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Visual attention in preterm born adults: Specifically impaired attentional sub-mechanisms that link with altered intrinsic brain networks in a compensation-like mode

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ABSTRACT

Although pronounced and lasting deficits in selective attention have been observed for preterm born individuals it is unknown which specific attentional sub-mechanisms are affected and how they relate to brain networks. We used the computationally specified 'Theory of Visual Attention' together with whole- and partial-report paradigms to compare attentional sub-mechanisms of pre- ($n = 33$) and full-term ($n = 32$) born adults. Resting-state fMRI was used to evaluate both between-group differences and inter-individual variance in changed functional connectivity of intrinsic brain networks relevant for visual attention.

In preterm born adults, we found specific impairments of visual short-term memory (vSTM) storage capacity while other sub-mechanisms such as processing speed or attentional weighting were unchanged. Furthermore, changed functional connectivity was found in unimodal visual and supramodal attention-related intrinsic networks. Among preterm born adults, the individual pattern of changed connectivity in occipital and parietal cortices was systematically associated with vSTM in such a way that the more distinct the connectivity differences, the better the preterm adults' storage capacity.

These findings provide first evidence for selectively changed attentional sub-mechanisms in preterm born adults and their relation to altered intrinsic brain networks. In particular, data suggest that cortical changes in intrinsic functional connectivity may compensate adverse developmental consequences of prematurity on visual short-term storage capacity.

Introduction

Preterm birth (<37 weeks of gestation) is a substantial risk factor for suboptimal neurocognitive development with disadvantages persisting into adulthood (Baron and Rey-Casserly, 2010; D'Onofrio et al., 2013; Wolke and Meyer, 1999). Due to improvements in medicine and demographic changes preterm birth and survival rates are increasing with a global prevalence of about 10% (Blencowe et al., 2012). In order to identify specific neurocognitive targets for potential intervention, it is important to scrutinize the long-term cognitive and neuronal changes following preterm birth.

Specific functional weakness in preterm born individuals, which persists into early adulthood and is not explained by global cognitive deficit, has been observed for visual attention (Anderson and Doyle, 2003; Atkinson and Braddick, 2007, 2012; Mulder et al., 2009; Shum

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et al., 2008; Strang-Karlsson et al., 2010; van de Weijer-Bergsma et al., 2008). Attention deficits and their long-term stability are documented, for example, by changed eye movement at infancy (Atkinson and Braddick, 2012; van de Weijer-Bergsma et al., 2008), by deficits in neuropsychological tests at school age (Anderson and Doyle, 2003; Atkinson and Braddick, 2007; Johnson, 2007; Luciana et al., 1999; Shum et al., 2008; Taylor et al., 2004), and by slower reaction times in perceptive–attentional tests in early adulthood (Strang-Karlsson et al., 2010). However, the specific cognitive mechanisms underlying such observable behavior are unknown.

The major forms of brain injury after preterm birth are subcortical white and gray matter lesions together with impaired structural connectivity (Ball et al., 2012; Eikenes et al., 2011; Ment et al., 2009; Nosarti et al., 2008; Padilla et al., 2014; Pierson et al., 2007; Srinivasan et al., 2007; Salmaso et al., 2014; Volpe, 1998, 2009). These initially rather localized lesions are assumed to lead to widespread and functionally relevant long-term consequences (Hack and Taylor, 2000; Volpe, 2009), particularly in intrinsic brain networks (Bäuml et al., 2014; White et al., 2014). Such networks organize brain activity (Fox and Raichle, 2007) and are relevant for specific cognitive functions (Laird et al., 2011; Smith et al., 2009).

In the current study, we wanted to specify sub-mechanisms of visual attention affected in adults born preterm on the basis of the “Theory of Visual Attention” (TVA) framework. Furthermore, we aimed to integrate potential cognitive changes in visual attention with changes in intrinsic functional connectivity (iFC) of intrinsic brain networks in preterm born adults.

