Changes in event-related brain responses and habituation during child development – A systematic literature review

Julia Hartkopf[1,2], Julia Moser[1,2], Franziska Schleger[1,2], Hubert Preissl[1,2], Jana Keune[2,3]

[1]Institute for Diabetes Research and Metabolic Diseases/German Center for Diabetes Research (DZD e.V.) of the Helmholtz Center Munich at the University of Tuebingen, Otfried-Mueller-Strasse 10, 72076 Tuebingen, Germany
[2]fMEG-Center, University of Tuebingen, Otfried-Mueller-Strasse 47, 72076 Tuebingen, Germany
[3]Department of Neurology, Klinikum Bayreuth GmbH, Hohe Warte 8, 95445 Bayreuth, Germany

julia.hartkopf@med.uni-tuebingen.de

julia.moser@student.uni-tuebingen.de

franziska.schleger@med.uni-tuebingen.de

hubert.preissl@uni-tuebingen.de

j.keune@mail.de

* Corresponding Author:

Julia Hartkopf

University of Tuebingen

fMEG-Center

Otfried-Mueller-Straße 47

72076 Tuebingen, Germany

Phone: +49-7071-29-87689, Fax: +49-7071-29-5706

Email: julia.hartkopf@med.uni-tuebingen.de

Abstract

Objective

This systematic review highlights the influence of developmental changes of the central nervous system on habituation assessment during child development. Therefore, studies on age dependant changes in event-related brain responses as well as studies on behavioural and neurophysiological habituation during child development are compiled and discussed.

Methods

Two PubMed searches with terms “(development evoked brain response (fetus OR neonate OR children) (electroencephalography OR magnetoencephalography))” and with terms “(psychology habituation (fetal OR neonate OR children) (human brain)” were performed to identify studies on developmental changes in event-related brain responses as well as habituation studies during child development.

Results

Both search results showed a wide diversity of subjects’ ages, stimulation protocols and examined behaviour or components of event-related brain responses as well as a demand for more longitudinal study designs.

Conclusions

A conclusive statement about clear developmental trends in event-related brain responses or in neurophysiological habituation studies is difficult to draw. Future studies should implement longitudinal designs, combination of behavioural and neurophysiological habituation measurement and more complex habituation paradigms to assess several habituation criteria.

Significance

This review emphasizes that event-related brain responses underlie certain changes during child development which should be more considered in the context of neurophysiological habituation studies.

Keywords

habituation; development; event-related brain responses; evoked brain responses

Highlights

- With habituation, grade of neuronal maturity/integrity can be investigated from an early age
- Behavioural studies are being increasingly complemented by neurophysiological measurements
- Developmental changes in event-related brain responses should be considered

Abbreviations

CNS	central nervous system
EEG	electroencephalography
MEG	magnetoencephalography
fMEG	fetal magnetoencephalography
GA	gestational age
P	positive electroencephalography components
N	negative electroencephalography components
CAEP	cortical auditory evoked potential
CVEP	cortical visual evoked potential
DTI	diffusion tensor imaging
ISI	inter-stimulus interval
SOA	stimulus onset asynchrony
iCNV	early component of contingent negative variation
MMN	mismatch negativity
ITI	inter-train-interval

1 Introduction

1.1 Development of the human central nervous system (CNS)

When a human develops up from a fetus over childhood to adolescence, the brain undergoes continuous changes. During the third week after conception, the development of the human nervous system proceeds by expanding the neural plate – the origin of most of the neurons in the CNS. The development of the human CNS is characterized by cell proliferation, cell division, cell migration, cell aggregation, apoptosis and formation of networks (for a detailed overview on intra-uterine anatomical brain development see (Pinel, 2003)). The development of white matter and the related progress of myelination begin before birth and persist, with area-specific differences, until adulthood (Lebel and Beaulieu, 2011; Lebel et al., 2008). The processes of CNS development are therefore not finished at birth but continue over the entire life span.

In earlier days, the development of the human brain, especially before birth, could be investigated only by post mortem studies. The invention of ultrasound observation of fetuses enabled the investigation of brain structure during the fetal period in vivo, as well as fetal inner organs and fetal movements. Moreover, as an indicator for stimulus perception and neuronal processing, fetal behavioural responses to external stimulation were evaluated by ultrasound. In most studies, the stimulation was acoustic or vibro-acoustic and applied outside of the maternal abdomen (Leader et al., 1982b; Bellieni et al., 2005; Shalev et al., 1989). However, despite providing important insight into brain development, behavioural studies could only indirectly explain brain functioning and were unable to directly illuminate functional brain processes. Thanks to technological advances, behavioural studies are now complemented by neurophysiological measurement methods.

Unlike behavioural observation, the neurophysiological measurement methods electroencephalography (EEG) and magnetoencephalography (MEG) meant that neuronal activity could be evaluated directly with a high spatial and temporal resolution. The first EEG recording of a human scalp was performed by Berger in 1911 (Berger, 1929). EEG measurements register changes in electrical neuronal activity on the scalp while MEG measurements register changes in the magnetic fields produced by neurophysiological activity. It should be noted that both methods are completely non-invasive. While in neonates both EEG and MEG are applicable, advances of the fetal magnetoencephalography (fMEG) technique allowed for neurophysiological measurement of event-related responses to auditory and visual stimulation already during the fetal period. In addition to fetal measurements, it is possible to measure event-related brain responses of neonates with fMEG devices. Both EEG and (f)MEG are suitable for measuring event-related responses in infants and children. However, depending on the age of the participants, the kind of stimulation and external conditions, each method has its advantages as well as its specific limitations. MEG devices tend to be more expensive and hence less available. Special MEG systems for children and fMEG devices are rarely accessible. One necessary prerequisite for the evaluation and interpretation of both behavioural and neurophysiological responses related to external stimulation is the functional development of the auditory and visual system. Prenatally, detection and discrimination of sounds is possible, and the development of sound localization, as well as improved sound source acuity and sound discrimination, occurs during the first years of life (Anbuhl et al., 2017). Shortly after the rapid anatomical maturation of the auditory system during the second trimester of pregnancy, the first studies evaluated auditory experiences in fetuses between the 25th and 30th week of gestational age (GA) (for review see (Moore and Linthicum, 2007)). Birnholz et al. detected first responses to vibroacoustic stimulation in fetuses between the 24th and 25th week GA by monitoring blink-startle reflexes ultrasonically (Birnholz and Benacerraf, 1983). Stable behavioural responses across the study group were observed at a GA of 28 weeks. Detection of different pure tone frequencies could be shown over the course of fetal development (Hepper and Shahidullah, 1994). First behavioural responses to 500 Hz tone stimuli in single subjects were detected at 19 weeks GA. At an age of 27 weeks GA, almost the whole sample of fetuses showed reactions to stimulation in the frequency range between 250 Hz and 500 Hz. The authors also ascertained that responses to higher frequencies of around 1000 Hz could be detected at 33 weeks GA, whereas responses to 3000 Hz tones were not detected until 35 weeks GA (Hepper and Shahidullah, 1994). Other groups confirmed similar gestational ages for fetal responses to auditory stimulation (Querleu et al., 1988).

Visual stimulation in the prenatal period has, by comparison, been less well researched than auditory stimulation. It is important to note that not all parts of the visual system are mature before birth, but mature further during the first year of postnatal life. While scotopic vision (vision under low-light condition) becomes functional during the prenatal period between the 24th and 40th week GA, photopic vision (vision under well-lit conditions) requires the influence of direct light and is not functionally mature before birth (Graven and Browne, 2008). First brain responses to light flashes in the prenatal period have been detected as early as at the age of 28 weeks GA (Eswaran et al., 2004).

