiderinablagerungen



Sequenzen



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RESEARCH ARTICLE

T1-MPRage & SWI

Routine Magnetic Resonance Imaging at Term-Equivalent Age Detects Brain Injury in 25% of a Contemporary Cohort of Very Preterm Infants

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Introduction

In recent years, significant investigation has been undertaken by means of magnetic resonance imaging (MRI) in an attempt to identify preterm infants at risk for adverse outcome. The primary objective is to provide a comprehensive characterization of cerebral injury detected by conventional MRI at term-equivalent age in an unselected, consecutive, contemporary cohort of preterm infants born <32 gestational weeks. Secondly, this study aims to identify risk factors for the different injury types in this population.

Methods

Data for all preterm infants born <32 gestational weeks and admitted to Innsbruck Medical University Hospital were prospectively collected (October 2010 to December 2015). Cerebral MRI was evaluated retrospectively using a validated scoring system that incorporates intraventricular haemorrhage (IVH), white matter disease (WMD) and cerebellar haemorrhage (CBH).

PLOS ONE

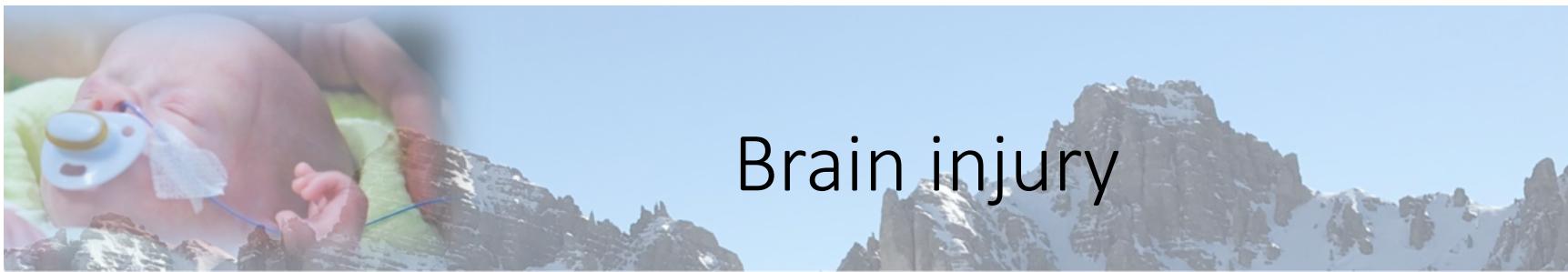
Results

300 infants were included in the study. MRI showed 24.7% of all infants to have some form of brain injury. The most common injury type was IVH (16.0%). WMD and CBH were seen in 10.0% and 8.0%. The prevalence of common neonatal risk factors was greater within the group of infants with CBH. In particular indicators for respiratory disease were observed more often: longer ventilation duration, more frequent need for supplemental oxygen at day 28, higher rates of hydrocortisone treatment. Catecholamine treatment was the only neonatal risk factor that was overrepresented in infants with WMD

Discussion

Cerebral MRI at term-equivalent age, as addition to cranial ultrasound, detected brain injury in 25% of preterm survivors. The diagnosis of IVH was already made by neonatal ultrasound in most cases. In contrast, only a minority of the CBH and none of the non-cystic WMD have been detected prior to MRI. Decreasing gestational age and neonatal complications involved with immaturity have been identified as risk factors for CBH, whereas WMD was found in relatively mature infants with circulatory disturbances.

Sequenzen – und was sagen sie uns?



