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„Differences in Attentional Functioning Between Preterm
and Fullterm Born Children and How These Differences
Are Mapped in the Brain“

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1. Theoretical Background

1.1. Preterm Birth

Preterm birth defined by the World Health Organization as a birth before the completion of 37 weeks or before 259 days from the first day of the last menstrual period is an emerging issue for the health care system and especially for expectant parents and their newborn children (WHO, 2018). Around 15 million babies are born preterm every year, which means that worldwide 10 % of the births happen before 36 weeks and 6 days of gestation. In Europe more specifically this applies to 8.7 % of the births and the frequency of preterm births overall increases steadily since 1980 (Malik & Baarda, 2021; Goldenberg, Culhane, Iams & Romero, 2008).

The developments that an unborn child goes through are essential for further survival, therefore a more precise distinction must be made. The definition regarding the degree of prematurity is dependent on the gestational age as well as the birth weight: extremely preterm birth (less than 28 weeks), very preterm (28-31 weeks) and moderate to late preterm birth (32-37 weeks) (Malik & Baarda, 2021). A distinction is made between children with extremely low birth weight (500-1000 grams), very low birth weight (1000-1500 grams) and low birth weight (2000-2500 grams). The weight of the newborn is also crucial regarding the probability of a positive outcome (Wense & Bindt, 2021; Malik & Baarda, 2021).

The importance of each individual day in the prenatal development is well illustrated by the example of brain development. In the 34th week of pregnancy the mass of the brain is only 65 % of the brain in the 40th week of pregnancy (Kinney, 2006). The dynamic process of differentiation can be observed from the surface structure of the fetus' brain during pregnancy. The differentiation and maturation processes are very dynamic at the level of the nerve cells as well which happens especially in the last weeks of pregnancy. There is not only a rapid increase in the number of neurons, but also a complex migration and sprouting of synapses as well as interconnection of neurons. In premature birth, this process does not take place in the womb but in a completely different environment with other stimuli than intended (Wense & Bindt, 2021) leading to the assumption that many difficulties this vulnerable population must face are based on the immaturity of the brain.

Due to improvements in perinatal care the survival rates for children born preterm and/or with low birth weight constantly increased over the last decades (Clark & Sand-Loud, 2018; Green et al., 2018). Whereas in 1970, the 30th week of pregnancy was considered as the limit of survivability, today the limit is extended to the 22nd to 24th week. The survival rate of extremely preterm infants

(≤ 27 weeks' gestation) is about 87 % (AKH Wien, 2021; Statistik Austria 2020; Kim et al., 2019). The later in gestation and the more weight the children have when being born plays an important role for the outcome of these children. In comparison, the chances of survival rate at 23 weeks of gestation are at 50 %, at 22 weeks they are significantly lower (Wense & Bindt, 2021). Therefore, the decision in this time frame whether life-sustaining measures should be taken is decided individually by medical care also in consensus with the parents. Preterm birth globally remains a major problem as 65 – 75 % of neonatal deaths and 75 % of neonatal morbidity needs to be attributed to preterm birth (Malik & Baarda, 2021).

1.2. Risk Factors

The reasons for premature birth seem to be complex and multifactorial. The need for research regarding the factors and the additive effects of those remains high. However, there are known risk factors that influence the probability of preterm birth. While infections are the most common cause for a preterm birth the risk profile also includes behavioral and psychosocial factors as well as sociodemographic characteristics, environmental exposure, infertility treatments and other biological factors (Butler & Behrman, 2007; Wense & Bindt, 2021). Two thirds of preterm births happen spontaneously due to premature labor with or without premature rupture of membranes (Berger et al., 2019), or by labour induction or caesarean delivery for maternal or fetal indications (Goldenberg, Culhane, Iams & Romero, 2008). There are different occurrences especially in pregnancy that are associated with preterm birth (see Table 1).

Table 1
Constellations with an increased risk of early childbirth

Maternal Causes
<ul style="list-style-type: none"> ○ Genital infections/infection of amniotic cavity ○ Premature rupture of the amniotic sac ○ Weakness of the cervical closure (cervical insufficiency) ○ Short interval to the previous pregnancy ○ HELLP syndrome (hemolysis, elevated liver enzymes, low platelets)
Placental issues
<ul style="list-style-type: none"> ○ Unfavorable placental location (e.g. placenta praevia with hemorrhage) ○ Placental insufficiency with growth retardation of the fetus ○ Premature placental abruption
Fetal problems

- Multiple pregnancy (twins, triplets,...)
- Increased amniotic fluid (e.g. fetal dysphagia)

Risks based on the life situation

- Underage pregnancy
- Higher age
- Significant psychosocial stress during pregnancy
- Difficult socioeconomic conditions

(Wense & Bindt, 2021, p. 33)

Various studies have tried to elicit risk profiles. Very common risk factors among women specific to preterm birth were various medical conditions, low educational level, or having a previous preterm birth, miscarriage, or abortion. A low weight gain during the pregnancy, short stature, and reporting life as stressful in the year prior to birth could be linked to preterm birth (Heaman et al., 2012). Indeed, it could be shown that mothers who report one or more highly stressful life events, especially during the pregnancy were 1.76 times more likely to experience a preterm delivery (Hedegaard et al., 1996). That stress is an important indicator in this context could be found in several studies early on. This was even the case after adjustments were made for maternal demographic and behavioral characteristics (Copper et al., 1996).

From a psychological perspective, stress is of particular interest. Stress is related to complex neuroendocrine processes which enables individuals to adapt and react to changes in the environment. When experiencing stress, the two main systems of stress regulators are activated – the hypothalamic-pituitary axis and the sympathetic-adrenal medullary axis (SAM). Both pathways are activated with the release of corticotropin-releasing hormone (CRH) from the hypothalamus further stimulating the release of adrenocorticotropin hormone (ACTH) from the pituitary gland resulting in the release of glucocorticoids, more specific cortisol, from the adrenal cortex. The stress response is then switched off by the cortisol, suppressing the release of ACTH and CRH. SAM is the more rapidly working pathway where the released ACTH stimulates the adrenal medulla resulting in a release of epinephrine in the adrenal medulla and norepinephrine from sympathetic nerve endings. Stress leads to various physiological changes such as mobilizing glucose, altering blood pressure and heart rate as well as redirecting the blood.

Neural, vascular, and other connections between mother and fetus are mediated through the placenta. The endocrine products alter the feedback and control mechanism of the maternal hypothalamic-pituitary-adrenal axis. The placental CRH (p-CRH) shows to play a crucial role

regarding the maternal stress response. Cortisol stimulates the p-CRH leading to increased levels of this hormone. CRH acts as a placental clock that rises with advancing gestation and controls the duration of pregnancy. Therefore, higher levels in early gestation are believed to support preterm birth as CRH levels increase and promote myometrial contractility (Najafzadeh, 2016).

Stress thus seems to play a relevant role. Although there are many useful approaches to explore the causes of preterm birth, the exact risk profile remains opaque. Research on risk profiles is far from complete and still leaves room for further questions and approaches.

1.3. Consequences of Preterm Birth

The premature birth of children is accompanied by many challenges from the day of birth. The children and their families face potential long-term somatic effects:

- Lung diseases
 - bronchopulmonary dysplasia
 - increased susceptibility to infections
 - more frequent hospitalizations in infancy and early childhood
 - increased incidence of early childhood asthma
 - increased risk of bronchial obstruction in young adulthood
 - questionable increase in risk of chronic obstructive pulmonary disease in late adulthood
- Cardiovascular diseases
- Sudden Infant Death Syndrome
- Growth and physical development
- Infantile cerebral palsy
- Visual disorders/Retinopathy
- Hearing impairments
 - Conductive hearing loss
 - Sensorineural hearing loss
 - Central hearing loss (Wense & Bindt, 2021)

A large area of research is devoted to the cause of the comparatively poorer development. The focus here is primarily on risk factors such as birth weight, gestational age, and medical complications. However, the factors are interrelated, making it difficult to interpret the contribution to the developmental outcome. Furthermore, a high in-group variability is observable.

Medical issues related to complex alterations in brain development are an amalgam of destructive and developmental mechanisms like inflammation of the brain and ischemia causing brain injuries, reduced white matter volume, ventricular dilation, and atrophy of the corpus callosum (Skranes et al., 2005). Those injuries of the brain affect the anatomical alterations long-term and lead to changes in the intrinsic networks (Bäumel et al., 2014). It seems that the neural plasticity of the brain is limited in preterm born children, leading to less functional adaption, less growth and higher stability in functions as attention (Luciana, 2003).

One important cause of long-term neurodevelopmental morbidity as well as deficits in language and motor development, cerebral palsy, hearing, and vision abnormalities are attributed to brain development. An occurrence with difficult prognostication of the outcome is the presence of an intraventricular hemorrhage (IVH). It occurs in 20-30 % of preterms born with less than 1500 g and in 45 % of infants with extremely low birth weight less than 1000. Severity of the IVH is described within the range of I and IV IVH (Jones et al., 2018). MRI scans at term-equivalent age show high correlations and a strong predictive validity in terms of neurodevelopment between 2 and 3 years of age (Goeral et al., 2021).

White matter damage, in particular the Periventricular Leukomalacia (PVL) is the main predictor of Cerebral palsy which represents a major concern in preterm infants. Prevalence is estimated to be around 14 % at 22 - 27 week of pregnancy and steadily decreases with ongoing gestational age (Arpino et al., 2010).

But medical problems aren't the only challenges premature children face. They have a global impact on other areas of life. Speech development for example is also something where prematurity shows effects as it has intrauterine roots. The auditory system of a fetus is developed in the 23rd to 25th week of gestation. The auditory input supports the acquisition of language as the prosody is learned and remembered postnatally. Preterm born children start their life in incubators with little speech stimulus during the developmental phase where they would need to be exposed to multiple sensory experiences. Whether the acoustic deprivation is the reason for the later often observed weakness in phonological short-term memory of language development disorders remains unclear. The lower the birth weight, the more frequently problems with the receptive and expressive language appear regarding the semantic as well as grammatical abilities independent of socio-demographic factors (Wense & Bindt, 2021).

At the age of 7 very preterm born children show three times the odds of meeting criteria for any psychiatric diagnosis. Those are predicted by the neonatal brain abnormalities as well as social-emotional problems (Treyvaud et al., 2013).

Extremely preterm children also show an increased risk for autism spectrum disorders (ASD) associated with neurocognitive outcomes suggesting that autism in this population may result from abnormal brain development (Johnson et al., 2010a; Pritchard et al., 2016). The prevalence of ASD is significantly high in this population with an overall prevalence rate of 7 % (Agrawal et al., 2018) compared to the estimation of 7 in 1,000 autistic children and adolescents in the general population (CDC, 2006).

It is also observable that premature infants are at increased risk for attention-deficit/hyperactivity disorder (ADHD) and ADHD-like symptoms (Rommel et al., 2019). More pronounced ADHD symptoms are related to greater executive dysfunction like inhibitory self-control, cognitive flexibility, and emergent metacognition. A lower IQ as well as higher perinatal clinical risks are associated with higher inattentive ADHD type symptoms (Montagna et al., 2020).