1.2 Auditory and visual event-related brain responses

Event-related brain responses show characteristic waveforms that consist of different components. The latter can be categorized into three types: exogenous components, endogenous components and motor components. Exogenous components, typically triggered by sensory stimuli, are modulated by characteristics of stimuli and occur in the first 150 ms after stimulus presentation. Unlike exogenous components, endogenous components are influenced by top-down-processes, consciousness and attention. This type of component is modulated by task relevant processes and is not entirely connected to the occurrence and physical aspects of a stimulus. The third category, motor components, emerges during preparation and execution of a motor response (Luck, 2005). Although in some cases the boundaries of these three categories are fluid, it is nevertheless a useful way of differentiating between event-related brain response components. The comparison of specific response components within participants of different age groups can therefore provide information about the development of distinct cognitive skills.

1.3 Habituation

The investigation of event-related responses facilitates the assessment of stimulus perception and processing by the direct examination of underlying neural correlates. The exploration of higher cognitive skills such as recognition or memory, however, requires complex stimulation paradigms. Habituation, as a form of basal learning competence, is one established concept for examining such higher cognitive processes. Habituation is commonly defined as "response decrement to repetitive stimulation" (Thompson and Spencer, 1966). However, alternative explanations for this process could be sensory adaptation or fatigue, defined as a state of decreased neuronal sensitivity as a result of constant stimulation (Carandini, 2000; Netser et al., 2011). To differentiate between these two possible sources of response decrement to repetitively presented stimulation, Thompson et al. developed criteria of habituation, which were later revised to provide ten characteristics of habituation by Rankin et al. (Supplementary Table 1) (Thompson and Spencer, 1966; Rankin et al., 2009).

In habituation studies, many different types of stimulation are applied. In addition to visual, tactile and auditory stimuli, combinations of two different sensory perceptions are used, e.g. vibroacoustic stimulation. The stimulation is selected on the characteristics and age of the participants and on the respective method of measuring habituation. In fetal studies, auditory stimulation is the predominant method. Visual stimulation is less feasible inside the maternal abdomen, even if stimulation with light flashes in fetal studies provides an additional possibility of stimulation. In neonates, visual and tactile stimuli gain importance in addition to auditory stimulation (Adams and Courage, 1995; Lejeune et al., 2014).

Characteristics of stimuli (loudness, time of repetition, intervals between or modalities of presentation) may affect the processes of habituation as well as the internal condition of the subject under investigation (motivational aspects, state of behaviour, inner evaluation processes and current interests) (Butler, 1968; Barry, 2004; Ponce et al., 2011; Gatchel and Lang, 1974).

The most frequently investigated premises of habituation over the last decades were the characteristics *response decrement*, *stimulus specificity* and *dishabituation*. Many studies reported habituation merely by the occurrence of *response decrement* over repetitively presented stimulation (Clifton et al., 1968; Groome et al., 1995; Hepper et al., 2012). Other studies used two or more of the characteristics to differentiate between habituation and sensory fatigue: *stimulus specificity* and *dishabituation* (Marcus et al., 2012; Lejeune et al., 2014). *Stimulus specificity* is defined by response recovery to a new stimulus (deviant), which is inserted into an array of repetitively presented standard stimuli and which is often wrongly labelled as *dishabituation.* Leader et al. discussed the lack of distinctiveness between stimulus specificity and dishabituation as early as 1982 (Leader et al., 1982a). The term *dishabituation*, however, should be used to describe response recovery to the habituated standard stimulus itself once the deviant stimulus has been inserted (Rankin et al., 2009).

To distinguish habituation clearly from other phenomena that may cause a response decrement (for example sensory fatigue, refractoriness or adaptation), several of the criteria postulated by Rankin et al. should be investigated simultaneously (Berry and Meister, 1998; Perez-Gonzalez and Malmierca, 2014; Rankin et al., 2009). Already Thompson and Spencer suggested that the process of dishabituation should be used as a main indicator for real habituation (Thompson and Spencer, 1966). Rankin et al. propose in addition to test for stimulus specificity and frequency-dependent spontaneous recovery (Rankin et al., 2009). Both, dishabituation and stimulus specificity are therefore particularly suitable criteria to confirm habituation that can easily be integrated into habituation paradigms (Figure 3).

To investigate habituation in humans, two different types of habituation paradigms are commonly used. In behavioural studies, stimulation is often repeated until response cessation, and habituation is quantified by the number of stimuli required before responses reach an asymptotic level (Kuhlman et al., 1988; Leader et al., 1982b). Alternatively, a predefined number of stimuli is presented and habituation is quantified by the amount of response decrement over this presented array (Sörös et al., 2001; Sheridan et al., 2008; Matuz et al., 2012). This method has the advantage of being less time consuming and is therefore often used in neurophysiological studies of infants and children.

Habituation is an established tool to investigate specific markers of behavioural and neurophysiological measures altered in disease states. Differences in habituation between patients and controls were found in migraine patients, in persons with autism spectrum disorder, with schizophrenia and with neurodegenerative disease (McDiarmid et al., 2017). For the field of neurodevelopmental research, habituation is particular well suitable because it can be applied without any specific behavioural response and is applicable over a wide age range. The recorded neurophysiological or behavioural correlates of habituation can be therefore used as markers for a healthy neurophysiological developmental process.

1.3.1 Behavioural habituation measurement

As early as 1963, Sokolov et al. described a decrement of the orienting reflex (a reaction to a novel or significant stimulus) which is characterized by three criteria: (1) nonspecificity with regard to the quality of the stimulus, (2) nonspecificity with regard to the intensity of the stimulus and (3) selectivity of extinction of various properties of the stimulus with repeated presentation (Sokolov, 1963a). While the term “extinction” is comparable to “habituation”, they used the term “disinhibition” similar to response recovery (Sokolov, 1963b). The first behavioural habituation studies were then published in the early 1980s (Schexnider et al., 1981; Leader et al., 1982b). To obtain higher objectivity in these trials, visual examination of a predefined behavioural response to a stimulus paradigm was often combined with videotaped recordings or other technology such as computer assisted recording programs, ultrasound monitoring of fetal behaviour, assessment of eye movements or fixation time (Groome et al., 1993; Groome et al., 1995; Leader et al., 1982b; Sommerville and Woodward, 2005). Moreover, implementation of special observer trainings, categorized documentation systems and calculation of inter-rater reliability are useful tools for minimizing observer effects that might influence data evaluation.

Reflexive action that is not controlled by conscious thoughts, such as the fetal startle response, is a behavioural component to assess habituation that is present in early fetal development. Its decrease is deemed a suitable marker for fetal habituation (Bellieni et al., 2005). The fetal startle response manifests itself not only by body movements but also by vegetative responses such as a change in heart rate (Buss et al., 2009; Sandman et al., 1997). A number of fetal studies therefore combine behavioural assessment and measurement of heart rate changes using ultrasound or transabdominal transducers (Groome et al., 1993; Leader et al., 1984). A further method of assessing habituation is to measure fixation time of participants to visual stimuli. In the past, gaze behaviour was mainly evaluated by observers. However, nowadays, eye-tracking-systems enable us to precisely and objectively record the direction and course of the subject's gaze (Streri and Pecheux, 1986).

Besides the reflexes, participants' conscious actions are an observable dependent variable in behavioural habituation studies. Tactile stimulation is a suitable method for examining habituation in neonates or premature infants and the duration of time that participants explore an object in their hands can be used as a marker for familiarization with its specific features (Lejeune et al., 2012; Sann and Streri, 2008; Lejeune et al., 2014; Streri and Pecheux, 1986).