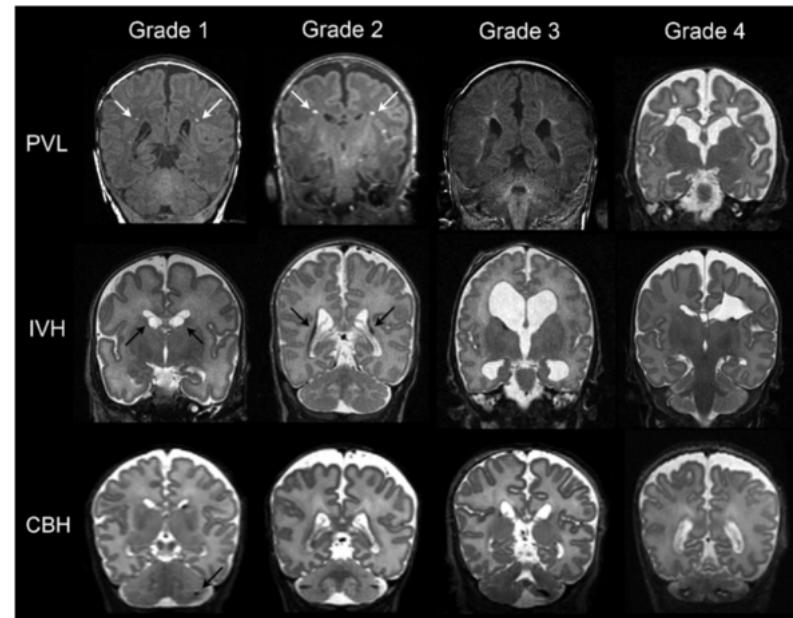
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Brain injury

Schädigung der weißen
Substanz/White matter disease

Intraventrikuläre Blutung/
Intraventricular hemorrhage

Kleinhirnblutung/
Cerebellar hemorrhage



Kidokoro et al., 2014

Sequenzen – und was sagen sie uns?



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- Hirnschädigung bei ca. 25 %
- schwere Hirnschädigung bei 6,3 %

	Pathologie	Sonographie %	MRI % (Grad 3-4 %)
2/3 isoliert	≥1 Pathologie	17,0	24,7 (6,3)
	IVH	15,3	16,0 (1,7)
	PVL	1,0	10,0 (3,3)
	CBH	0,7	8,0 (2,0)
2/3 kombiniert mit supratentorieller Läsion			

Sequenzen – und was sagen sie uns?

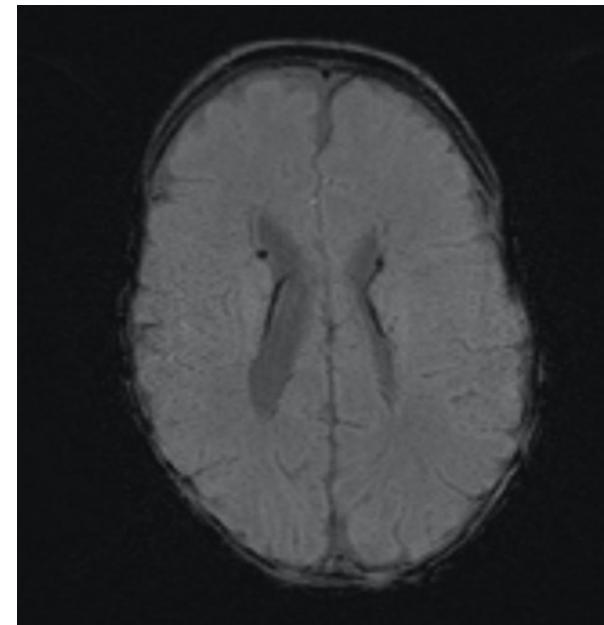


Intraventrikuläre Blutung

Sonographie



MRT



Sequenzen – und was sagen sie uns?



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White Matter Disease

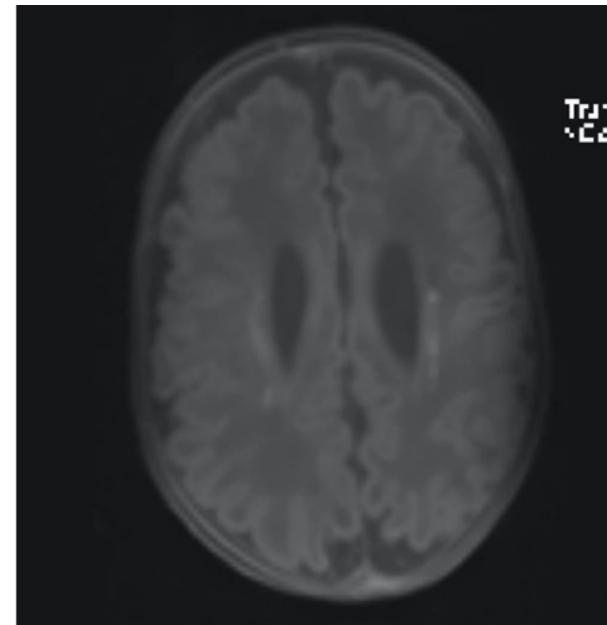


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Sonographie



MRT



Sequenzen – und was sagen sie uns?