But the most common developmental impairment after preterm birth are global and specific cognitive impairments with a much higher prevalence than motor, visual or hearing impairments (Arpino et al., 2010; Vanderbilt & Gleason, 2010). Many studies showed that preterm born children show an overall worse performance in developmental tests from infancy onwards and later also in intelligence tests (Wense & Bindt, 2021). Fortunately, severe cognitive disabilities are comparatively rare (Hille et al., 2007, Serenius et al., 2016). However, there is empirical evidence that very preterm and/or very low birth weight (VPT/VLBW) children show a higher risk for neurodevelopmental impairment and in school age more deficits in academic achievement, attention problems as well as internalizing behavioral problems attributed to immaturity at birth (Mulder et al., 2009). In fact, preterm born children use special educational services proportionately more often, even without severe disabilities or intellectual deficits (Nyman et al., 2019; Aylward, 2002; Walther, den Ouden & Verloove-Vanhorick, 2000). The extent of the difficulties is influenced by gestation age, whereas it is observable that skills can catch up with age in children with mean gestational age above 26 weeks (Mulder et al., 2009; Johnson et al., 2010b; Jaekel et al., 2013b), but especially deficits in higher-order neurocognitive functions persist throughout childhood and young adulthood (Aarnoudse-Moens et al., 2009; Breeman et al., 2016). Attention development seems to be less optimal in preterm born infants with increasing severity when they grow into toddlers (van de Weijer-Bergsma, Wijnroks & Jongmans, 2007). More precisely VPT children show poor attention performance in sustained attention, focused attention

and distractibility and show a reduced processing speed in divided attention and flexibility tasks (Anderson et al., 2011; Giordano et al., 2016). Differences in early orienting as well as sustained attention are predictive of later attentional, cognitive, and behavioral functioning (van de Weijer-Bergsma et al., 2007).

These problems are observable with ongoing age. Children at 4 years of age show significantly lower abilities regarding their working memory, cognitive flexibility, and inhibition (van Houdt et al., 2019). Even into young adulthood these problems persist. Specific executive function impairments in task that involve response inhibition and mental flexibility are observable in young adults born very preterm, even when adjusting for IQ, gender, and age (Nosarti et al., 2007).

Those deficits are also perceived by parents. It could be shown that poor performance in psychological assessments is significantly related to the evaluation of the parents. Children who are described by their parents as being conspicuous in terms of behavior or performance also show greater difficulties during psychological assessments (Lowe et al., 2019).

1.4. Attention

Attention is seen as a core neuropsychological component and presents a pre-requisite for effective cognitive functioning. It is the base for the ability of thinking and acting in a flexible way, establishing action goals, and handling conflicting situations. Attention is not one consistent process, but a multidimensional construct based on different attentional mechanisms (Byrne, 2010). According to the neurocognitive model of Peterson and Posner (2012; 1990), the sources of attention form a system of anatomical areas, which includes three neural networks: alerting, orienting, and executive control. While the alerting network supports (phasic alertness) and maintains (tonic alertness or vigilance) a general state of activation, the orienting network is the base for selecting and focusing on specific information. The executive network manages the ability to solve incongruent information. It is believed that the three networks function independently from each other. However, although the three attentional networks are independent from each other it can be assumed that the three network interact and that the interaction of the attentional system ensures an efficient performance as a whole. The Alerting network for example produces an inhibitory effect on the Executive Function network and therefore enhances a fast response to sensory input. Also, the Orienting and Executive Function network seem to interact. It was found that in congruent trials participants are able to react faster than in incongruent ones, leading to the conclusion that congruency helps to focus attention and making it easier to ignore incongruent flankers. The influence of the Alerting network on the Orienting network seems to be an acceleration of its function rather than an increase (Fan et al., 2002).

The alerting network is associated with frontal and parietal regions predominantly in the right hemisphere (Posner & Peterson, 1990). The orienting system is associated with areas of the parietal and frontal lobes, more specific the superior parietal lobe and the temporal-parietal junction (Corbetta et al., 2000). When investigating the activated areas while the executive network is active, it depends on the tasks used. However, different types of conflict tasks activated similar areas within the anterior cingulate cortex (Fan et al., 2003).

1.5. Attention Deficits in Preterm Children

Addressing the development and deficits of attention is particularly important in this population, as it has been shown that attention significantly influences the further development of preterm infants (van de Weijer-Bergsma, Wijnroks & Jongmans, 2007). A relatively permanent pattern of difficulties regarding selective attention, shifting and effortful control can be observed. Applying the model of Peterson & Posner (1990), various studies could show that preterm born infants show less efficient attention behaviors compared to full-term born children already in the first 6 months of life (Stroganova, Posikera & Pisarevskii, 2005; Stroganova, Posikera, Pisarevskii & Tsetlin, 2006) and show less mature shifting behavior (Hunnius, 2004; Mulder, Pitchford, Hagger & Marlow, 2009) as well as higher distractibility (Sun, 2003) and attention inhibition (Woodward, Edgin, Thompson & Inder, 2005). Even with ongoing age at 12 months it is observable that preterms had lower scores on eye-tracking measures of orienting and alerting compared to their full-term born peers (de Jong, Verhoeven & van Baar, 2015). At preschool age, it can be observed that compared to full-term born children preterm children show lower attentional performance in alerting and orienting (Pizzo et al., 2009; Giordano et al., 2016; Snyder et al. 2007) and deficits in executive control (Pizzo et al., 2009; Geldof et al., 2013). Deficits in executive functioning seem to become more apparent with increasing demands and workload (Wehrle et al., 2015; Jaekel et al., 2013a). Even if deficits in attention are often accompanied by cognitive impairments, it is observable that also preterm born children who have average cognitive abilities show difficulties in their attentional performance (Bayless & Stevenson, 2006; Taylor, Hack & Klein, 1998; Böhm et al., 2007).

However, it remains unclear if preterm born children are selectively impaired only in single domains of attention or if all domains of attention are less optimal compared to full-term born peers. Nevertheless, it is also observable that preterm born children show higher rates of test-aborts, decreased motivation and parents also rate their children poorer regarding their attention and cognitive abilities (Giordano et al., 2014) as well as in terms of behavioral and temperament problems (Klein et al., 2013).

1.6. Neurobiological base of attention deficits

Murray et al. (2014) could show that the adverse attention and processing speed results preterm children show at 7 years of age are associated with neonatal brain pathology. More specific, abnormalities in gray and white matter as well as cerebellar abnormality were predictive of attention and processing speed outcomes. Further studies support the hypothesis that brain anatomy has a predictive impact on higher order cognitive functions especially executive functioning (Woodward et al., 2011; Goeral et al., 2021).

Based on previous research and the fact that the brains of premature infants are extremely immature at birth, it is natural to further investigate the brain structure and functionality of preterm born children in more detail. Even if results are not always clear, it can be assumed that the premature birth is reflected in further development of the brain and has an effect on the behavioral level in the long term. MRI scans conducted shortly after birth and at term-equivalent age showed that the relative volumes of the cortical gray matter, cerebellum and cerebrospinal fluid increased while the relative volumes of unmyelinated white matter as well as subcortical gray matter decreased. Lower gestational age is associated with lower growth rates (Gui et al., 2019).

To examine the neural architecture of the brain, functional MRI characterizes the blood-oxygen-level-dependent (BOLD) signal. Task-based fMRI examines task-evoked fluctuations in brain activity, whereas resting state-fMRI (rs-fMRI) assesses intrinsic fluctuations in brain activity and measures the connectivity of intrinsic brain networks (Cole et al., 2014). Typically, studies focus either on resting state or task-based fMRI data, although prior research has shown that combining both approaches deliver additional information as it is possible to compare the results (Harrewijn et al., 2019). Studies applying fMRI offer heterogeneous findings. Some found different patterns of activation in preterm born children indicating that alternative pathways or networks do exist in this population (Constable et al., 2013). A few fMRI studies support the behavioral data mentioned above with anatomical correlates, although these studies are comparatively rare. Nassar et al. (2019) found that VPT born adults showed deficits on the executive component of the Attentional Network Task (ANT) at age 26 years. The gestational age correlated with ANT-evoked activity in the dorsal anterior cingulate cortex as well as lateral occipital regions. Wheelock et al. (2021) used a rs-fMRI to examine the functional connectivity of 12-year-old VPT born children. They observed poorer sustained, shifting, and divided attention compared to their full term born peers. Furthermore, the impairments in attention were associated with alterations of functional connectivity. However, fMRI studies often find no relevant evidence for differences between preterm born children and their full-term born peers (de Kieviet et al.,

2014) or reduced activation in task-related brain networks (Griffiths et al., 2013; Daamen et al., 2015).

1.7. Attention Assessment

There are a variety of tests to measure attention. Nevertheless, there are several methodological issues regarding the assessments in general that need to be noted. Different tasks may assess similar underlying functions but also face the struggle of confounding additional functions. There are always multiple processes and different subcomponents involved when a task is performed. It is additionally challenging when assessing children due to the rapid development at a young age, the age of the test person must also be considered depending on the test. Similar tasks can also vary in their focus. While some tasks are developed to measure primarily accuracy others measure speed (Mulder, Pitchford, Hagger & Marlow, 2009; Giordano et al., 2016). This is especially relevant when testing the vulnerable population of preterm born children. For example, it seems that preterm born children have a greater disadvantage in tasks that rely on the speed component (Bohm, Smedler & Forssberg, 2004; Rose, Feldman & Jankowski, 2002) which reduces the comparability when a speed component is a prerequisite while accuracy of preterm born children is within the normal range (Snyder et al., 2007). In addition, the question arises which assessments are particularly suitable for measuring attention in specific age groups like preschool children.

Table 2 lists the most common procedures used to measure attention in preschool to elementary school aged preterm born children in alphabetical order. The assessments differ regarding the underlying definition and subarea of attention measured as well as whether a questionnaire or a (computerized) test is used.

Table 2
Attention Assessments used in preterm born population

Name	Author(s)	Year of Publication	Type of Test	Construct of Interest
ANT	Fan, McCandliss, Sommer, Raz, & Posner	2002	Computerized Assessment	Alerting, Orienting, Executive Control
BRIEF-P	Daseking, & Petermann,	2013	Questionnaire	Executive Functioning

BVN/NPS	Bisiacchi, Cendron, Gugliotta, Tressoldi & Vio	2005	Assessment	Attention, Executive Functioning
CBCL	Achenbach	2014	Questionnaire	Attention Problems
CogState	Collie, Maruff, Darby & McStephen	2003	Computerized Assessment	Detection speed, visual attention, vigilance
CPT-K	Rosvold, Mirsky, Sarason, Bransome & Beck	2003	Computerized Assessment	Response Inhibition, Sustained Attention
KITAP	Zimmermann, P.; Gondan, M., Fimm, B.	2003	Computerized Assessment	Distractibility, Alertness, Continuous Attention, Flexibility, Divided Attention, Go/NoGo, Vigilance, Scanning
NEPSY-II	Korkman, Kirk & Kemp	2007	Assessment	Selective Attention, Focused Attention
STROOP	Golden	1978	(Computerized) Assessment	Selective Attention
TEA-Ch	Manly et al.	2010	Assessment	Selective Attention, Attention Control & Response Inhibition, Concentration & Sustained Attention, Divided Attention,
Verbal Cancellation Test	Montiel & Seabra	2012	Assessment	Selective Attention
Tester's Rating of Child Behavior	Wolke	2012	Questionnaire	Attention Span
Strengths and Difficulties Questionnaire	Goodman, R.	1997	Questionnaire	Hyperactivity and Inattention

Flexible Item Selection Task	Jacques & Zelazo	2001	Assessment	Cognitive flexibility
Visual Search Task	Welsh	1991	(Computerized) Assessment	Selective Attention
CANTAB	Robbins & Sahakian	1980	Computerized Assessment	Executive Functioning, Attention, Reaction Time, Response Control
Tower of Hanoi	Lukas	1883	(Computerized) Assessment	Executive Functioning
Hayling Sentence Completion Test	Burgess & Shallice	1997	Assessment	Response Inhibition

1.7.1. Assessment

Assessments based on paper-pencil or with a toolbox are relatively rarely used. The most common assessment is the TEA-CH, a test battery for assessing multiple types of attention whereby not only one but sometimes two tasks have to be completed in parallel (Murray et al., 2014; Anderson et al., 2011; Bayless & Stevenson, 2006; Wheelock et al., 2021). Other tasks used are for example the Visual Search Task (Geldof et al., 2013; Woodward et al., 2011), the Flexible Item Selection Task (Woodward et al., 2011), NEPSY (Shum et al., 2008) or the Hayling Sentence Completion Test (Nosarti et al., 2007) which differentiate between the attentional functioning of preterm and full-term born children.