1.3.2 Neurophysiological habituation measurement

As technology advanced, the behavioural concept of habituation was complemented by studies that analyse neurophysiological activity directly (Weber et al., 2016; Muenssinger et al., 2013c). Habituation, investigated with neurophysiological measurements, enables us to examine the underlying neuronal processes responsible for observable changes in behavioural habituation. In this context, amplitudes of event-related responses are used to detect habituation criteria analogous to behavioural responses (for details, see chapter 2).

However, to date, most studies investigating habituation have been based on behavioural observations and only a small number of studies used neurophysiological measurement methods.

1.4 Objective

The aim of this review was to summarize results of habituation studies during child development with a focus on neurophysiological habituation measurements, based on the analysis of event-related brain responses.

Particularly during the first years of life, there is progressive development of the CNS (e.g. myelination, synaptic plasticity, formation of networks). These developmental changes cause changes in event-related responses (especially alterations in amplitude and latency). As the investigation of event-related responses therefore allows to draw inferences in regard to the development of neural structures and/or neural functions, a general overview of studies on *“age-related changes in event-related brain responses”* is included. Here, the focus is on alterations in amplitude and latency linked to auditory and visual stimulation in the prenatal, postnatal and childhood period as the analysis of event-related brain responses is the most common technique for the investigation of neurophysiological habituation. We then performed a PubMed search on *“habituation studies during child development”* to analyse different methods of stimulation, response evaluation and the criteria used to differentiate between habituation and receptor fatigue. Finally, having drawn conclusions from the insights of both queries, we make recommendations for the evaluation of earlier studies and design of future trials.

2 Methods

This systematic review summarizes research data of studies investigating the development of event-related brain responses and habituation during childhood. For this purpose, relevant literature from the PubMed database was thoroughly reviewed in two independent searches. To summarize studies relating to *“age-related changes in event-related brain responses”,* a first search with certain terms “(development evoked brain response (fetus OR neonate OR children) (electroencephalography OR magnetoencephalography))” was performed. The term “evoked” was sought instead of “event-related” since use of the former has become more widespread in the last few decades. A second search with the terms “(psychology habituation (fetal OR neonate OR children) (human brain)” was used to identify *“habituation studies during child development”*.

Studies resulting from the search *“age-related changes in event-related brain responses”* were screened for the following inclusion criteria:

- Youngest age group <12 years
- Measurement of brain activity by EEG or (f)MEG
- Developmental processes within research question, including a comparison between at least two different age groups (cross-sectional or longitudinal)
- Healthy subjects or healthy control groups (except preterms)
- Original research articles

To enable a better comparison, it is generally established to label EEG components time-locked to a stimulus by the following definitions: “P” or “N” (P = positivity; N = negativity) combined with an integer number that approximately represents the mean latency of occurrence in milliseconds or the component number (for example “P100” or “P1”). Similarly, responses in (f)MEG studies are typically labelled with “M” followed by latency in ms or by component number (for example “M100", “M1”). Moreover, the respective amplitudes of event-related responses can be analysed. The typically described and frequently analysed components of a “Cortical Auditory Evoked Potential” (CAEP) include P1, followed by N1, P2 and N2 and P300 (Figure 1). The typical “Cortical Visual Evoked Potential” (CVEP) shows components N1, P1, N2 and P300 (Figure 2).

In neurophysiological habituation studies, characteristics of habituation can be observed by changes in amplitudes of event-related responses elicited by stimuli arranged in habituation paradigms (Muenssinger et al., 2013b). The observed components depend on the measurement method, the respective stimulation modality (auditory/visual/tactile) and the features of applied stimuli.

Studies resulting from the second search "*habituation studies during child development"* were screened for the following inclusion criteria:

- Youngest age group <12 years
- Healthy subjects or healthy control groups (except preterms)
- Repeated stimulation with evaluation of response characteristics
- Original research articles

Reference sections of studies that fulfilled inclusion criteria were also screened for further potentially relevant articles. Figures 4 and 5 show the systematic literature review process. Characteristics, methods and results, as well as limitations and perspectives of exemplary studies, are summarized and discussed in the following sections.

3 Results and Discussion

To simplify the overview of studies, age was grouped as depicted in Table 1 (Schneider and Lindenberger, 2012).

3.1 Age-related changes in event-related brain responses

In our first query, we searched for studies investigating event-related brain responses during child development. Table 2 shows a total of 85 studies that fulfilled the inclusion criteria for the first query. The number of participants varied between 10 and 586 with a median of 56. A longitudinal design (identified by "*") was chosen in 13 trials. A total of 72 studies recorded event-related responses by EEG and 12 studies by MEG or fMEG. One study used both EEG and MEG (Figure 6).

In one study, MEG was complemented with DTI (Diffusion Tensor Imaging), a non-invasive method for determining the anatomical connectivity of different brain regions by tracking white matter fibres, while another study used MRI alongside MEG to investigate the anatomical brain structure in more detail (Chen et al., 2010).

Changes in event-related brain responses during child development were shown in 73 of 85 studies. These changes may comprise different aspects of event-related brain responses. For example, an MEG-study using visual stimulation that compared children and adults (mean age 11 and 30 years respectively) showed a decrease of latency and an increase of response amplitudes with increasing age (Chen et al., 2010). Although a majority of studies investigated age-related changes of event-related brain responses in 0-2 year old children, the changes appeared to persist up until late adolescence (Mahajan and McArthur, 2012). Importantly, fMEG studies demonstrated that developmental changes are already observable during the fetal period (Schneider et al., 2004; Eswaran et al., 2004).

For further investigation, we decided to focus on two component ranges: first, developmental changes in the exogenous components N1 (first negativity) and P1 (first positivity) and second, developmental changes in the later components P2, N2 and P300.

3.2 Age-related changes in primary exogenous event-related brain responses

3.2.1 Auditory P1

Seven studies using auditory stimulation investigated age-related changes in component P1 (Table S2). Two studies showed that a typical P1 was not identifiable in very young participants. While one of these studies investigated preterm infants, and ascertained that the P1 component emerged between 37 and 38 weeks of gestational age, a second trial did not detect the component until an age of about 5 years (Weitzman et al., 1967; Lippe et al., 2009). However, different kinds of stimulation were used. The three studies analysing latency reported a decrease of latency with increasing age. Stimulation features such as inter-stimulus interval (ISI) and stimulus onset asynchrony (SOA) also have an influence on the latency and amplitude of the P1 component.

3.2.2 Auditory N1

Four studies investigated changes of the N1 component by comparing latencies and/or amplitudes between different age groups (Table S3). However, these studies all differed with respect to the stimulation applied. Two studies showed an increase of the N1 amplitude. In one of these two trials, a go-/no-go task and a stop-signal-task were presented to children between seven and nine years of age, and the increase of amplitude was detectable only for auditory stop-signals in the parietal region (Johnstone et al., 2007). The second study showed an increased amplitude of evoked responses after presenting pure tones and syllables in children and adolescents aged between 10 and 18 years than in adults (Mahajan and McArthur, 2012). A further study, in which clicks were used to stimulate a younger group of children between 23 and 47 weeks of age, reported a decrease in latency (Weitzman et al., 1967). Sussman et al. investigated the influence of different kinds of pure tones with changing stimulation paradigm features (Sussman et al., 2008). Differences in amplitude and latency between age groups were, however, not statistically analysed and the N1 component, which was probably dependent on the stimulus rate, was visible in only a small number of the participants aged between 8 and 11 years.