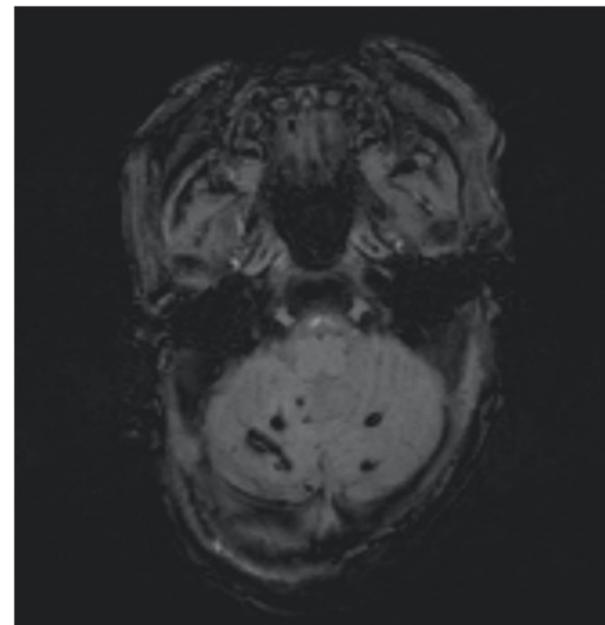
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Kleinhirnblutung

Sonographie



MRT



Sequenzen – und was sagen sie uns?



Brain injuries und Outcome

- IVH I-II° mit Entwicklungsverzögerung assoziiert
Patra et al., 2006; Bolisetty et al., 2014
- schwere PVL mit auffälligem MDI und PDI im Alter von 1 und 2 Jahren assoziiert
Kidokoro et al., 2014; Hammerl, 2020
- Kleinhirnblutungen:
 - Effekte auf Motorik, Kognition, Sprache, Sozialverhalten, Autismus
Limperopoulos et al., 2007; Hortensius et al., 2018; Hammerl, 2020
 - höhere Raten an Entwicklungsverzögerung (auch bei milder CBH)
Hammerl, 2020

Sequenzen – und was sagen sie uns?



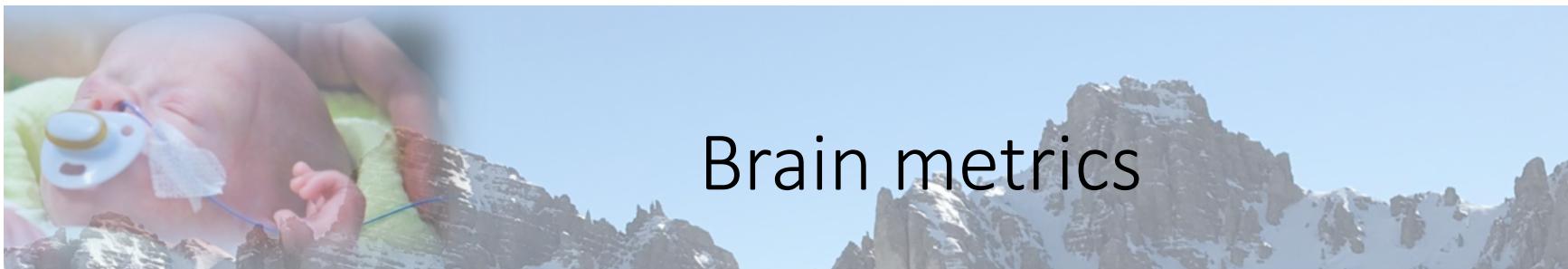
Brain metrics



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- FG <32 SSW haben ein kleineres Gehirn in der Adoleszenz – Gehirnvolumen erklärt 20-40% der IQ- und Bildungsoutcome-Unterschiede
Cheong et al., 2013
- bereits am errechneten Termin Unterschiede in den Gehirnvolumina feststellbar
Lind et al., 2010; Keunen et al., 2016
- 2D-Messungen als (leicht einsetzbare) Alternative
Nguyen The Tich et al., 2009

Sequenzen – und was sagen sie uns?