In some cases, different test batteries such as BVN/NPS (Iono et al., 2022), NEPSY (Iono et al., 2022; Di Lieto et al., 2017), Verbal Cancellation Test (Da Nobre et al., 2019) are used to assess partial aspects of attention or well-known test paradigms are used like the STROOP (Shum et al., 2008) or the Tower of Hanoi (Sheehan et al., 2017). However, this is mostly done in combination with other procedures.

1.7.2. Computerized Assessments

The comparatively most common test paradigm that is used is the Attentional Network Task which was assess the efficiency of the three attentional networks and is based on the Cued Reaction Time (Posner, 1980) and the flanker paradigm (Eriksen & Eriksen, 1974). The ANT enables a simultaneous and rapid evaluation of the attentional networks. Although children can work on the ANT, the child-friendly version ANTI-Birds was found to be more suitable for assessing children

aged 3 through 6 years and has the additional advantage that the interaction between the networks can also be captured but also leading to different versions of the ANT that are in use (Casagrande et al., 2021; Pizzo et al., 2009; Geldof et al., 2013; Forns et al., 2014; Snyder et al., 2007; Winders Davis et al., 2007; de Keviet et al., 2012; Reijneveld et al., 2021; Walczak-Kozłowska et al., 2020). Other computerized assessments used are the Test of Attentional Performances (KiTAP; Giordano et al., 2016; Nosarti et al., 2007), CogState (Murray et al., 2014; Suikkanen et al., 2021), CANTAB (Bayless & Stevenson, 2006), and computerized versions of the Visual Search Task (Datin-Dorrière et al., 2020)

1.7.3. Questionnaires

Assessments based on either observation or interviewing of caregivers are used in almost every study, at least as a supplement. The most common used questionnaires to assess attention are the CBCL (Gaspardo et al., 2018; Johnson et al., 2010; Winders Davis et al., 2007; de Keviet et al., 2012; Cosentino-Rocha et al., 2014; Klein et al., 2013; Eryigit-Madzwamuse & Wolke, 2014; Iono et al., 2022) followed by the Tester's Rating of Child Behavior (Breeman et al., 2016; Jaekel et al., 2013) and the Strengths and Difficulties Questionnaire (Giordano et al., 2016; Johnson et al., 2010; Schnider et al., 2020; Bachiller-Carnicero et al., 2019).

An assessment particularly used to query executive functions is the BRIEF-P (Zvara et al., 2019; Hodel et al., 2019; García-Bermúdez et al., 2019; Anderson et al., 2015)

Overall, it is observable that conclusions drawn from the studies based on the attention assessments are heterogenous. It seems profitable to combine different types of attention tests to gain a comprehensive and holistic impression of the children's attentional abilities and deficits. Some studies combined the results of multiple tests and compiled a value for Executive Functioning for example, further supporting the approach of a combination of methods (Woodward et al., 2011)

1.8. Questions and Hypotheses

The interest of this study is to complement the data of attentional performance embedded in the neuroanatomical model of Posner and Peterson (1990) with functional MRI data to evaluate the performance in the individual networks but also the connectivity between these networks. Based on the literature following questions and hypotheses are elaborated:

K-ABC II

H1: Preterm born children show poorer performance in K-ABC II than full-term born children.

KiTAP

H2: Preterm born children show poorer performance in the flexibility task of the KiTAP compared to their full-term born peers.

H3: Preterm born children show poorer performance in the go/no-go task of the KiTAP compared to their full-term born peers.

ANTI-Birds

H4: Preterm born children overall show longer reaction times than full-term born children.

H5: Preterm born children show a poorer performance in the alerting network in comparison to full-term born peers.

H6: Preterm born children show a poorer performance in the orienting network compared to full-term born children.

H7: Preterm born children show a poorer performance in their executive control compared to full-term born children.

H8: Preterm born children show greater attentional costs than full-term born children.

H9: Preterm born children show less attentional benefits than full-term born children.

H10: The performances in K-ABC II, KiTAP and ANTI-Birds show significant correlations.

fMRI

Q1: Is the Attentional Network Task Interaction – Birds is a valid assessment to show the performance of the three attentional networks Alerting, Orienting and Executive Control as well as the connectivity between those networks in this population?

H11: Preterm born children show poorer network connectivity compared to the full-term born control group.

Q2: Is it possible to measure this population in the fMRI with appropriate preparation?

Preterm birth and attention

H12: Children with lower gestational age show poorer performance in terms of attention

H13: Children with lower birth weight show poorer performance in terms of attention

2. Method

The study was conducted at the University Children's Hospital of the Medical University of Vienna at the Follow up Clinic. Supervision at the hospital was provided by Priv. Doz.ⁱⁿ Dr.ⁱⁿ Karin Pichler, PhD, Dr. Vito Giordano, Dr.ⁱⁿ Renate Fuiko and support for the fMRI scans and calculations was provided by Mag. Dr. rer. nat. Florian Fischmeister. Internal supervision at the University of Vienna was provided by Univ.-Prof.ⁱⁿ Dr.ⁱⁿ Stefanie Höhl.

2.1. Recruitment

The sample was recruited at University Children's Hospital of the Medical University as part of the follow-up program of the aftercare of preterm born children. The full-term born children were friends or family of the preterm children, were recruited through colleagues at the Medical University of Vienna and through a flyer posted by the Vienna Children Studies (Wiener Kinderstudien). The initial recruitment of the preterm born children was conducted during the regular check-up of the follow-up program of the preterm born children. Parents received a flyer with the most important information and had the chance to ask additional questions in a phone call afterwards. The full-term born peers were recruited via phone call directly and received the information of the study per mail. All participants signed an informed consent form for the study itself and also for the fMRI measurement.

To participate in the study, children had to be 5 years old and clearly premature (< 32 weeks' gestation) or full-term born (> 37 weeks' gestation) for the control group. Due to the medical consequences of prematurity, children were excluded with problems like cerebral palsy, motor disabilities, hearing impairments or deficits in cognitive functioning. The children also had to be MRI compatible.

2.2. Procedure & Study Design

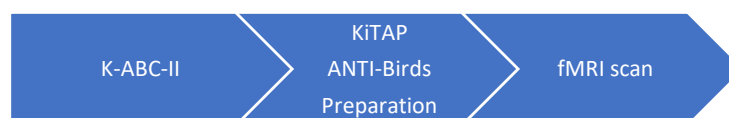


Figure 1: Procedure schedule appointments

First, the children perform the Kaufman Assessment Battery for Children – II (K-ABC-II, Kaufman & Kaufman, 2015) to assess if the children are cognitively developed according to their age and the parental ratings of behavioral data, including attentional skills, is assessed using the

CBCL. While the preterm born children are tested with the K-ABC II as part of the follow-up program at the clinic at 5.6 years of age, an extra appointment is needed for the mature control group. Children with cognitive impairment will not be included in the study. In order to provide a deeper understanding of the preterm infants and a more comprehensive description of the experimental group, the data from the regularly given Child Behavior Checklist for Ages 1.5-5 (Achenbach & Rescorla, 2000) are used.

At a second appointment, the children perform the Attentional Network Test for Interaction – Birds (ANTI-Birds) as well as the two subtests for cognitive flexibility and a go/no-go task of Test of Attentional Performance for Children (KiTAP, Zimmermann et al., 2002). Then the children are prepared for the fMRI scan in a playful way. The adapted logbook “Ich schaffe das MRT” (Weiler-Wichtl et al., 2019) is used and the procedure of the scan is demonstrated with a small wooden MRI and a stuffed animal. Meanwhile, the parents are informed about the fMRI scan by a doctor and sign a consent form. It is ensured that the children are fMRI compatible and, for example, have no metal in their bodies. Afterwards, the children get the chance to get to know the real fMRI. The children can walk around the fMRI and lie down or more specifically have a look inside the fMRI.

At the third and last appointment, the scan in the fMRI is performed, where the anatomy of the brain while the children watch a cartoon and a resting state while the children look at a black cross on white background are recorded, and the children complete the ANTI-Birds task in the fMRI.

After the second and third appointment the children receive a small reward for their participation.

2.3. Sample

The total sample size consisted of $n = 9$ children, $n = 6$ born preterm (3 female) and $n = 3$ full-term born peers (2 female). On their first appointment the children were on average 5 years and 8 months old ($SD = 2.7$ months). The preterm born sample had a mean gestational age of 28 weeks ($SD = 2$ weeks) and a mean birth weight of 1066 grams ($SD = 410$ grams). All children were described by their parents using the CBCL as having no attention problems. Two participants (one preterm and one full-term born child) could not be measured with the fMRI, resulting in a sample size of $n = 6$, $n = 4$ preterm born children and $n = 2$ full-term born children for the fMRI data. Two participants (preterm born children) dropped out of the flexibility task of the KiTAP due to motivational reasons (see table 3).

The a priori conducted power analysis calculated with G*Power suggested a total sample size of 102 participants, 51 for each group, assuming a medium-sized effect with a power of 80 % and a

type 1 error of $\alpha < .0$ (Faul et al., 2007; Casagrande et al., 2021). Due to the COVID-19 pandemic and especially the Omikron variant, resulting in difficulties in recruiting the samples, the desired sample size could not be reached.

Table 3
Overview of the assessed data of the sample

	Group	Week of pregnancy	K ABC II	KiTAP Flexibility	KiTAP Go/No-Go	ANTI-Birds	fMRI
ID 001	PT	30 + 3	X	X	X	X	X
ID 002	PT	30 + 3	X	X	X	X	X
ID 003	PT	27 + 6	X	X	X	X	X
ID 004	PT	26 + 3	X	-	X	X	X
ID 005	PT	25 + 1	X	-	X	X	-
ID 006	PT	30 + 0	X	X	X	X	X
ID 007	FT	-	X	X	X	X	X
ID 008	FT	-	X	X	X	X	-
ID 009	FT	-	X	X	X	X	X

2.4. Instruments

2.4.1. Kaufmann Assessment Battery for Children – II

The K-ABC-II (Kaufmann & Kaufmann, 2015) is an individual test to assess cognitive abilities in children and adolescents aged 3 to 18 years. The theoretical construct is based on Luria's theory of neuropsychological processing and the Cattell-Horn-Carroll model (CHC-model). With this test battery the general cognitive ability is assessed with an overall score composed of a sequential and simultaneous thinking scale and a learning scale.

2.4.2. The Child Behavior Checklist for Ages 1.5-5

The CBCL (Achenbach & Rescorla, 2000) is a checklist filled in by parents to describe children's behavior using 99 problem items. The scale goes from 0 for not true, 1 for somewhat or sometimes true and 2 for very true or often true. The item scores are summed and converted to t-scores while higher scores represent deviant behavior on seven syndrome scales grouped into two syndromes:

(a) Internalizing, consisting of Emotionally Reactive, Anxious/Depressed, Somatic Complaints and Withdrawn and (b) Externalizing including Attention Problems and Aggressive Behavior. Sleep Problems are analyzed independently.

2.4.3. Test of Attentional Performance for Children

The KiTAP (Zimmermann et al., 2002) is a Test Battery for Attention Assessment especially designed for children with the aim of promoting motivation of children. Performance is assessed based on the number of omissions and errors as well as reaction times using the two subtests of the KiTAP “House of the Dragons” to measure cognitive flexibility and the go/no-go task “The Bat” to assess inhibition.

The subtest “House of the Dragons” measures attention selectivity and cognitive flexibility. In this test, a green and a blue dragon appear simultaneously to the left and right of the center of the screen (a goal). The target stimulus alternates: first, the button on the side on which the green dragon is located must be pressed; in the next presentation, the button on the side on which the blue dragon appears should be pressed. The task is to press the correct key as quickly as possible and then independently redetermine the respective target criterion.