The latency of the early auditory components P1 and N1 as exogenous components showed a tendency of becoming shorter as age increased. From the 11 studies that investigated either the auditory component N1 or P1, five studies confirmed this tendency by statistical analysis. Due to the fact that the focus was on changes in amplitudes, latency was not analysed in the other six studies. The phenomenon of a decrease of latency with age could be explained by the myelination of nerves that accelerates conduction (Pihko et al., 2009).

Findings were diverse with regard to the amplitudes of event-related responses. Most trials included participants of various age ranges, and almost all of the studies used different kinds of stimuli and stimulation paradigms. Given that age is associated with the degree of maturity of the CNS and that the applied stimulation impacts the elicited event-related responses, the lack of a developmental trend in amplitude heights of the compiled studies seems natural.

3.2.3 Visual N1

In all four studies, an age-dependent decrease in latency of the visual N1 was shown independent of the kind of stimulation and age of the participants (Table S4). One of the studies also detected an increase in the amplitude of N1 with age; in the other trials there was no consistent age-related effect on the amplitude of N1. (Hirai et al., 2009; Lippe et al., 2007; Tremblay et al., 2014). In addition to stimulation type and age, the hemisphere under investigation seemed to have an influence on the amplitude and its potential developmental changes, thus contributing to the heterogeneous results.

3.2.4 Visual P1

Four out of eight studies observed a decrease in latency of the visual P1 with increasing age, while one showed only a partial decrease (Table S5). An increase in amplitude was shown in only two studies, one of which did not perform a statistical test for significance. Five trials reported a decrease in amplitude as age increased. This observation was independent of stimulation conditions (all five studies applied different stimuli) and observable over various age groups. In three of these five studies, participants were six years of age and older, while very young participants (aged between 0 and 2 years) were investigated in the other two studies.

The type of visual stimulation varied in all five studies and an influence of stimulus complexity on the development of the component P1 can be excepted (Sokol and Jones, 1979). The diversity in age of the participants and the methodical differences of conditions mean that it is difficult to draw a firm conclusion with regard to the developmental changes observed in visual P1.

3.3 Age-related changes in primary endogenous event-related brain responses

3.3.1 Auditory P2

The four studies that investigated auditory P2 did not show consistent results with regard to age-related changes (Table S6). P2 component appears to become more prominent during the first months of life and is influenced by the type of stimulation (Lippe et al., 2009). SOA levels of pure tones, as well as different conditions at a go-/no-go-task (response inhibition vs. response execution) affect the P2 (Sussman et al., 2008; Johnstone et al., 2007). Although amplitude of P2 was found to increase in one study stimulating with broadband noise, the P2 did not emerge until about the fifth year of life. Only one study carried out with premature infants registered a decrease in latency of P2 with increasing age within the first weeks after birth (Weitzman et al., 1967).

3.3.2 Auditory N2

There is no consistency in age-dependent latency changes of N2 (Table S7). Four of the seven studies investigating the N2 showed that the development of this component is dependent on the type of stimulus and the location of the electrodes. A decrease in latency was registered in one study only; all other studies found no consistent trend. Changes in amplitude are also heterogeneous. Two studies found no consistent changes, while two others reported that amplitude decreased as age increased.

3.3.3 Auditory P300

Development of auditory P300 was analysed in six trials (Table S8). Albeit a decrease in latency with increasing age was found in three trials, two of these showed only a partial decrease, depending on what stimulation was applied. By contrast, one study showed an increase in latency. An increase in amplitude was observed in four studies, even though these changes depended on the kind of stimuli applied. The auditory P300 is supposed to represent higher cognitive processes related to working memory such as context information, recognition or categorisation (Duncan et al., 2009). The development of this component is assumed to continue until at least adolescence.

3.3.4 Visual N2

The visual N2 was taken into consideration in twelve studies and was therefore the most frequently investigated component (Table S9). An age-related decrease in latency was observed in six studies, however, in four of these trials the investigated age groups had a difference of at least six years. A decrease in latency of N2 with increasing age therefore seems to occur relatively slowly (Luck and Kappenman, 2011).

Although an increase of amplitude was established in four studies, one did not report a statistical test for significance (Waxer and Morton, 2011b). A further six studies registered a decline or no change of amplitude. It is, therefore, not possible to draw any conclusions about developmental changes in amplitude of the visual N2 component.

3.3.5 Visual P300

Visual P300 component was analysed in five studies (Table S10). The majority of the studies that investigated P300 used go-/no-go or novel-target detection stimulation paradigm. One study, which used a congruency/incongruency task as its stimulus, observed a decrease in latency with age (Rueda et al., 2004). An increase in amplitude was detected in another study that investigated novelty processing by presenting faces and patterns (Kihara et al., 2010).

None of the other trials showed consistent results for either a decrease in latency or/and an increase in amplitude for the visual event-related P300 component. The visual P300 is presumably influenced by memory and attention processes (Polich, 2007). The low number of studies and the inconsistent results do not permit us to make any valid conclusion with regard to developmental trends of the P300. Furthermore, the complex and diverse stimulation paradigms complicated the comparison and conclusions from these results.

3.4 Habituation studies during child development

In our second quest, we searched for studies that evaluated habituation during child development. Table 3 summarizes a total of 52 studies and shows the methods applied, type of stimulation and types of habituation criteria tested (Supplementary Table S1).

3.4.1 Participants

A total of 15 of the habituation studies were fetal studies, while 27 studies investigated habituation in infants aged between 0-2 years and a further 4 studies examined both fetuses and infants aged between 0 and 2 years. In all, 46 of the 52 trials investigated participants between fetal age and 24 months, thus supporting the particular suitability of habituation for the examination of early learning capability and – directly with measurement of brain activity or indirectly by behavioural analysis – for drawing conclusions about the function of the developing CNS.

3.4.2 Stimulation

Most studies used visual or auditory stimulation (14 visual stimulation, 21 auditory or vibroacoustic stimulation). Tactile/vibrotactile stimulation (passive as well as active) was applied in 11 trials, one of which also combined tactile stimulation with visual stimulation. Six studies applied a combination of visual stimulation and auditory stimulation. In addition to response decrement following repeated stimulation, which was analysed in all of the studies, 26 trials also analysed stimulus specificity. The criterion of response decrement was found to be fulfilled in 35 of the trials, and partially fulfilled in 13 of the studies. Twenty-eight of the studies tested for two criteria (response decrement & stimulus specificity, response decrement & dishabituation or response decrement & spontaneous recovery). Of these, 12 reported that both criteria were fulfilled. Habituation paradigms, which allow the investigation of three or more habituation criteria, were used in only 5 trials. In a tactile habituation study, Marcus et al. ascertained that premature infants already show response decrement, stimulus specificity and dishabituation to a wooden object (Marcus et al., 2012). The authors concluded that premature infants already display developed skills of memorization, discrimination and recognition to tactile explored objects. In a fetal behavioural habituation study, Leader et al. investigated 40 fetuses with vibrotactile stimulation and found evidence of habituation and dishabituation (Leader et al., 1982a). The paradigm design would even have been suitable to test for stimulus specificity, but this step was not performed since the data had not been analysed for this purpose.

3.4.3 Neurophysiological habituation studies

Of all the studies that fulfilled the inclusion criteria, habituation was analysed by direct visual observation of behavioural responses (including videotaped recordings and observation by ultrasound) in 38 studies. Eight studies evaluated changes in heart rate partly in combination with other response types such as respiration or behavioural observation. The neurophysiological activity was directly measured during the habituation procedure to examine habituation criteria in only 8 studies (Table 4).