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Brain metrics

- Kinder ohne Gehirnläsion gelten als „Low-Risk“ Gruppe für auffälliges Outcome
- entwicklungsneurologische Auffälligkeiten häufiger als Gehirnläsionen

Serenius et al., 2013; Blencowe et al., 2012; Hammerl et al., 2019

Neonatology

Original Paper

Neonatology
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Neonatology

Original Paper

Neonatology 2020;117:287–293
DOI: 10.1159/000506836

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Published online: May 12, 2020

Reduced Cerebellar Size at Term-Equivalent Age Is Related to a 17% Lower Mental Developmental Index in Very Preterm Infants without Brain Injury

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Supratentorial Brain Metrics Predict Neurodevelopmental Outcome in Very Preterm Infants without Brain Injury at Age 2 Years

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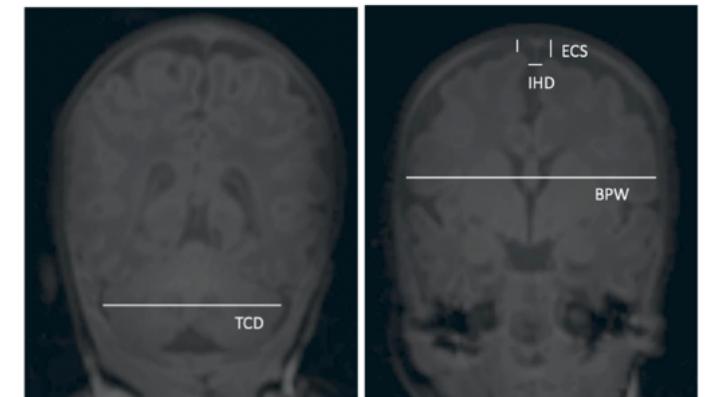
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Sequenzen – und was sagen sie uns?



Brain metrics und Outcome

- Messung u.a. der biparietalen Weite, des Interhemisphärenspaltes und des transcerebellären Durchmessers in T1-MPRage Bildern
- PPV:
 - BPW z-score <-0,5 und IHD ≥ 4 mm:
41% für auffälliges Outcome im Alter von 1 a
 - TCD <50 mm:
45% für auffälliges Outcome im Alter von 2 a
- NPV – keine abnormalen Brain metrics:
 - 97% für kognitive Auffälligkeiten im Alter von 1 a
 - 96% für motorische Auffälligkeiten im Alter von 2 a



Hammerl et al., 2019; Hammerl et al., 2020; Hammerl, 2020

Sequenzen – und was sagen sie uns?



Brain metrics und Outcome



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- kleineres Gehirn (BPW oder TCD auffällig)
→ niedrigerer Verbal-IQ (WPSSI-III)
- TCD <50 mm: Verbal-IQ <85 häufiger
(50% vs. 2%)

Hammerl, 2020

Sequenzen – und was sagen sie uns?



Diffusion Tensor Imaging



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- unterschiedliche Diffusionseigenschaften von Wassermolekülen in Abhängigkeit von ihrer Umgebung
- Brown'sche Molekularbewegung

isotrope Diffusion (z.B. in Liquorräumen):
Wassermoleküle sind in ihrer Bewegung kaum beeinträchtigt – mehr Diffusion – starke Signalreduktion – in der Aufnahme dunkel

Stegemann et al., 2006

Sequenzen – und was sagen sie uns?



Diffusion Tensor Imaging



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- weiße Substanz: strukturelle Barrieren für Wassermoleküle (Zellmembranen, Myelinscheiden) - schnellere Bewegung in der Längsrichtung der Axone = anisotrope Diffusion

Wassermoleküle sind durch strukturierte Anordnung des Gewebes in der Diffusion stark eingeschränkt
– in der Aufnahme hell

Sequenzen – und was sagen sie uns?