TVA, attentional sub-mechanisms, and its neural correlates

TVA is a mathematically formulated model of selective attention (Bundesen, 1990; Bundesen et al., 2005). In TVA, visual processing is conceived of as a parallel-competitive race. Visual objects in a given display are supposed to compete for selection, i.e., conscious representation, into the capacity-limited visual short-term memory (vSTM) store. Bottom-up and top-down generated bias signals determine ‘attentional weights’ for objects. Depending on their relative weights, some objects are thus favored for selection. The probability of selection is determined by an object's processing rate v, which depends on the attentional weight (w) that it receives, on sensory effectiveness, and the capacity of the vSTM store (if the store is filled, the selection process terminates). In TVA, the processing speed, C, for a display is defined as the sum of all v values in the display and, thus, characterizes the visual information processing rate of a given participant. Methods that have been previously used to disentangle impaired and preserved parameters of visual attention and short-term memory in neurodevelopmental disorders such as dyslexia, ADHD and spina bifida myelomeningocele (Bogon et al., 2014; Caspersen and Habekost, 2013; Finke et al., 2011; McAvinue et al., 2012; Stenneken et al., 2011) are simple psychophysical tests of whole and partial report of briefly presented letter arrays. Integrated within the TVA framework these tests permit different parameters of visual attention in a given participant to be extracted and quantified independently, and in measurements that are not confounded by, for example, cognitive or motor slowing. Such cognitive specificity is the optimal basis for relating quantified basic parameters of visual attention performance to underlying neural networks in healthy and patient populations (Gillebert et al., 2012; Peers et al., 2005; Sorg et al., 2012; Wiegand et al., 2013). We used the TVA based approach in order to collect estimates of visual perceptual processing speed (parameter C), vSTM storage capacity (parameter K), top-down control (parameter α), and spatial laterality of attention (parameter w_λ).

With respect to normally developed brains, the neural interpretation of TVA (NTVA) (Bundesen et al., 2005) specifies that posterior visual perceptual areas are governed by bias signals generated in frontoparietal areas and by a salience map putatively located in the pulvinar (Corbetta and Shulman, 2002; Kanwisher and Wojciulik, 2000; Kastner and Ungerleider, 2000). Visual perception is assumed to rely on a parallel race of visual objects that compete for access to the limited vSTM store (Bundesen, 1990). Thalamo-cortical feedback loops are suggested to (re)-activate the same visual neurons in posterior parts of the cortex coding and maintaining the winner objects (Gillebert et al., 2012; Magen et al., 2009; Todd and Marois, 2004; Xu and Chun, 2006). Due to their reliance on widespread interconnected brain areas the TVA parameters, and particularly vSTM storage capacity, are vulnerable to interruptions or connectivity changes within large-scale brain networks (Habekost and Rostrup, 2007). Based on these areas relevant for TVA-related mechanisms, we focused our analysis on intrinsic brain networks of the posterior brain that might be a brain base for impaired attentional sub-mechanisms in preterm born adults.

Intrinsic brain networks after preterm birth and its potential link with altered attention

Large-scale intrinsic functional connectivity is organized in intrinsic brain networks, which are defined by synchronous ongoing activity (i.e. iFC) in the frequency range of 0.01–0.1 Hz (Fox and Raichle, 2007). Intrinsic networks are consistent across individuals (Damoiseaux et al., 2006), development (Fransson et al., 2007), different behavioral states (Horovitz et al., 2008), and even species (Vincent et al., 2007), and possibly represent a basic organization principle of the mammalian brain. They are functional networks i.e. their areas commonly coactivate during both non-task and task states, suggesting intrinsic networks to implement specific aspects of cognition and behavior (Laird et al., 2011; Smith et al., 2009). One possible explanation for this functional specificity is that functional connectivity at rest reflects the history of correlated activity changes during goal-directed behavior (Berkes et al., 2011; Lewis et al., 2009; Riedl et al., 2011). By the use of resting-state functional resonance imaging (rs-fMRI), precursors of intrinsic brain networks are already detectable in newborns (Fransson et al., 2009) and even preterm born infants (Doria et al., 2010), with the latter showing subtle alterations in network connectivity (Damaraju et al., 2010; Smyser et al., 2010). Recently, changed intrinsic networks have been demonstrated for preterm born adults (Bäuml et al., 2014; White et al., 2014; Wilke et al., 2013), indicating distinct developmental trajectories for intrinsic networks after preterm delivery.

Given the functional–cognitive relevance of intrinsic networks, it seems reasonable to expect that impaired mechanisms of visual attention might be related to changes of intrinsic networks, which cover posterior areas of the brain relevant for visual attention, i.e. thalamic, visual, and dorsal attention networks. In principle, two types of relationship are possible: (i) the more attention is impaired the more intrinsic connectivity is changed from that of healthy controls, reflecting detrimental effects of preterm birth; (ii) the less attention is impaired the more intrinsic connectivity is changed from that of healthy controls, reflecting compensatory response on effects of preterm birth. Beyond the pattern of altered attentional sub-mechanisms in preterm born adults, the present study investigates the nature of the relationship between altered visual attentional mechanisms and intrinsic networks of the posterior brain.

Materials and methods

Participants

Participants were recruited as part of the prospective Bavarian Longitudinal Study (BLS) (Riegel et al., 1995; Wolke and Meyer, 1999), a geographically defined whole-population sample of preterm born children and full-term controls. Of the initial sample, 33 preterm adults and 32 healthy term controls (all aged 25 to 27 years)