The first habituation study we identified that used a neuroimaging method was published in the early 1990s and recorded event-related brain responses in children by EEG (McIsaac and Polich, 1992). Beside MEG or fMEG, EEG is still the most widely used neurophysiological approach in habituation studies. Besides its feasibility, the applied method depends on the aims of a study and the respective trial design. EEG, which is feasible in children and adults, is suitable not only for the measurement of temporal dynamics of event-related brain responses but also for examining spatial information by comparing signals at different electrodes. In the search, three EEG studies were found to investigate habituation in children. The study populations of these three studies varied between preterm infants, babies, children and adolescents and investigated habituation in different components of the event-related brain responses, depending on the kind of stimulation and the research question. To compare habituation in 10 infants of approximately 6 months of age with that of a group of 10 young adults, McIsacc et al. chose a paradigm that uses single tones presented in sequences (McIsaac and Polich, 1992). The component P300 was found to have a similar morphology in both groups, but peaked earlier and with lower amplitudes in infants than in adults, indicating a developmental effect. Interindividual differences in P300 were more pronounced in infants. There was no significant response decrement to repeated stimulation in either the group of infants or within young adults. The authors therefore suggested that the kind of stimulation (a passive stimulation paradigm) and the related attention processes inhibited response decline. However, the small sample size limited the generalisability of these results.

Kropp et al. used an auditory two-stimulus reaction time go/no-go task to examine habituation in migraine and healthy participants (Kropp et al., 1999). The early component of contingent negative variation (called iCNV) following the reaction to the go-stimulus was investigated. Response decrement in healthy children was not shown, whereas healthy adults habituated to the stimulation.

The third EEG-study, conducted by Weber et al., examined habituation in 17 healthy preterm infants and 16 term infants with an auditory oddball-paradigm (Weber et al., 2016). The mismatch negativity (MMN) component in both groups was investigated at the term-equivalent age of approximately 40.8 weeks of GA. The MMN is assumed to reflect a pre-attentive cognitive discrimination capacity. No significant differences in MMN amplitude and latency between preterm and term infants were found. However, response decrement and stimulus specificity were found in both groups. It is also interesting to note that the authors were able to show a positive correlation between habituation and the scores of a developmental follow-up assessment at approximately 20 months of age in both preterm and term infants.

While the above studies examined endogenous components and MMN, the remaining five developmental related habituation studies analysed exogenous components of event-related brain responses. One research question in the neurophysiological habituation field addressed whether exogenous components, also referred as early components, actually show habituation or if a response decline is potentially caused by adaptation phenomena like refractoriness processes or sensory fatigue (Barry et al., 1992; Verbaten et al., 1986; Budd et al., 1998). However, there is evidence that habituation occurs also in early components, like N1/P1. In adults, for example, habituation of visual N1 was shown. By using a long, varying ISI, refractoriness could be excluded as reason for response decline, since the length of the ISI exceeded the refractory time (Verbaten et al., 1986). It should be mentioned that the variation of the length of the ISI influences the amplitudes of event-related responses and is in general a factor known to influence neurophysiological habituation (Pereira et al., 2014; Miltner et al., 1991). The length of the ISI can modulate how fast habituation occurs and how long the effects persist (Fruhstorfer et al., 1970; Gatchel, 1975; Davis, 1970). Habituation of auditory N1 was moreover shown by Woods and Elmasian, presenting speech sounds and tones (Woods and Elmasian, 1986). Here, the long ISI-condition (1000 ms duration) should be long enough to enable recovery of N1 (Cowper-Smith et al., 2013). The applied paradigm allowed testing for stimulus specificity that was shown additionally to response decrement. The authors examined habituation of N1 by comparing amplitudes of responses and stimulus-specificity across stimulation blocks. This procedure served as a further criterion to exclude adaptation, as the time interval between blocks is usually longer than the ISI.

An MEG-study by Muenssinger et al. examined auditory habituation of component M1 in a sample of 29 children and 14 adults (Muenssinger et al., 2013c). The habituation paradigm consisted of five equal tones, with an inserted different tone followed by two tones as previously, to allow assessment of response decrement, stimulus specificity and dishabituation following the recommendations of Rankin et al. (Rankin et al., 2009). Response decrement caused by sensory adaption or neuronal fatigue is implausible using this approach, if several habituation criteria are met. In the group of children, none of the three tested habituation criteria within-trains could be confirmed and only response decrement across the stimulation blocks was found. By comparison, the adult group showed response decrement and stimulus specificity within-blocks. Rankin et al. describe stimulus specificity next to frequency-dependent spontaneous recovery as an appropriate marker to prove for habituation (see table S1) (Rankin et al., 2009). The study by Muenssinger et al. also suggested that developmental changes occur in habituation processes across different age groups, as supported by the diverse results in children and adults.

Four neurophysiological habituation studies measured event-related responses with fMEG, where the first detectable peak is examined. This can be interpreted as early component. Sheridan et al. presented repeated trains of four light flashes to 25 fetuses and 12 newborns (Sheridan et al., 2008). In the group of neonates, all infants with detectable event-related responses (9 out of 12) showed a decline in amplitude from the first to the last flash of light. About a third of the fetuses showed detectable event-related response components with a decrement after the first stimulus. The ISI between the stimuli in a block with two seconds should enable recovery of the measured component, however, there is little knowledge about the recovery time of event-related components in fetuses. The second fMEG visual habituation study of Matuz et al. used an advanced version of the light flash paradigm of the recent study by Sheridan et al. (Matuz et al., 2012; Sheridan et al., 2008). In the light flash paradigm, a burst tone was also implemented to allow the examination of stimulus specificity. Moreover, two different conditions of inter-train-interval (ITI) duration were implemented to exclude sensory fatigue. In neonates, under the long ITI condition, both response decrement and stimulus specificity could be shown. However, in fetuses, the response rates to the visual stimuli were at a similarly low level as in the study of Sheridan et al. and habituation was not demonstrated consistently (Sheridan et al., 2008). Muenssinger et al. conducted an fMEG study for fetuses and neonates with an auditory habituation paradigm consisting of eight pure tones with one inserted deviant in place of the sixths tone similar to the paradigm as depicted in Figure 3

(Muenssinger et al., 2013b). The paradigm allowed investigation of response decrement, stimulus specificity and dishabituation. A significant response decrement between the second and the last tone was detected in fetuses, and stimulus specificity was present in both fetuses and neonates. Dishabituation was found neither in fetuses nor in neonates. In a further fMEG study, an auditory habituation paradigm (Figure 3) consisting of syllables was presented to fetuses and neonates (Hartkopf et al., 2016). Stimulus specificity was demonstrated in neonates only; neither response decrement nor dishabituation could be shown in either age group.

Generally, in future research of neurophysiological habituation studies, the impact of adaptation phenomena on response decrement should be consequently excluded by testing for stimulus specificity and dishabituation. Furthermore, the influence of the ISI should be investigated systematically in this context, with a differentiation of early and late components during child development.

3.4.4 Longitudinal studies

Habituation is widely accepted as a suitable tool for the investigation of the development of early cognitive skills (for example cognitive encoding, information processing skills, discrimination and memory; for a review, see (Kavsek and Bornstein, 2010). Longitudinal designs are particularly suitable for investigating development, for example the timing of specific cognitive changes during childhood. None of the eight neurophysiological habituation studies used the same stimulation paradigm to compare changes in neural correlates from more than two timepoints during child development. Further studies should seek to bridge this gap, even if longitudinal research is more time-consuming than cross-sectional studies.

4 Conclusion:

In this review, we aimed to collect and describe studies investigating habituation in the context of developmental processes in growing children with an emphasis on neurophysiological habituation measurements, based on the analysis of event-related brain responses.