The subtest “The Bat” is a classical go/no-go task to measure inhibition ability and impulse control. In this test, either a vampire bat or a cat is seen, and only the bat is to be reacted to (Zimmermann et al., 2002).

2.4.4. Attentional Network Test for Interaction – Birds

In the ANTI-Birds (Casagrande et al., 2021), each trial begins with the presentation of a nest which is the fixation point over a tree. Above and below the fixation point is a horizontal row of five yellow eggs. The targets are a yellow and an orange bird in the middle of a horizontal row of five birds, whereas the two birds on each side are used as flankers. The task is to identify the color of the centrally presented bird by clicking the right button if a yellow bird is in the middle of the row and the left button if the bird is orange.

Due to the combination of a flanker paradigm and a cuing task there are different condition combinations of 2 (Alerting) x 3 (Cueing) x 2 (Congruency).

Alerting consists of a short duration of a high frequency tone that has two levels – presence or absence. The auditory warning stimulus is a 98-dB and 2000 Hz sound, lasting 50 ms. Sometimes there is a cue presented where the eggs get a thicker contour which would present the position of the upcoming target. When they are presented at the position of the upcoming target the cue is

valid, when they are in the opposite location the cue is invalid and sometimes the cue is absent (no cue). On congruent trials, the targets are flanked with birds of the same color. On incongruent trials, the target bird is flanked with birds of the different color.

In the trial run the children also received feedback. For correct responses, the visual feedback was several birds and additional auditory feedback of birds chirping. For incorrect responses, the visual feedback was a nest with two sad birds and auditory feedback of people saying “Nooo”. Performance is assessed through reaction times for the correct responses.

The task consists of a 12-trial practice block and six experimental blocks of 72 trials. Each trial begins with a fixation period of 400 ms, followed by a warning stimulus, a flash or nothing in one third of the trials each. After that there is a fixation period of 350 ms, followed by a cue that is presented for 100 ms. One third of the trials consists of valid conditions, one third of invalid and the last third of no cue conditions. After a variable interstimulus interval (ISI, 100 – 150 ms) the target is presented, and participants need to response in a time frame of 2000 ms (see Figure 2). Test duration at the second appointment was 12 minutes, in the fMRI scan duration was 6 minutes.



Figure 2: Representation of procedure and stimuli ANTI-Birds (Casagrande et al., 2021)

2.4.5. Ich schaffe das fMRT

The handbook "Ich schaffe das MRT" (I can do the MRI) used and tested at the Neuro-oncology unit at the University Children's Hospital of the Medical University Vienna prepares children for an MRI examination in a playful way (Weiler-Wichtl et al., 2019). For this study an adapted version was used with additional pictures of the fMRI (Appendix A).

2.5. Analysis

Due to the small sample size nonparametric Mann-Whitney-U-Tests were calculated to determine differences between preterm and full-term born children in their results in K-ABC II, KiTAP and ANTI-Birds using SPSS 27.0.1.0.

In K-ABC the overall score as well as the three subscales sequential score, simultaneous score and learning scale were investigated.

The analysis of the KiTAP results was based on the reaction times and errors in the two subtests. For ANTI-Birds the different conditions were compared after checking for differences in accuracy between the experimental and the control group and attentional effects were computed by subtracting from specific conditions: a) Alerting effect: tone – no tone conditions; b) Orienting effect: invalid – valid cue conditions; c) Executive Control: incongruent – congruent conditions; d) Attentional costs: invalid – no-cue conditions and e) Attentional benefits: no-cue – valid conditions.

The fMRI data was acquired at a 3 Tesla Siemens Vida scanner (Siemens Medical Solutions, Erlangen, Germany), equipped with a 64-channel head coil at the Department of Biomedical Imaging and Image-guided Therapy at the Medical University of Vienna. 3D structural MRI scans are performed using a standard 3D MPRAGE sequence. fmRI images are acquired using a multiband echo planar imaging (EPI sequence) (TE/ER = 30/650 ms, 60 axial slices, slice thickness = 3 mm). Stimuli for the experimental paradigms are presented using an MR compatible visual stimulation device (Nordic Neurolab, NNL, Bergen Norway). MR-compatible response pads are used to record the button presses (Nordic Neurolab, NNL, Bergen Norway). The imaging is performed in one session with a total scanning time of 30 minutes.

Data processing was performed with SPM12 implemented in Matlab 9.3.0.713579 including a motion correction, spatial normalization, and spatial smoothing. For the task-based fMRI single subject analysis of the data was performed as well as a fixed effects analysis was carried out for contrast pointing out the differences. Functional Connectivity analysis was performed using CONN functional connectivity toolbox version 17.

3. Results

3.1. K-ABC II

A Mann-Whitney-U-Test was calculated to determine differences in K-ABC II scores between preterm born children ($n = 6$) and their full-term born peers ($n = 3$). There was no statistically significant difference in the overall score ($U = 8.000$, $Z = -.264$, $p = .905$), the sequential score ($U = 7.500$, $Z = -.389$, $p = .714$), the simultaneous score ($U = 7.500$, $Z = -.389$, $p = .714$) or the learning scale ($U = 8.500$, $Z = -.131$, $p = .905$). Table 4 shows the mean standard scores for the K-ABC II results for both groups.

Table 4
K-ABC II results

	Overall		Sequential		Simultaneous		Learning	
	Preterm	Full-term	Preterm	Full-term	Preterm	Full-term	Preterm	Full-term
Mean	110.83	107.00	109.83	105.33	110.33	108.33	100.66	99.33
SD	17.74	3.46	22.19	9.71	12.16	4.16	12.29	6.35
Min.	83	105	80	97	94	105	87	92
Max.	134	111	146	116	123	113	115	103

3.2. KiTAP

A Mann-Whitney-U-Test was assessed to show differences between preterm and full-term born children regarding the errors as well as the reaction times in the subtest flexibility as well as the go/no-go task. There was no statistically significant difference regarding the errors ($U = 3.000$, $Z = -1.146$, $p = .4$) and mean reaction times ($U = 5.000$, $Z = -.354$, $p = .857$) in the flexibility task. In the go/no-go condition there was no significant difference between the experimental and the control group regarding the errors ($U = 6.000$, $Z = -.781$, $p = .548$) or the mean reaction times ($U = 7.000$, $Z = -.516$, $p = .714$).

Table 5
KiTAP results description

	Flexibility Errors		Flexibility Mean		Go/No-Go Errors		Go/No-Go Mean	
	Preterm	Full-term	Preterm	Full-term	Preterm	Full-term	Preterm	Full-term
Mean	6.50	5.33	1522.34	1538.21	3.83	2.33	576.05	566.24
SD	1.73	0.58	389.38	331.65	2.86	1.53	18.98	59.58
Min.	5	5	1234.79	1292.92	0	1	544.54	511.85
Max.	9	6	2097.5	1915.54	8	4	601.28	629.92

3.3. ANTI-Birds

In order to compare the reaction times of the preterm and full-term born children the accuracy of the two groups was compared using a Mann-Whitney-U-Test. Preterm and on term born children did not differ in terms of the made errors ($U = 0.000$, $Z = -1.000$, $p = 1.000$). Table 5 shows the mean reaction times and errors as well as the standard deviations for both groups in each condition.

Table 6

Description errors and reaction times for all conditions in ANTI-Birds

	Group	Mean Errors	SD Errors	Mean RT	SD RT
NoTone_Invalid_Congruent	PT	10.667	1.966	1164.083	39.770
	FT	11.667	0.577	808.000	92.580
NoTone_Invalid_Incongruent	PT	10.333	2.066	1160.083	106.996
	FT	11.333	0.577	952.333	53.463
NoTone_NoCue_Congruent	PT	10.000	3.521	1134.833	63.515
	FT	11.333	1.155	909.333	64.866
NoTone_NoCue_Incongruent	PT	10.333	2.160	1113.500	65.941
	FT	12.000	0.000	846.500	78.581
NoTone_Valid_Congruent	PT	10.500	2.739	1019.250	25.861
	FT	11.667	0.577	787.667	56.003
NoTone_Valid_Incongruent	PT	9.833	2.563	1013.083	39.631
	FT	11.333	0.577	770.167	79.348
Tone_Invalid_Congruent	PT	10.000	2.966	1117.917	107.841
	FT	11.667	0.577	904.000	28.553
Tone_Invalid_Incongruent	PT	10.333	2.875	1083.167	138.502
	FT	11.667	0.577	888.667	62.302
Tone_NoCue_Congruent	PT	10.000	2.191	1064.833	131.527
	FT	10.667	0.577	872.000	70.873
Tone_NoCue_Incongruent	PT	9.667	2.944	1093.250	67.872
	FT	11.000	1.000	968.500	150.817
Tone_Valid_Congruent	PT	10.333	2.875	1053.667	92.251
	FT	11.333	0.577	840.500	32.898
Tone_Valid_Incongruent	PT	10.833	2.401	969.833	87.343
	FT	12.000	0.000	874.667	118.822

A significant difference regarding the reaction times was observable in the conditions NoTone x Invalid x Congruent, NoTone x NoCue x Congruent, NoTone x NoCue x Incongruent, NoTone x Valid x Congruent, NoTone x Valid x Congruent, Tone x Invalid x Congruent and Tone x Valid x Congruent. In the conditions NoTone x Invalid x Incongruent, Tone x Invalid x Incongruent, Tone x NoCue x Congruent, Tone x NoCue x Incongruent and Tone x Valid x Incongruent no significant difference was observable.

Table 7
Group differences for all conditions ANTI-Birds

	U	Z	p
NoTone_Invalid_Congruent	.000	-2.334	.024*
NoTone_Invalid_Incongruent	2.000	-1.807	.095
NoTone_NoCue_Congruent	.000	-2.324	.024*
NoTone_NoCue_Incongruent	.000	-2.324	.024*
NoTone_Valid_Congruent	.000	-2.334	.024*
NoTone_Valid_Incongruent	.000	-2.324	.024*
Tone_Invalid_Congruent	.000	-2.324	.024*
Tone_Invalid_Incongruent	2.000	-1.807	.095
Tone_NoCue_Congruent	2.000	-1.807	.095
Tone_NoCue_Incongruent	3.000	-1.549	.167
Tone_Valid_Congruent	.000	-2.324	.024*
Tone_Valid_Incongruent	5.000	-1.037	.381

To compare the reaction times over all conditions between the preterm and full-term born children a Mann-Whitney-U-Test was assessed. It is observable that full-term born children generally show significant shorter reaction times compared to the preterms ($U = .000$, $Z = -2.324$, $p = .024$).