Apparent Diffusion Coefficient



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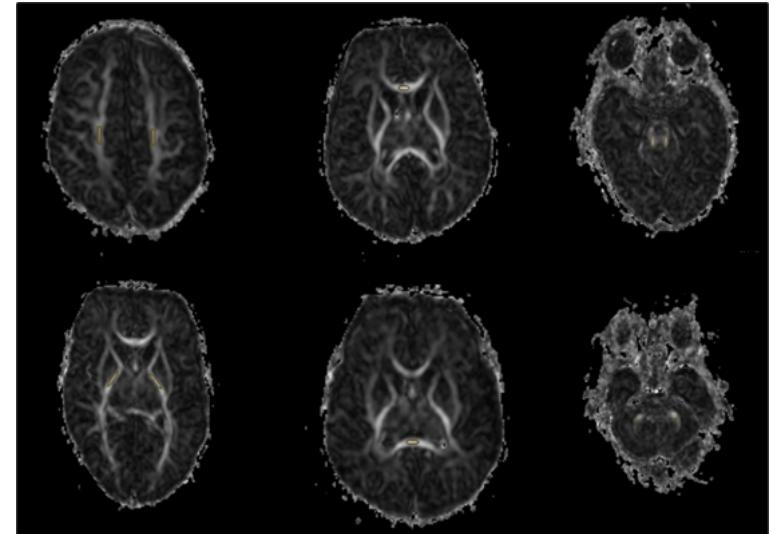
- scheinbarer Diffusionskoeffizient, ADC
- durchschnittliche Diffusionsgeschwindigkeit der Wassermoleküle in der Richtung des geschalteten Gradienten
- niedrig bei Diffusionsbarrieren

Sequenzen – und was sagen sie uns?



Fraktionale Anisotropie (FA)

- Maß für die Stärke der Anisotropie ohne Berücksichtigung der Vorzugsrichtung
- Grad der Anisotropie liefert Informationen über die strukturelle Integrität
- höhere Werte bei stark vorgegebener Richtung (z.B. viele Faserstränge)



Sequenzen – und was sagen sie uns?



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Neonatology

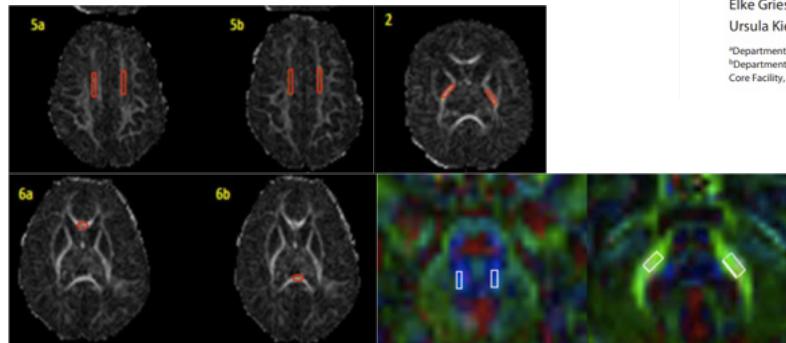
Neonatology 2018;113:93–99
DOI: 10.1159/000480695

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Accepted after revision: August 26, 2017
Published online: November 9, 2017

The Cerebellar-Cerebral Microstructure Is Disrupted at Multiple Sites in Very Preterm Infants with Cerebellar Haemorrhage

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Neonatology

Original Paper

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Prophylactic Low-Dose Paracetamol Administration for Ductal Closure and Microstructural Brain Development in Preterm Infants

Maria Sappeler^a Marlene Hammerl^a Yasmin Pellkofer^a
Elke Griesmaier^a Michaela Höck^a Tanja Janjic^{b,c} Elke Ruth Gizewski^{b,c}
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RESEARCH ARTICLES | AUGUST 25 2023

The Effect of Postnatal Cytomegalovirus Infection on (Micro)structural Cerebral Development in Very Preterm Infants at Term-Equivalent Age

Subject Area: Women's and Children's Health

Yasmin Pellkofer; Marlene Hammerl; Elke Griesmaier; Maria Sappeler; Elke Ruth Gizewski;
Ursula Kiechl-Kohlendorfer; Vera Neubauer

Neonatology (2023) 120 (6): 727–735.
<https://doi.org/10.1159/000532084> Article history
PubMed:37634498

Sequenzen – und was sagen sie uns?