Age-related changes of event-related brain responses themselves are linked to an increasing maturity of the sensory organs and the central nervous system and, indeed, a large number of the reviewed studies reported age-related changes in components of event-related responses (Birbaumer and Schmidt, 2006). However, the developmental changes observed were not consistent. Although general trends such as a decrease in latency and an increase in amplitude, which can reflect structural or functional maturation processes of the CNS (e.g. increasing myelination or formation of neural networks) are presumed to exist particularly in exogenous components, it is challenging to confirm this on the basis of the studies included in our review. The diversity in methods, selected age groups, chosen stimulation paradigms and investigated components, drastically restricts the comparability of the results.

To facilitate better comparability, the studies were divided according to specific methodical characteristics: a) the kind of investigated component(s) (exogenous versus endogenous components) and b) the stimulus modality (auditory versus visual). In addition, the separate components of the typical CAEP and CVEP were taken into consideration. However, even this differentiated overview did not lead to a generally valid statement about developmental trends in components of event-related brain responses.

Nearly all of the included studies used different stimuli/stimulation paradigms, investigated participants in different age groups and analysed their data on the basis of various methods. Besides the age of participants – and hence the state of maturity of the CNS – changes in event-related brain responses are strongly related to different types of stimulation. Fuchigami et al., for example, showed that response latencies decreased more rapidly with increasing age for complex stimuli than for simple tones (Fuchigami et al., 2009). Moreover, further attributes of the stimuli such as novelty, the emotional context or spatial motion impacted characteristics of event-related brain responses during development (Kihara et al., 2010; Mecklinger et al., 2011; Lamm and Lewis, 2010; van der Meer et al., 2012). This wide range of different study designs and methods limits the interpretation of developmental trends of event-related brain responses or their components and does not endorse a general trend in developmental changes of latency and amplitude during childhood.

Habituation, a basic form of learning, which is manifest very early in development, is a concept to assess cognitive function. It can be measured by two main approaches: the observation of behavioural changes and neurophysiological measurements of event-related brain responses, which enable for a direct evaluation of brain developmental processes. Components of event-related responses measured by EEG and (f)MEG/MEG seem to be suitable for investigating changes in habituation during child development. Studies with fetuses demonstrated that brain responses to auditory and visual stimulation are already measurable during the third trimester of pregnancy, meaning that it is possible to investigate event-related brain responses from an early stage of development. It should be mentioned that fMEG as measuring method has some limitations, for example a low signal-to-noise ratio or the sensitivity to environmental artefacts. The stimuli should met certain criteria so that they can be perceived by the fetus through tissue layers and amniotic fluid. Therefore, visual light stimuli need to be in a defined range of wavelenghts and auditory stimulation in a certain range of frequency to ensure a satisfactory transferability (Preissl et al., 2004; Sheridan et al., 2010). Most of the habituation studies examining changes in latency and amplitude of event-related responses or their particular components in different age groups found differences that were possibly related to age-dependent stimulus processing. However, it is still difficult to rule out whether other variables, such as the type and the context of the applied stimuli, the examined brain region and the selection of the analysed components impact the results. Unlike behavioural habituation studies, the number of neurophysiological habituation studies remains low.

To rule out sensory fatigue as the driving mechanism for response decrement, habituation studies should use at least three of the postulated habituation criteria: “response decrement”, “stimulus specificity” and “dishabituation”. Despite the fact that these criteria can be easily implemented in most habituation paradigms, only very few of the included studies used all them.

A large number of studies that do not examine these criteria thus lose quality, as it is not possible to draw clear conclusions about habituation as a driving mechanism for response decrement. This should be also taken into account in future habituation studies.

Despite the large number of studies investigating event-related brain responses and habituation in early development, it is currently not possible to make any conclusive statements about developmental trends. This is mainly due to the fact that stimulation protocols are very diverse. More consistent stimulation paradigms are needed to replicate findings and to better compare different study populations. An interesting issue would also be the combination of behavioural and neurophysiological habituation assessment in order to compare results of both approaches directly with each other. Ultimately, more trials with longitudinal designs are needed to provide clearer information about maturational changes of event-related responses during the process of growing up.

Conflicts of interest

None of the authors have potential conflicts of interest to be disclosed.

Funding

This word was partially supported by the Luminous project (EU-H2020-FETOPEN GA No.686764) and a grant (01GI0925) from the Federal Ministry of Education and Research (BMBF) to the German Center for Diabetes Research (DZD e.V.).

Acknowledgements

We are grateful to Shirley Wuerth for help with editing the manuscript.

References

Adams RJ, Courage ML. Development of chromatic discrimination in early infancy. Behav. Brain Res. 1995;67(1):99-101.

Adams RJ, Courage ML, Mercer ME. Deficiencies in human neonates' color vision: photoreceptoral and neural explanations. Behav. Brain Res. 1991;43(2):109-14.

Agyei SB, van der Weel FR, van der Meer AL. Longitudinal study of preterm and full-term infants: High-density EEG analyses of cortical activity in response to visual motion. Neuropsychologia 2016;84:89-104.

Anbuhl KL, Uhler KM, Werner LA, Tollin DJ. Early Development of the Human Auditory System. Fetal and Neonatal Physiology (Fifth Edition). Elsevier; 2017, p. 1396-411. e3.

Anderson S, Parbery-Clark A, White-Schwoch T, Kraus N. Development of subcortical speech representation in human infants. J. Acoust. Soc. Am. 2015;137(6):3346-55.

Atchley RA, Rice ML, Betz SK, Kwasny KM, Sereno JA, Jongman A. A comparison of semantic and syntactic event related potentials generated by children and adults. Brain Lang. 2006;99(3):236-46.

Babkirk S, Rios V, Dennis TA. The late positive potential predicts emotion regulation strategy use in school-aged children concurrently and two years later. Dev Sci 2015;18(5):832-41.

Barry RJ. Stimulus significance effects in habituation of the phasic and tonic orienting reflex. Integr. Physiol. Behav. Sci. 2004;39(3):166-79.

Barry RJ, Cocker KI, Anderson JW, Gordon E, Rennie C. Does the N100 evoked potential really habituate? Evidence from a paradigm appropriate to a clinical setting. Int. J. Psychophysiol. 1992;13(1):9-16.

Bellieni CV, Severi F, Bocchi C, Caparelli N, Bagnoli F, Buonocore G, et al. Blink-startle reflex habituation in 30-34-week low-risk fetuses. J. Perinat. Med. 2005;33(1):33-7.

Berger H. Über das elektrenkephalogramm des menschen. Arch. Psychiatr. Nervenkr. 1929;87(1):527-70.

Berry MJ, 2nd, Meister M. Refractoriness and neural precision. J. Neurosci. 1998;18(6):2200-11.

Birbaumer N, Schmidt RF. Biologische Psychologie.(6., vollständig überarbeitete und ergänzte Auflage). Heidelberg: Springer; 2006.

Birnholz JC, Benacerraf BR. The development of human fetal hearing. Science 1983;222(4623):516-8.

Brinkman MJ, Stauder JE. Development and gender in the P50 paradigm. Clin. Neurophysiol. 2007;118(7):1517-24.

Brinkman MJ, Stauder JE. The development of passive auditory novelty processing. Int. J. Psychophysiol. 2008;70(1):33-9.

Brusini P, Dehaene-Lambertz G, Dutat M, Goffinet F, Christophe A. ERP evidence for on-line syntactic computations in 2-year-olds. Dev. Cogn. Neurosci. 2016;19:164-73.