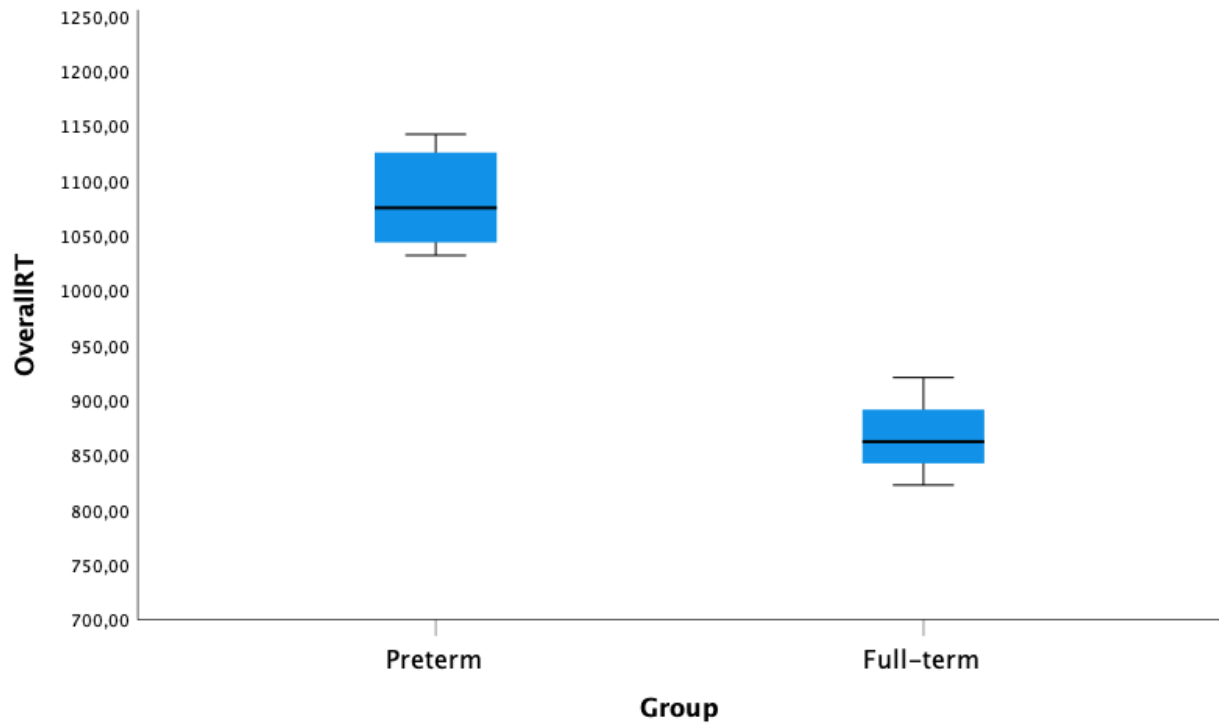


Figure 3: Boxplot Mean Reaction times of all conditions ANTI-Birds

3.3.1. Alerting

Mann-Whitney-U-Test showed a significant difference in terms of Alerting between preterm and on term born children ($U = 1.000$, $Z = -2.066$, $p = .048$).

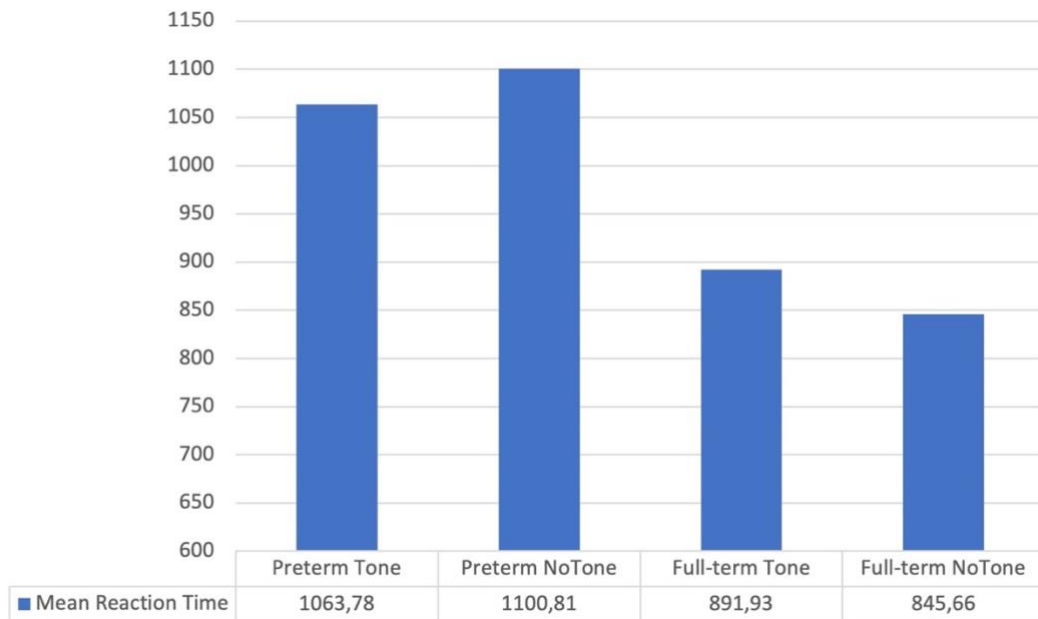


Figure 4: Mean reaction time comparison Alerting

3.3.2. Orienting

A conducted Mann-Whitney-U-Test showed no significant differences between preterm and full-term born children regarding their Orienting ability ($U = 4.000$, $Z = -1.291$, $p = .262$).

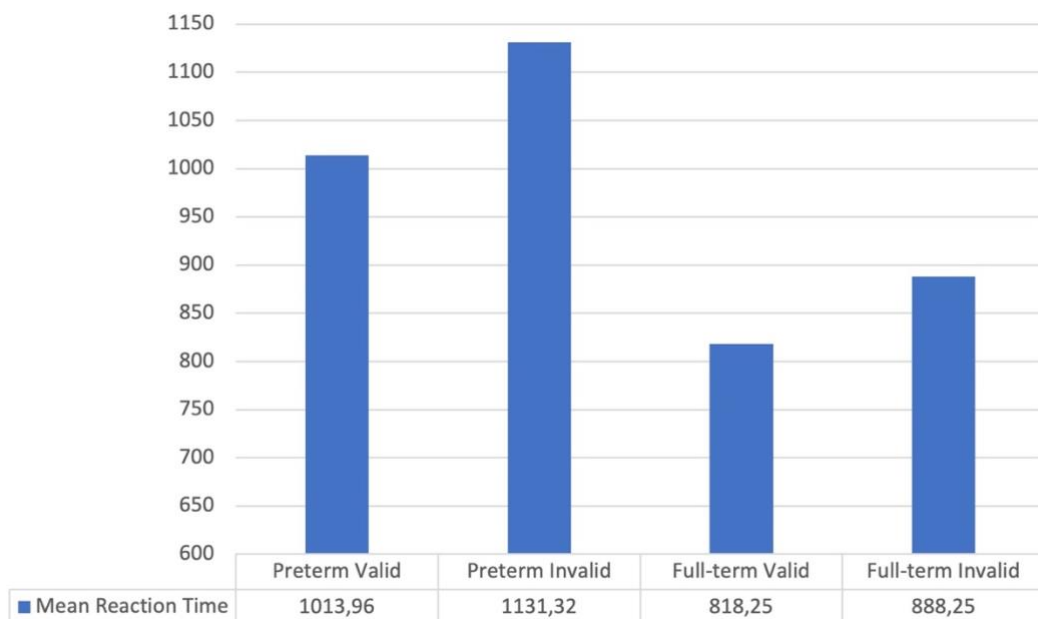


Figure 5: Mean reaction time comparison Orienting

3.3.3. Executive Control

Using a Mann-Whitney-U-Test no significant differences between preterm born children and their full-term born peers were found regarding their Executive Control ($U = 5.000$, $Z = -1.033$, $p = .381$).

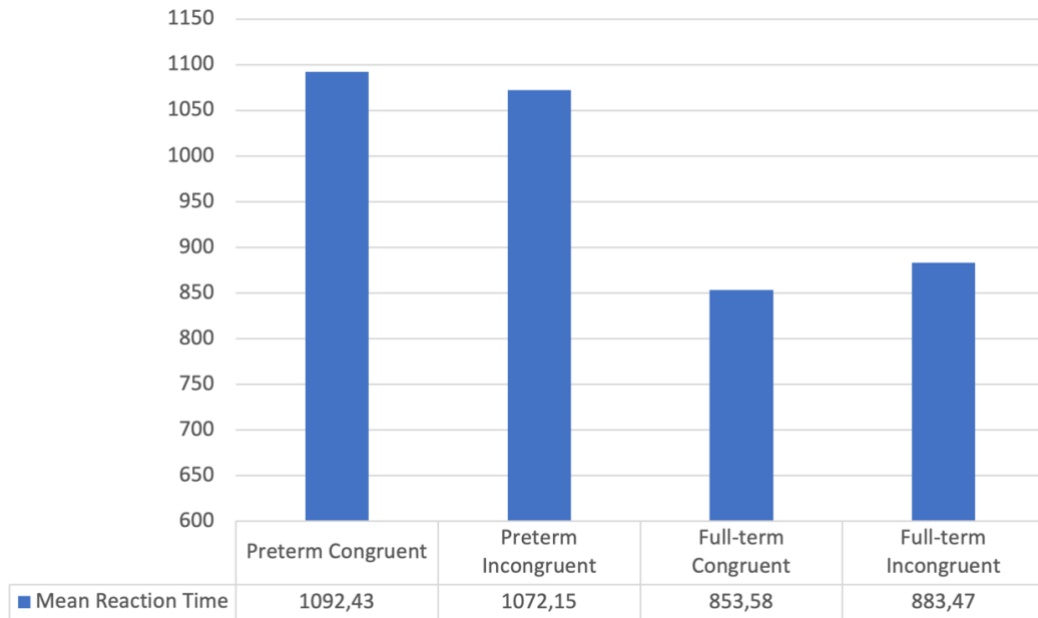


Figure 6: Mean reaction time comparison Executive Control

3.3.4. Attentional Cost

An applied Mann-Whitney-U-Test showed no significant difference regarding Attentional Costs ($U = 3.000$, $Z = -1.549$, $p = .167$) between the preterm born children and the control group.

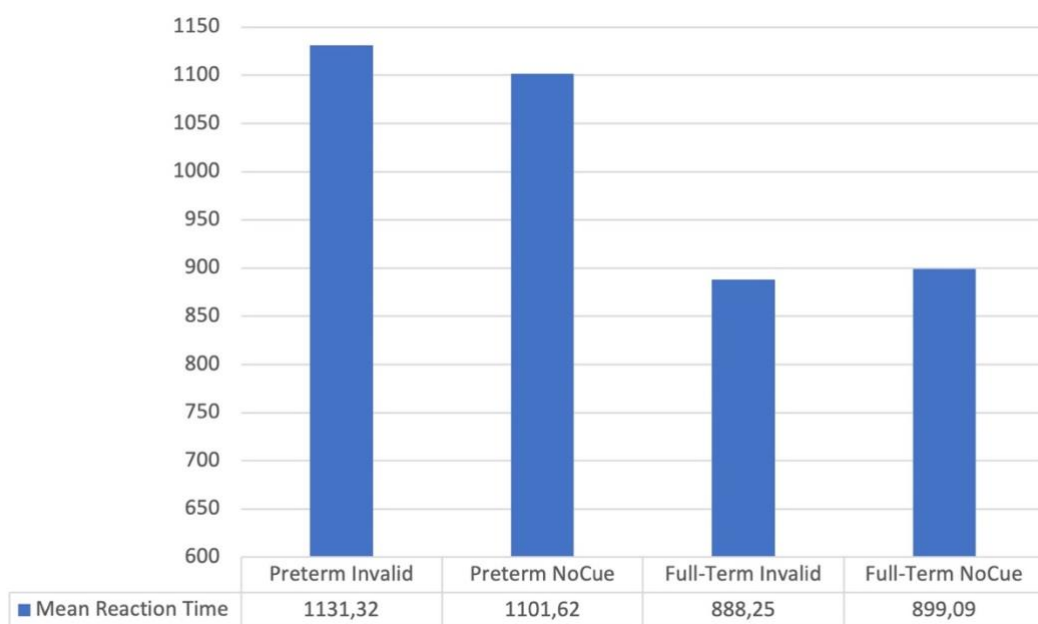


Figure 7: Mean reaction time comparison Attentional Costs

3.3.5. Attentional Benefits

No difference was observable in the Attentional Benefits between preterm and full-term born children ($U = 9.000$, $Z = .000$, $p = 1.000$) applying a Mann-Whitney-U-Test.