Traktographie



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- basierend auf DTI – 3D Rekonstruktion
- ermöglicht Darstellung und Analyse von Nervenfaserbündeln im Gehirn

DEVELOPMENTAL MEDICINE & CHILD NEUROLOGY

ORIGINAL ARTICLE

Tractography of white-matter tracts in very preterm infants: a 2-year follow-up study

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ANNETTE A VAN DEN BERG-HUYSMANS¹ | MONIQUE RIJKEN³ | MARK A VAN BUCHEM¹ |
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Perspektiven



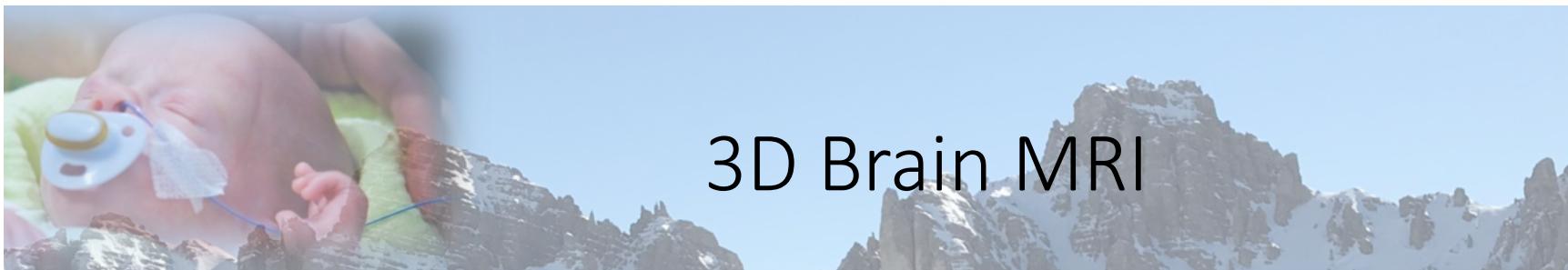
Funktionelles MRI



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- misst Veränderungen der Gewebsdurchblutung, die durch Energiebedarf von Nervenzellen hervorgerufen werden
 - Blutflussmessung: erhöhte Durchblutung in aktiveren Gehirnregionen
 - Sauerstoffgehaltmessung: sauerstoffreiches Blut magnetisch reaktiver → BOLD-Effekt
- resting state fMRI: keine bestimmten Aufgaben müssen ausgeführt werden
→ spontane Aktivität wird gemessen
- aktuell laufende Studie in Innsbruck

Lordier et al., 2019



ORIGINAL
ARTICLES

www.jpeds.com • THE JOURNAL OF PEDIATRICS



Brain Volumes at Term-Equivalent Age in Preterm Infants: Imaging Biomarkers for Neurodevelopmental Outcome through Early School Age

Kristin Keunen, MD^{1,2}, Ivana Isgum, PhD^{2,3}, Britt J. M. van Kooij, MD, PhD¹, Petronella Anbeek, PhD^{1,3}, Ingrid C. van Haastert, PhD¹, Corine Koopman-Esseboom, MD, PhD¹, Petronella C. Fieret-van Stam, PhD⁴, Rutger A. J. Nieuvelstein, MD, PhD⁵, Max A. Viergever, PhD^{2,3}, Linda S. de Vries, MD, PhD^{1,2}, Floris Groenendaal, MD, PhD^{1,2,*}, and Manon J. N. L. Benders, MD, PhD^{1,2,3}

Pediatr Radiol (2011) 41:953–961
DOI 10.1007/s00247-011-2071-x

ORIGINAL ARTICLE



Associations between regional brain volumes at term-equivalent age and development at 2 years of age in preterm children

Annika Lind · Riitta Parkkola · Liisa Lehtonen ·
Petriina Munck · Jonna Maunu · Helena Lapinleimu ·
Leena Haataja · PIPARI Study Group

OPEN ACCESS Freely available online

PLOS ONE

Contribution of Brain Size to IQ and Educational Underperformance in Extremely Preterm Adolescents

Jeanie L. Y. Cheong^{1,2,*}, Peter J. Anderson^{2,4,6}, Gehan Roberts^{2,5,6}, Alice C. Burnett^{2,4}, Katherine J. Lee^{2,6}, Deanne K. Thompson^{2,7,8}, Carly Molloy², Michelle Wilson-Ching², Alan Connelly⁸, Marc L. Seal^{6,7}, Stephen J. Wood⁹, Lex W. Doyle^{1,2,3}

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Chou et al., 2012

Perspektiven

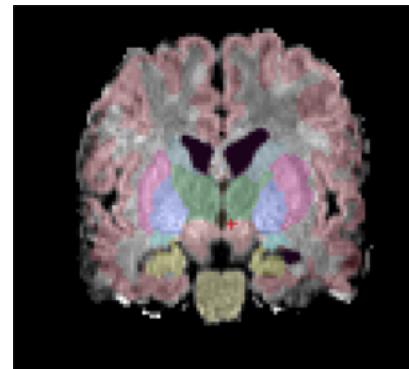


Automatisierte Segmentierung



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- verschiedene Programme/Atlanten
- FreeSurfer Infant: Erkennen von 31 Gehirnregionen - Volumetrie