Budd TW, Barry RJ, Gordon E, Rennie C, Michie PT. Decrement of the N1 auditory event-related potential with stimulus repetition: habituation vs. refractoriness. Int. J. Psychophysiol. 1998;31(1):51-68.

Buss C, Davis EP, Class QA, Gierczak M, Pattillo C, Glynn LM, et al. Maturation of the human fetal startle response: evidence for sex-specific maturation of the human fetus. Early Hum. Dev. 2009;85(10):633-8.

Butler BE, Trainor LJ. Brief pitch-priming facilitates infants' discrimination of pitch-evoking noise: evidence from event-related potentials. Brain Cogn. 2013;83(3):271-8.

Butler RA. Effect of changes in stimulus frequency and intensity on habituation of the human vertex potential. J. Acoust. Soc. Am. 1968;44(4):945-50.

Byrne JM, Connolly JF, MacLean SE, Dooley JM, Gordon KE, Beattie TL. Brain activity and language assessment using event-related potentials: development of a clinical protocol. Dev. Med. Child Neurol. 1999;41(11):740-7.

Carandini M. Visual cortex: Fatigue and adaptation. Curr. Biol. 2000;10(16):R605-7.

Chan PY, Cheng CH, von Leupoldt A. The Effect of Development in Respiratory Sensory Gating Measured by Electrocortical Activations. Neural Plast. 2015;2015:389142.

Chen Y, Xiang J, Kirtman EG, Wang Y, Kotecha R, Liu Y. Neuromagnetic biomarkers of visuocortical development in healthy children. Clin. Neurophysiol. 2010;121(9):1555-62.

Chevalier N, Martis SB, Curran T, Munakata Y. Metacognitive processes in executive control development: the case of reactive and proactive control. J. Cogn. Neurosci. 2015;27(6):1125-36.

Cho RY, Walker CP, Polizzotto NR, Wozny TA, Fissell C, Chen CM, et al. Development of sensory gamma oscillations and cross-frequency coupling from childhood to early adulthood. Cereb. Cortex 2015;25(6):1509-18.

Clery H, Roux S, Besle J, Giard MH, Bruneau N, Gomot M. Electrophysiological correlates of automatic visual change detection in school-age children. Neuropsychologia 2012;50(5):979-87.

Clifton RK, Graham FK, Hatton HM. Newborn Heart-Rate Response and Response Habituation as a Function of Stimulus Duration. J. Exp. Child Psychol. 1968;6(2):265-&.

Cody DT, Townsend GL. Some physiologic aspects of the averaged vertex response in humans. Audiology 1973;12(1):1-13.

Colombo J, Kannass KN, Shaddy DJ, Kundurthi S, Maikranz JM, Anderson CJ, et al. Maternal DHA and the development of attention in infancy and toddlerhood. Child Dev. 2004;75(4):1254-67.

Cowper-Smith CD, Green J, Maessen H, Bance M, Newman AJ. Refractory effects of the N1 event-related potential in experienced cochlear implant patients. Int. J. Audiol. 2013;52(2):104-12.

Cragg L, Fox A, Nation K, Reid C, Anderson M. Neural correlates of successful and partial inhibitions in children: an ERP study. Dev. Psychobiol. 2009;51(7):533-43.

Cummings A, Ceponiene R, Dick F, Saygin AP, Townsend J. A developmental ERP study of verbal and non-verbal semantic processing. Brain Res. 2008;1208:137-49.

Davies PL, Segalowitz SJ, Gavin WJ. Development of error-monitoring event-related potentials in adolescents. Ann. N. Y. Acad. Sci. 2004a;1021:324-8.

Davies PL, Segalowitz SJ, Gavin WJ. Development of response-monitoring ERPs in 7- to 25-year-olds. Dev. Neuropsychol. 2004b;25(3):355-76.

Davis M. Effects of interstimulus interval length and variability on startle-response habituation in the rat. J. Comp. Physiol. Psychol. 1970;72(2):177.

Duncan CC, Mirsky AF, Lovelace CT, Theodore WH. Assessment of the attention impairment in absence epilepsy: comparison of visual and auditory P300. Int. J. Psychophysiol. 2009;73(2):118-22.

Eswaran H, Lowery CL, Wilson JD, Murphy P, Preissl H. Functional development of the visual system in human fetus using magnetoencephalography. Exp. Neurol. 2004;190(S52-S58).

Eswaran H, Lowery CL, Wilson JD, Murphy P, Preissl H. Fetal magnetoencephalography--a multimodal approach. Brain Res. Dev. Brain Res. 2005;154(1):57-62.

Fabrizi L, Slater R, Worley A, Meek J, Boyd S, Olhede S, et al. A shift in sensory processing that enables the developing human brain to discriminate touch from pain. Curr. Biol. 2011;21(18):1552-8.

Fiser J, Aslin RN. Statistical learning of new visual feature combinations by infants. Proc. Natl. Acad. Sci. U. S. A. 2002;99(24):15822-6.

Fox AM, Anderson M, Reid C, Smith T, Bishop DV. Maturation of auditory temporal integration and inhibition assessed with event-related potentials (ERPs). BMC Neurosci. 2010;11:49.

Friedrich M, Friederici AD. Phonotactic knowledge and lexical-semantic processing in one-year-olds: brain responses to words and nonsense words in picture contexts. J. Cogn. Neurosci. 2005;17(11):1785-802.

Fruhstorfer H, Soveri P, Järvilehto T. Short-term habituation of the auditory evoked response in man. Electroencephalogr. Clin. Neurophysiol. 1970;28(2):153-61.

Fuchigami T, Okubo O, Fujita Y, Kohira R, Arakawa C, Endo A, et al. Event-related potentials in response to 3-D auditory stimuli. Brain Dev. 2009;31(8):577-81.

Fuchigami T, Okubo O, Fujita Y, Okuni M, Noguchi Y, Yamada T. Auditory event-related potentials and reaction time in children: evaluation of cognitive development. Dev. Med. Child Neurol. 1993;35(3):230-7.

Fujioka T, Ross B, Kakigi R, Pantev C, Trainor LJ. One year of musical training affects development of auditory cortical-evoked fields in young children. Brain 2006;129(Pt 10):2593-608.

Gatchel RJ. Effects of interstimulus interval length on short-and long-term habituation of autonomic components of the orienting response. Physiological Psychology 1975;3(2):133-6.

Gatchel RJ, Lang PJ. Effects of interstimulus interval length and variability on habituation of autonomic components of the orienting response. J. Exp. Psychol. 1974;103(4):802-4.

Gebuis T, Herfs IK, Kenemans JL, de Haan EH, van der Smagt MJ. The development of automated access to symbolic and non-symbolic number knowledge in children: an ERP study. Eur. J. Neurosci. 2009;30(10):1999-2008.

Gorga MP, Kaminski JR, Beauchaine KL, Jesteadt W, Neely ST. Auditory brainstem responses from children three months to three years of age: normal patterns of response. II. J. Speech Hear. Res. 1989;32(2):281-8.

Graven SN, Browne JV. Visual Development in the Human Fetus, Infant and Yound Child. Newborn Infant. Nurs. Rev. 2008;8(4):194-201.

Groome LJ, Gotlieb SJ, Neely CL, Waters MD. Developmental trends in fetal habituation to vibroacoustic stimulation. Am. J. Perinatol. 1993;10(1):46-9.

Groome LJ, Singh KP, Burgard SL, Neely CL, Deason MA. Motor responsivity during habituation testing of normal human fetuses. J. Perinat. Med. 1995;23(3):159-66.