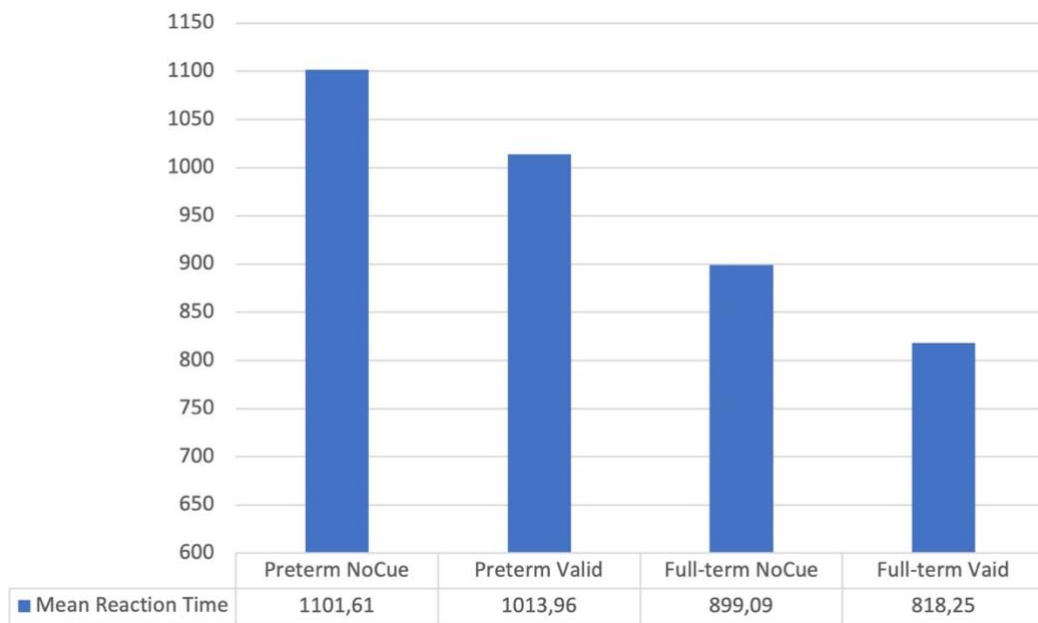


Figure 8: Mean reaction time comparison Attentional Benefits

3.4. Correlations

Correlational analysis revealed significant positive correlations between the K-ABC II overall score and K-ABC II Sequential subscale ($r = .907, p < .001$), K-ABC II Simultaneous Subscale ($r = .907, p < .001$) and Orienting ($r = .714, p = .031$). Attentional Costs and Orienting also correlated highly positive significant ($r = .901, p < .001$). Performance in the KiTAP subtask flexibility and K-ABC II overall score ($r = -.791, p = .034$) as well as K-ABC II Sequential ($r = -.812, p = .027$) showed a significant negative correlation.

No significant correlation was observable between the three attentional networks.

Table 8
Correlational analysis of instruments

Variable	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
1. KABC overall										
2. KABC Sequential	.939**									
3. KABC Simultaneous	.907**	.857**								
4. KABC Learning	.457	.268	.098							
5. Alerting	-.119	.206	-.179	.149						
6. Orienting	.714*	.703*	.716*	.072	.178					
7. Executive Control	.426	.301	.368	.342	-.398	.359				
8. Attentional Costs	.599	.520	.515	.280	.286	.901*	.319			
9. Attentional Benefit	.510	.630	.669*	-.355	-.125	.598	.222	.191		
10. Go/NoGo	.274	.325	.210	.063	.489	.368	-.015	.258	.356	
11. Flexibility	-.791*	-.812*	-.620	-.317	-.159	-.650	-.314	-.744	-.036	-.504

3.5. fMRI

The fMRI scans of the children show the following activation in the brain regions:

For the alerting network, representing a change in internal state, includes frontal and parietal regions, particularly of the right hemisphere. The orienting network, involved in selection of information, consists of frontal eye fields, the inferior parietal lobe, and midbrain as well as thalamic regions. The executive control network, representing more complex mental operations like monitoring conflicting information involved midline frontal areas like the anterior cingulate cortex, lateral prefrontal cortex and basal ganglia.

Please note, that the images are thresholded to show the different networks and originate from a fixed effects model.

Unfortunately, the connectivity of the networks could not be investigated further due to delays in the workflow and the data not being available in time.

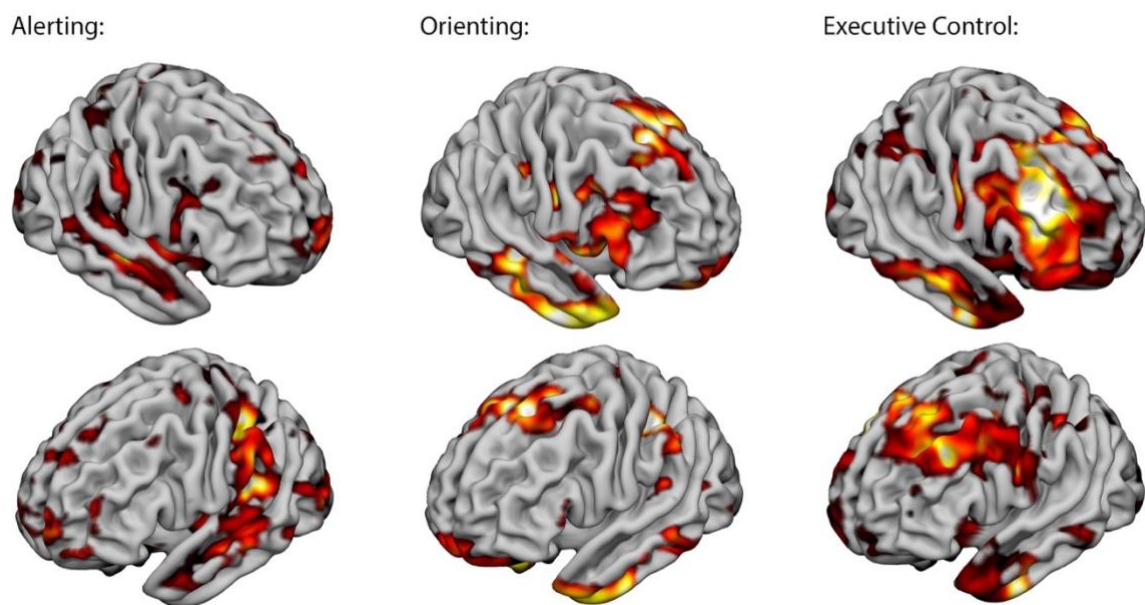


Figure 9: fMRI Images of the three networks

3.6. Preterm birth and attention

As gestational age and birth weight correlate highly significant ($r = .939$, $p < .001$) a linear regression with gestational age only was applied. Linear regression showed that gestational age is a significant predictor of reaction time on the ANTI-Birds task ($F(1,7) = 39.086$, $p < .001$) with variance resolution of $R^2 = .848$.

Gestational age cannot predict performance on the Go/No-go task ($F(1,7) = .001$, $p = .973$) or the Flexibility Task ($F(1,5) = .162$, $p = .704$).

4. Discussion

Summary

The aim of this study was to investigate the differences between preterm and full-term born children regarding their attentional abilities and complement the findings with fMRI data. In order to comprehensively assess the cognitive abilities as well as the attentional performance multiple tasks were assessed. Results were expected to provide a deeper understanding for the attentional functioning of preterm born children and the neuroanatomical structures of the preterm born children's brain.

Considering the background of the study, cognitive performance was assessed at baseline to ensure that there was no confounding by general cognitive impairment, which is comparatively common in this population as preterm infants with good medical outcomes and age-appropriate cognitive abilities also often show poorer performances in assessments such as the K-ABC II (Wolke & Meyer, 1999; Schermann & Sedin, 2004). However, this was not observable in this sample. The preterm and full-term born children did not differ in performance on the K-ABC II. This may be due to the small sample size and thus lack of variance. In addition, in the experimental group, one child with an above-average value in the overall score of the K-ABC II is present. Nevertheless, it also not uncommon for preterms to have equally good cognitive abilities especially with ongoing age as skills can catch up (Mulder et al., 2009; Johnson et al., 2010b; Jaekel et al., 2013b) which also could be the case in this sample.

Regarding the performance in the KiTAP in the two subtests flexibility and go/no-go no significant differences were observable, neither regarding the errors nor the mean reaction times. These results are contrary in terms of flexibility according on current research where preterm children show significantly worse performance on this task (Giordano et al., 2017; Giordano et al., 2014). In the go/no-go task it is not uncommon that no differences are found between preterms and their full-term born peers (Potharst et al., 2013; Giordano et al., 2017; Nosarti et al., 2007). Assessing response inhibition with other assessments than the KiTAP, inhibitory control difficulties are observed more frequently (Rommel et al., 2017; Lawrence et al., 2008). Indeed, this sample with homogenous cognitive abilities does not show high variability in the response behavior in the two subtests of the KiTAP. This can again be attributed to the small sample size and to the fact that two children did not complete the flexibility task. However, the subtests of the KiTAP are conceptualized separately which means that one subtest focuses on one type of attention. Previous studies discovered that performance in preterms is also partly dependent on the workload (Wehrle et al., 2015; Jaekel et al., 2013a). Since the workload is not very high in the subtests of the KiTAP,

as the children are able to focus on one aspect, it could be possible that in the sample of this study, consisting of preterm born children with good cognitive abilities, the KiTAP is not demanding enough to challenge the abilities of the children.

Assessment with the ANTI-Birds lead to contradictory results. Preterm children have also been shown to have significantly longer reaction times compared to full-term born peers in this data, which replicates the findings of Pizzo et al. (2009) where preterms showed slower reaction times in the conditions of the ANT. These findings are also consistent with previous research where preterms show longer reaction times even until adulthood (Kurpershoek et al., 2016; Suikkanen et al., 2021; Strang-Karlsson et al., 2010).

A closer look at the attention networks also reveals a significant difference in Alerting between preterm and full-term born children in these data. Interestingly, the preterm born children showed the expected responding behavior of reacting faster in conditions with a tone than in the conditions without a tone. The opposite is observable for their full-term born peers. This has not been reported in previous literature. Even if it is due to the small sample, the response behavior could be studied more closely in the future. Because of this, it is questionable to what extent the significant difference in alerting can be interpreted, since the mature children did not benefit at all from the condition with the tone and the calculation, after all, assumes that the condition with tone is accompanied by lower reaction times.

In this study no significant difference was found between preterms and full-term born children in their ability of Orienting. Pizzo et al. (2009) as well as Geldoff et al. (2013) also failed to observe group differences in orienting abilities. Both groups showed faster reactions in the valid conditions compared to the invalid conditions which is expected behavior. Comparing valid and invalid conditions in this task provides evidence that more time is needed to disengage and reorient from an attended location. Assumptions are made, that the orienting network develops earlier in life which could supported by the data of this study (Rueda et al., 2004) assuming that preterm born children may have caught up their orienting skills at preschool age in this sample.

Also, in terms of Executive Function no difference was found between preterms and their full-term born peers. While full-term born children showed the expected behavior of being faster in congruent conditions, the opposite was the case in the experimental group. For the preterm born children, it seemed to not matter if the conditions were congruent or incongruent.

No significant differences were observable regarding the Attentional Costs and Benefits between preterms and the control group. Based on the reaction times, it is observable that it seemed to make

little difference to the children whether there was no cue or an invalid cue. While premature children seemed to be more distracted by the invalid cue and had longer reaction times, the opposite was true for the comparison group. In invalid conditions they reacted faster than in those without a clue. Comparing the conditions without a cue and those with a valid cue the same response behavior can be observed in the experimental and the control group. In valid conditions, both the preterm and the full-term born children benefited from the cue and showed faster responses. The Attentional costs and benefits seem to be the same for both groups in the ANTI-Birds.

Correlational analyses revealed no significant correlation between the two attentional assessments KiTAP and ANTI-Birds. An explanatory approach would again be that the two different design rationales of the assessments may be the reason for this and that the KiTAP, because of the smaller workload and the less monotonous tasks, is more manageable in terms of attentional resources than the ANTI-Birds task.

The three attentional networks Alerting, Orienting and Executive Control did not show any correlations further supporting the assumption that the networks function quite independently from each other. However, the lack of correlation also may indicate a lack of reliability, especially when looking at the variation in response behavior and the lack of attentional costs or benefits (Rueda et al., 2004).