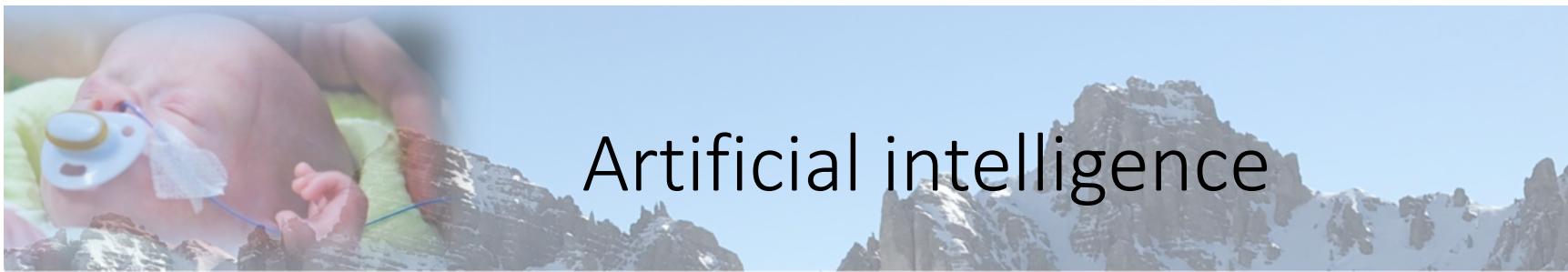
<https://surfer.nmr.mgh.harvard.edu>

Perspektiven



Artificial intelligence/Radiomics

- artificial intelligence:
 - imitiert menschliche Intelligenz
 - maschinelles Lernen/Deep Learning – Verbesserung der Interpretation Entscheidungsfindung
- Radiomics:
 - quantitative Analyse von Bildmerkmalen, die über das hinausgehen, was das menschliche Auge erkennen kann



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NEURO



Feed-forward neural networks using cerebral MR spectroscopy and DTI might predict neurodevelopmental outcome in preterm neonates

T. Janjic^{1,2} · S. Pereverzyev Jr^{1,2} · M. Hammerl³ · V. Neubauer³ · H. Lerchner^{1,2} · V. Wallner¹ · R. Steiger^{1,2} · U. Kiechl-Kohlendorfer³ · M. Zimmermann³ · A. Buchheim⁴ · A. E. Grams^{1,2} · E. R. Gizewski^{1,2}

Results By employing the constructed fNN predictors, we were able to predict cognitive delays of VPIs with 85.7% sensitivity, 100% specificity, 100% positive predictive value (PPV) and 99.1% negative predictive value (NPV). For the prediction of motor delay, we achieved a sensitivity of 76.9%, a specificity of 98.9%, a PPV of 90.9% and an NPV of 96.7%.

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Research paper

A deep learning pipeline for the automated segmentation of posterior limb of internal capsule in preterm neonates

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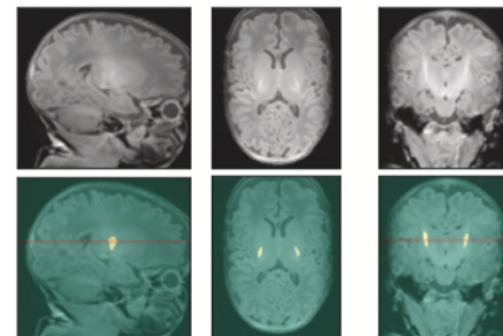
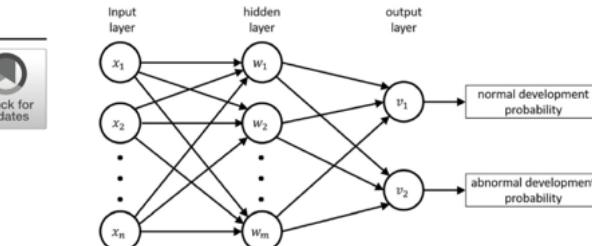
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Perspektiven



Vielen Dank!

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