Interestingly Orienting and only Attentional Costs correlated highly positive significant leading to the assumption that the higher the attentional costs are the more demanding the orientation performance.

Flexibility and the overall score as well as the sequential subscale show a negative significant correlation. The sequential subscale captures short-term memory and working memory. Children with shorter reaction times in the flexibility task have higher scores in the K-ABC II implying that good working memory skills and a flexible handling of attention relate to each other which is well examined in previous literature (Rosa-Alcázar et al., 2021; Blackwell et al., 2009; Bouchacourt & Buschmann 2019)

The fMRI data add a visual component to the previous assumptions. Although the images are thresholded and not significant, the three networks can nevertheless be perceived as separate from each other. The brain regions involved in the sample are consistent with the brain regions described in theory and found in previous research (Posner & Peterson, 1990; Corbetta et al., 2000; Fan et

al., 2003) supporting the assumption that the ANTI-Birds is an appropriate assessment for the three attentional networks and further suitable for application in fMRI.

It could be shown that it is possible to measure this population in fMRI. The children have particularly benefited from the extensive preparation. In addition, it was advantageous to be present during the fMRI measurement to reassure the children when they became motorically restless. It has also been shown to be beneficial when the children were with another child during both the preparation and the measurement. The same people were always present throughout the study, which meant that the children were surrounded by familiar people. A special help to shorten the time in the fMRI subjectively was the showing of child-friendly videos during the anatomy. The resting state was between video and measurement with ANTI-Birds, which gave the children input again after the resting state.

In the data of this study, it was observable that gestational age is a predictor for reaction times in the ANTI-Birds task. This is consistent with previous data, as it has been shown that the earlier children are born the worse their general outcome (Mulder et al., 2009; Johnson et al., 2010b; Jaekel et al., 2013b). However, this finding could not be found regarding the KiTAP subtests further supporting the assumption that the assessment may be not differentiating well between the experimental and the control group.

Limitations and further research

It is important to note that this study is very underpowered, and the results should therefore be interpreted with caution. The conducted power analysis suggested an ideal sample size of 102 participants which could not be reached due to the Covid-19 pandemic. Furthermore, two children did not finish the flexibility task of the KiTAP, leading to an even smaller sample size regarding this subtest. In addition to this, the distribution in the two groups was also not balanced, as there were only half of the participants in the control group compared to the experimental group further diminishing the comparability between the two groups and the representativeness for the population.

In addition, from the group of preterm infants, the participant with the lowest gestational age has not been measured with fMRI, allowing mainly more mature preterm children to be used for imaging. The study will continue at the clinic with focus on recruiting preterm infants of different, especially smaller, gestational ages.

Another limitation refers to the recruiting of participants, especially concerning the control group. As at least three different appointments were necessary it was easier to reach preterm born children as the first appointment was within the regular check-up at the clinic. It was observable that especially those families with dedicated parents who also support their children's development extensively were more interested in participating at the study. Accordingly, the preterm born participants may also not be representative of most preterm children, especially in terms of general cognitive abilities. Even if deficits were found in these children, the lack of variance cannot rule out the possibility that the social aspects play a role in those areas especially where no difference was found.

Recruiting the on term born participants was particularly challenging, as only a few parents saw a need in participating. Accordingly, the sample is also homogeneous, since only children of health care workers participated in the study.

For further research especially the response behavior in the ANTI-Birds task should be further investigated. As there are various versions of the ANT and the ANTI-Birds is a relatively new one it may be the case that the response behavior really is only observable in this version of the ANT. Furthermore, the convergent validity between KiTAP and ANTI-Birds could be an interesting topic, as both assessments both measure similar types of attention but did not show any significant correlation in this study.

Conclusion

The current study aimed to investigate the attentional functioning of preterm born children, to compare it to a on term born control group and provide neurological correlates in form of fMRI data.

The comprehensive approach with different attention assessments and imaging techniques provides a base for further research. In addition, the findings that this vulnerable population can be measured with fMRI relatively easily with sufficient preparation, even over a longer period in the scan, can be used in further studies. Although this small sample clearly showed significant results in terms of reaction time and alerting, it also left unanswered questions that require further research. Questions have arisen regarding the response behavior in the ANTI-Birds task and convergent validity between the different procedures.

In conclusion, the study has supported the current state of research with some initial findings and provided a foundation for further research that can contribute to a better understanding of the attentional functioning in preterm children.

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6. Appendix

6.1. Abstract

6.1.1. Englisch

Birth before the completed 37th week of gestation is associated with various risks and challenges related to the development of the preterm born children. Although the possible outcomes of preterm infants are no longer characterized by dramatic effects, due to the advancing medical standards, lasting consequences are evident, particularly in the areas of attention. It remains unclear, however, whether infants born prematurely are selectively impaired only in individual areas of attention or whether all areas of attention are less optimal compared with on term born peers. Based on the neuroanatomical model of Posner and Petersen (1990), the aim of this study was to investigate to what extent premature and mature children differ in the three networks 'Alerting', 'Orienting', and 'Executive Control' and to complement the data with images collected by functional magnetic resonance imaging.

To assess children's attentional performance, both the Test Battery for Attention Assessment - Child Version (KiTAP) and a child-friendly version of the Attentional Network Task Interaction - Bird were used. In addition, children underwent fMRI measurement with sufficient preparation.

The results show that preterm born children in this sample showed no difference, neither in their cognitive abilities nor in the two subtests of the KiTAP compared to their fullterm born peers. In the ANTI-Birds, however, significantly slower reaction times were observed for the premature born children. Regarding the three neuroanatomical networks, there was a significant difference in Alerting, with unexpected response behavior observable for the control group. No differences in orienting, executive control, or attentional costs/benefits were evident between the two groups. Neural structures assumed by Posner & Peterson to be activated could be supported by the fMRI data.

Despite the very small sample, this master thesis was able to support the current state of research with some initial findings and has laid a foundation for further research, which contributes to a better understanding of attentional function for preterm infants.

6.1.2. Deutsch

Eine Geburt vor der vollendeten 37. Schwangerschaftswoche geht mit einigen Risiken und Herausforderungen in Bezug auf die Entwicklung der frühgeborenen Kinder einher. Die Outcomes von Frühgeborenen werden dank fortschreitender medizinischer Standards zwar nicht mehr von dramatischen Auswirkungen geprägt, es zeigen sich jedoch nachhaltige Konsequenzen, vor allem in den Bereichen der Aufmerksamkeit. Es bleibt jedoch unklar, ob zu früh geborene Kinder nur in einzelnen Aufmerksamkeitsbereichen selektiv beeinträchtigt sind, oder ob alle Aufmerksamkeitsbereiche im Vergleich zu reifgeborenen Gleichaltrigen weniger optimal sind. Basierend auf dem neuroanatomischen Modell von Posner und Petersen (1990) war es Ziel dieser Masterarbeit herauszufinden, in welchem Ausmaß sich früh- und reifgeborene Kinder in den drei Netzwerken ‚Alerting‘, ‚Orienting‘ und ‚Executive Control‘ unterscheiden und diese Unterschiede mit Bildern erhoben durch funktionelle Magnetresonanztomographie zu ergänzen.

Um die Aufmerksamkeitsleistung der Kinder zu erfassen, wurde sowohl die Testbatterie zur Aufmerksamkeitsprüfung – Kinderversion (KiTAP) als auch eine kinderfreundliche Version des Attentional Network Task Interaction – Bird verwendet. Zusätzlich wurden die Kinder mit ausreichend Vorbereitung einer fMRT Messung unterzogen.

Die Ergebnisse zeigen, dass Frühgeborene im Vergleich zu reifgeborenen Kindern in dieser Stichprobe keinen Unterschied, weder in Bezug auf ihre kognitiven Fähigkeiten, noch in den beiden Subtests der KiTAP aufweisen. Im ANTI-Birds waren jedoch signifikant langsamere Reaktionszeiten bei den Frühgeborenen zu beobachten. In Bezug auf die drei neuroanatomischen Netzwerke zeigte sich ein signifikanter Unterschied im Alerting, wobei hier ein unerwartetes Antwortverhalten bei den reifgeborenen Kindern beobachtbar war. Es zeigten sich keine Unterschiede im Orienting, der Executive Control oder den Attentional Costs/Benefits zwischen den beiden Gruppen. Durch das bildgebende Verfahren konnten von Posner & Peterson angenommen neuronalen Strukturen aktiviert durch das Verfahren untermauert werden.

Trotz der sehr kleinen Stichprobe konnte diese Masterarbeit den aktuellen Forschungsstand mit einigen ersten Erkenntnissen untermauern und eine Grundlage für weitere Forschungen schaffen, welche zu einem besseren Verständnis der Aufmerksamkeitsfunktion bei Frühgeborenen beiträgt.

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6.4. Abbreviations

VPT	Very Preterm
VLBW	Very low birth weight
SAM	Sympathetic-adrenal medullary axis
CRH.....	corticotropin-releasing hormone
ACTH.....	adrenocorticotropin hormone
p-CRH	placental CRH
IVH.....	intraventricular hemorrhage
PVL	Periventricular Leukomalacia
ASD.....	Autism spectrum disorders
ADHD	Attention-deficit/hyperactivity disorder
BOLD	blood-oxygen-level-dependent
rs-fMRI.....	resting state-fMRI

Appendix A

Ich schaffe das fMRT

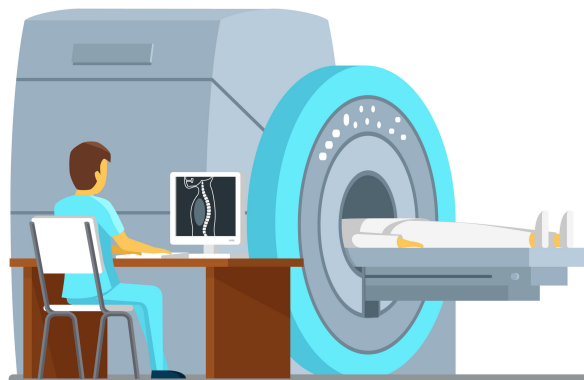
Weiler-Wichtl, L.J., Fohn-Erhold, V., Leiss, U. & Schwarzing, A.



Infos zum funktionellen fMRT

Alles, was ich über das fMRT wissen muss!

Die Magnetresonanztomographie, kurz MRT, ist wie eine ganz große Kamera mit der man Bilder vom Körperinneren machen kann, um zu sehen, was in deinem Körper los ist.



Beim **fMRT**, das ist die Abkürzung für das komplizierte Wort **funktionelle Magnetresonanztomographie**, wird geschaut, wie genau dein Körper arbeitet. Wie dieses Wort schon verrät, hat das etwas mit einem Magneten zu tun. Wie du wahrscheinlich schon weißt, ziehen Magnete metallische Dinge an. Der Magnet vom MRT befindet sich in einem großen Gehäuse in einem eigenen Raum. Manche nennen das fMRT auch **Röhre**, weil es irgendwie ja auch so aussieht.



Weißt du was man alles über das fMRT wissen muss?



Jetzt bekommst du ein paar ganz wichtige Informationen, wie die fMRT-Untersuchung abläuft.





Damit die Bilder von deinem Körper gemacht werden können, legst du dich auf die Liege des fMRT-Geräts.

Wer soll dich zur
Untersuchung
begleiten?

Um gute Bilder zu bekommen, ist es besonders wichtig, ganz ruhig liegen zu bleiben. Zur Unterstützung gibt es daher oft sogenannte **Lagerungshilfen**, die sind so ähnlich wie große Polster.



Werden Bilder von deinem Kopf gemacht, bekommst du so eine Art Spezialhelm (**Spule**) aufgesetzt. Über einen Spiegel kannst du einen Cartoon anschauen oder das Computerspiel durchführen.

Puuh, da muss man
eine ganze Menge
beachten.

Wenn die Bilder dann gemacht werden, macht der Magnet richtig laute **Klopfgeräusche**. Damit das aber nicht stört, bekommst du dicke Kopfhörer und/oder Ohrstöpsel. In die Hände bekommst du eine Joystick, mit dem du das Übungsspiel durchführen kannst.

Frag nach, wie die
meisten Kinder das
so machen – da
gibt es bestimmt
ein paar Tipps und
Tricks!

Lass uns gemeinsam herausfinden, wie du dich am besten vorbereiten kannst!

SO BEREITE ICH MICH VOR



Weißt du eigentlich,
warum du ein fMRT
machen musst?

☐

☐

☐

☐

☐

☐

Ich schaffe das fMRT!!!

SO BEREITE ICH MICH VOR



Was musst du
machen, bevor das
fMRT beginnt.

✓

✓

✓

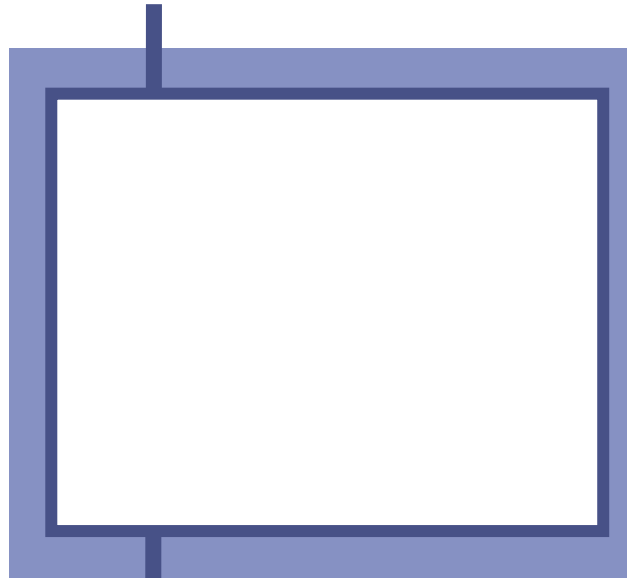


Achtung! Es gibt fünf
Dinge, die beim
fMRT besonders
wichtig sind und
beachtet werden
müssen. Versuche
sie dir zu merken!



DAS KANN MIR HELFEN, DAS PROBIER ICH AUS!

Person →



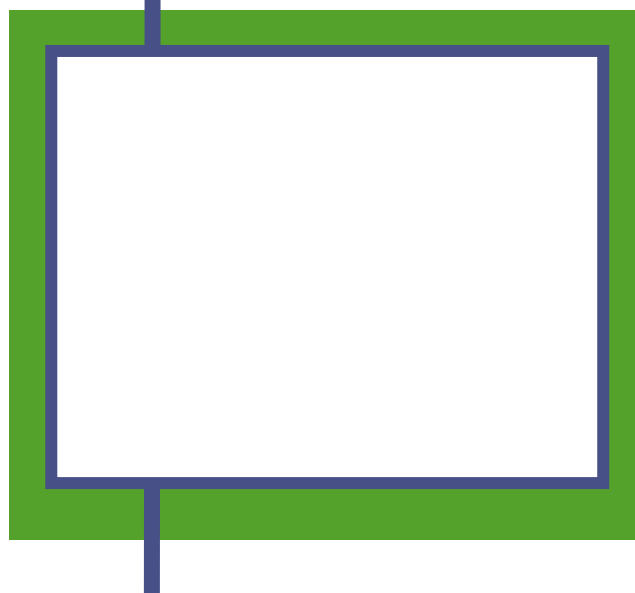
← Helferlein, z.B.
dein Kuscheltier



Wer kann dir beim
fMRT helfen?

Hier kannst du
zeichnen oder ein
Foto einkleben.

Meine eigene
Idee ... →



TRAINING – ICH HABE FLEISSIG GEÜBT!

Bitte übe, ruhig liegen zu bleiben, zusammen mit der Person, die dich zum fMRT begleitet. Für jede Übungseinheit kannst du dies hier kennzeichnen!

Trainings- kalender

MO

DI

MI

DO

FR



MEINE BESTZEIT

— : —



Die Geräusche vom fMRT findet man auch im Internet ... und mit ein bisschen Fantasie kann man sich ein MRT zum Üben bauen.



So lange kann ich schon ruhig liegen bleiben! Notiere deine Bestzeit!

IM fMRT ...



Welche Wörter
haben sich in
diesem Rätsel
versteckt?

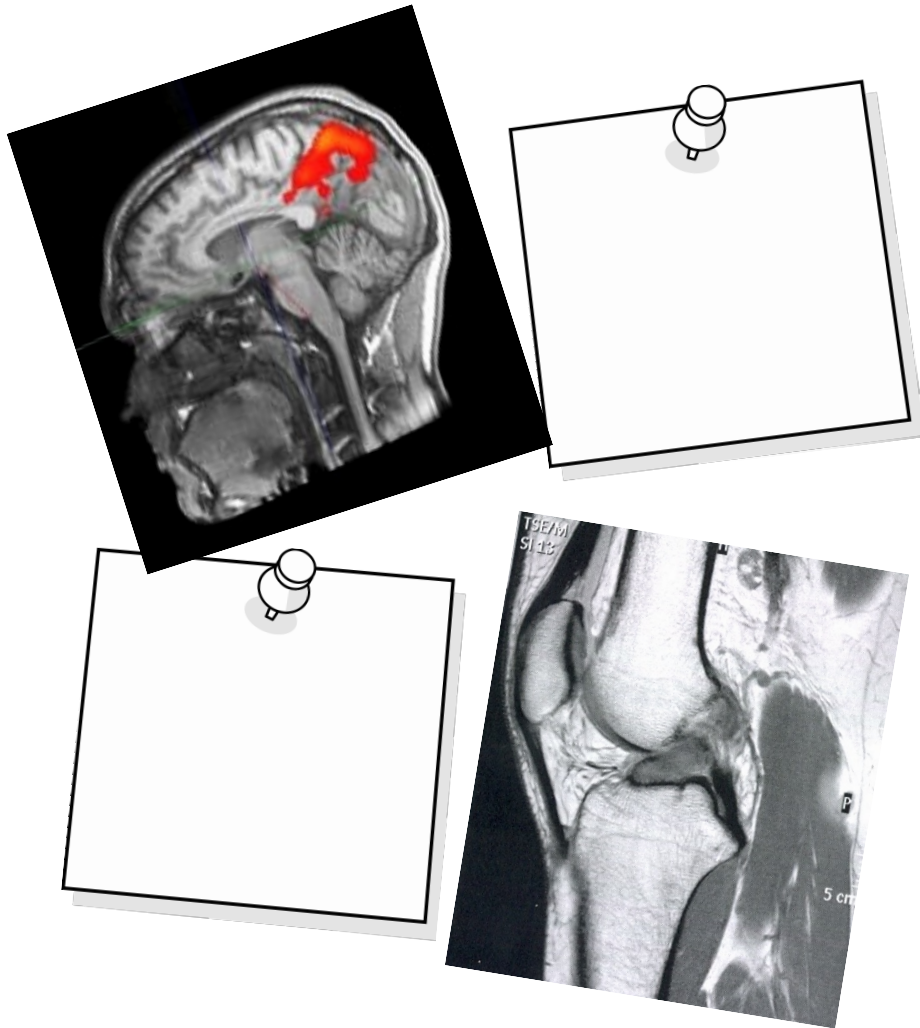
D	F	G	C	H	A	I	D	G	H	R	E	H	A	V	G	R	S	K	K	G	S	A	R	A
D	F	G	H	J	K	A	J	K	P	O	P	W	R	S	T	U	N	J	L	J	K	L	A	G
F	D	F	G	C	H	A	I	D	G	H	L	E	D	F	G	T	R	O	O	T	O	K	Q	L
G	C	M	E	I	N	L	O	G	B	U	C	H	F	G	H	J	N	Ö	P	P	R	T	Z	U
U	V	X	R	S	T	K	X	O	P	W	S	T	U	N	A	S	A	K	F	H	S	D	F	E
I	F	R	Z	H	G	J	U	I	W	Q	U	I	U	D	L	Y	R	H	G	F	G	K	O	Q
A	D	G	C	H	A	I	D	G	K	F	G	T	Z	U	I	X	K	Q	E	Q	T	Z	H	T
M	A	G	N	E	T	R	E	S	O	N	A	N	Z	T	O	M	O	G	R	A	P	H	I	E
D	E	F	X	F	G	K	L	J	N	S	F	G	Z	U	I	O	S	U	Ä	H	J	U	K	I
F	W	K	O	N	T	R	A	S	T	M	I	T	T	E	L	S	E	H	U	D	G	G	U	O
L	E	D	F	G	T	R	G	H	R	S	F	F	T	H	J	A	D	V	S	W	Q	R	Z	T
A	R	S	T	A	H	K	P	N	O	E	R	T	Z	U	G	S	A	R	C	G	S	A	R	A
X	R	S	T	R	U	H	I	G	L	I	E	G	E	N	J	K	L	A	H	J	K	L	A	G
G	D	X	D	F	G	K	O	Z	L	Q	E	R	R	Q	T	O	K	Q	E	T	O	K	Q	L
H	S	D	F	E	R	T	H	M	E	T	A	L	L	F	R	E	I	W	R	Z	J	T	K	L



Heute geht

zum fMRT!

MRT Profi – was kannst du auf den Bildern erkennen?



So sieht ein fMRT-Bild aus!

Was kannst du auf den Bildern erkennen?

Warum muss ich ruhig liegen?



Ahhh – jetzt sehe ich den Unterschied!

Im fMRT.



Wie war dein
Besuch beim fMRT?



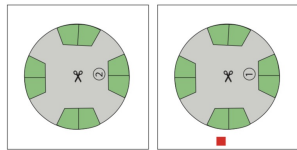
Hier hast du Platz
für ein Foto von dir
beim MRT.



Bastelanleitung für dein eigenes MRT

Wir beginnen mit der Röhre:

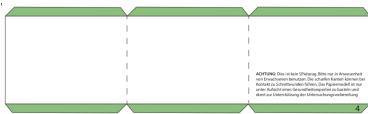
Gestalte zuerst die Oberfläche des MRTs wie du gerne möchtest.



- Schneide Nr.1 und Nr.2 des Vorlagebogens aus und die graue Fläche in der Mitte. Die Klebeflächen mit den Punkten bleiben erhalten und werden entlang des Kreises nach innen gebogen.



- Schneide nun Nr.3 aus und falte die Flächen an der gekennzeichneten Linie. Nun kannst du diesen Teil so um die beiden ersten Teile kleben, dass eine Röhre entsteht.

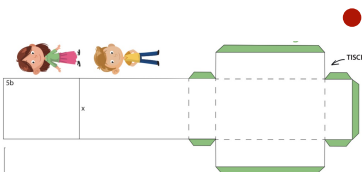


- Nr.4 wird die Hülle des MRTs. Schneide sie aus, falte sie an den gekennzeichneten Stellen und klebe sie um die Röhre.

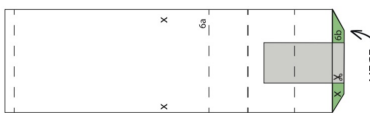


Du brauchst
1 Schere, 1 Kleber
& bunte Stifte ...
Überlege wer dir
dabei helfen kann!

Nun gestalten wir die Liege:



- Schneide Nr.5 aus und falte die gekennzeichneten Linien. Klebe die Kreuzchen zusammen, sodass eine kleine Box mit Verlängerung entsteht. Du kannst nun den Tisch mit der Verlängerung in die Röhre legen.



- Die verschiebbare Liege (Nr.6) wird nun ebenfalls ausgeschnitten, gefaltet und an den Kreuzchen zusammengeklebt. Sie ist nun bereit, dass du sie in das MRT hineinlegst.

Jetzt musst du dir nur noch eine Figur suchen, die darin Platz hat und dein MRT ausprobieren kann.