Hadley H, Pickron CB, Scott LS. The lasting effects of process-specific versus stimulus-specific learning during infancy. Dev Sci 2015;18(5):842-52.

Hartkopf J, Schleger F, Weiss M, Hertrich I, Kiefer-Schmidt I, Preissl H, et al. Neuromagnetic signatures of syllable processing in fetuses and infants provide no evidence for habituation. Early Hum. Dev. 2016;100:61-6.

Hepper PG, Dornan JC, Lynch C. Fetal brain function in response to maternal alcohol consumption: early evidence of damage. Alcohol. Clin. Exp. Res. 2012;36(12):2168-75.

Hepper PG, Shahidullah BS. Development of fetal hearing. Arch. Dis. Child. 1994;71(2):F81-7.

Hirai M, Watanabe S, Honda Y, Kakigi R. Developmental changes in point-light walker processing during childhood and adolescence: an event-related potential study. Neuroscience 2009;161(1):311-25.

Horst JS, Oakes LM, Madole KL. What does it look like and what can it do? Category structure influences how infants categorize. Child Dev. 2005;76(3):614-31.

Jansen-Osmann P, Heil M. Developmental aspects of parietal hemispheric asymmetry during mental rotation. Neuroreport 2007;18(2):175-8.

Jeng FC, Schnabel EA, Dickman BM, Hu J, Li X, Lin CD, et al. Early maturation of frequency-following responses to voice pitch in infants with normal hearing. Percept. Mot. Skills 2010;111(3):765-84.

Johnstone SJ, Dimoska A, Smith JL, Barry RJ, Pleffer CB, Chiswick D, et al. The development of stop-signal and Go/Nogo response inhibition in children aged 7-12 years: performance and event-related potential indices. Int. J. Psychophysiol. 2007;63(1):25-38.

Jonkman LM, Lansbergen M, Stauder JE. Developmental differences in behavioral and event-related brain responses associated with response preparation and inhibition in a go/nogo task. Psychophysiology 2003;40(5):752-61.

Kavsek M, Bornstein MH. Visual habituation and dishabituation in preterm infants: a review and meta-analysis. Res. Dev. Disabil. 2010;31(5):951-75.

Kihara M, Hogan AM, Newton CR, Garrashi HH, Neville BR, de Haan M. Auditory and visual novelty processing in normally-developing Kenyan children. Clin. Neurophysiol. 2010;121(4):564-76.

Kimura I, Kubota M, Hirose H, Yumoto M, Sakakihara Y. Children are sensitive to averted eyes at the earliest stage of gaze processing. Neuroreport 2004;15(8):1345-8.

Kirkham NZ, Slemmer JA, Richardson DC, Johnson SP. Location, location, location: development of spatiotemporal sequence learning in infancy. Child Dev. 2007;78(5):1559-71.

Kropp P, Siniatchkin M, Stephani U, Gerber WD. Migraine--evidence for a disturbance of cerebral maturation in man? Neurosci. Lett. 1999;276(3):181-4.

Kuhlman KA, Burns KA, Depp R, Sabbagha RE. Ultrasonic imaging of normal fetal response to external vibratory acoustic stimulation. Am. J. Obstet. Gynecol. 1988;158(1):47-51.

Kujawa A, Proudfit GH, Kessel EM, Dyson M, Olino T, Klein DN. Neural reactivity to monetary rewards and losses in childhood: longitudinal and concurrent associations with observed and self-reported positive emotionality. Biol. Psychol. 2015;104:41-7.

Kushnerenko E, Ceponiene R, Fellman V, Huotilainen M, Winkler I. Event-related potential correlates of sound duration: similar pattern from birth to adulthood. Neuroreport 2001;12(17):3777-81.

Lamm C, Lewis MD. Developmental change in the neurophysiological correlates of self-regulation in high- and low-emotion conditions. Dev. Neuropsychol. 2010;35(2):156-76.

Lasky RE. A developmental study on the effect of stimulus rate on the auditory evoked brain-stem response. Electroencephalogr. Clin. Neurophysiol. 1984;59(5):411-9.

Laucht M, Esser G, Schmidt MH. Contrasting infant predictors of later cognitive functioning. J. Child Psychol. Psychiatry 1994;35(4):649-62.

Lauronen L, Nevalainen P, Wikstrom H, Parkkonen L, Okada Y, Pihko E. Immaturity of somatosensory cortical processing in human newborns. Neuroimage 2006;33(1):195-203.

Leader LR, Baillie P, Martin B, Molteno C, Wynchank S. Fetal responses to vibrotactile stimulation, a possible predictor of fetal and neonatal outcome. Aust. N. Z. J. Obstet. Gynaecol. 1984;24(4):251-6.

Leader LR, Baillie P, Martin B, Vermeulen E. The assessment and significance of habituation to a repeated stimulus by the human fetus. Early Hum. Dev. 1982a;7(3):211-9.

Leader LR, Baillie P, Martin B, Vermeulen E. Fetal habituation in high-risk pregnancies. Br. J. Obstet. Gynaecol. 1982b;89(6):441-6.

Lebel C, Beaulieu C. Longitudinal development of human brain wiring continues from childhood into adulthood. J. Neurosci. 2011;31(30):10937-47.

Lebel C, Walker L, Leemans A, Phillips L, Beaulieu C. Microstructural maturation of the human brain from childhood to adulthood. Neuroimage 2008;40(3):1044-55.

Lee J, Birtles D, Wattam-Bell J, Atkinson J, Braddick O. Latency measures of pattern-reversal VEP in adults and infants: different information from transient P1 response and steady-state phase. Invest. Ophthalmol. Vis. Sci. 2012;53(3):1306-14.

Lejeune F, Audeoud F, Marcus L, Streri A, Debillon T, Gentaz E. The manual habituation and discrimination of shapes in preterm human infants from 33 to 34+6 post-conceptional age. PLoS One 2010;5(2):e9108.

Lejeune F, Berne-Audeoud F, Marcus L, Debillon T, Gentaz E. The effect of postnatal age on the early tactile manual abilities of preterm infants. Early Hum. Dev. 2014;90(5):259-64.

Lejeune F, Marcus L, Berne-Audeoud F, Streri A, Debillon T, Gentaz E. Intermanual transfer of shapes in preterm human infants from 33 to 34 + 6 weeks postconceptional age. Child Dev. 2012;83(3):794-800.

Lippe S, Martinez-Montes E, Arcand C, Lassonde M. Electrophysiological study of auditory development. Neuroscience 2009;164(3):1108-18.

Lippe S, Roy MS, Perchet C, Lassonde M. Electrophysiological markers of visuocortical development. Cereb. Cortex 2007;17(1):100-7.

Lo YH, Liang WK, Lee HW, Wang CH, Tzeng OJ, Hung DL, et al. The neural development of response inhibition in 5- and 6-year-old preschoolers: an ERP and EEG study. Dev. Neuropsychol. 2013;38(5):301-16.

Luck SJ. An introduction to the event-related potential technique MIT press. Cambridge, Ma 2005:45-64.

Luck SJ, Kappenman ES. The Oxford handbook of event-related potential components. Oxford university press; 2011.

Madison LS, Adubato SA, Madison JK, Nelson RM, Anderson JC, Erickson J, et al. Fetal response decrement: true habituation? J. Dev. Behav. Pediatr. 1986;7(1):14-20.

Mahajan Y, McArthur G. Maturation of auditory event-related potentials across adolescence. Hear. Res. 2012;294(1-2):82-94.

Mahajan Y, McArthur G. Maturation of the auditory t-complex brain response across adolescence. Int. J. Dev. Neurosci. 2013;31(1):1-10.

Marcus L, Lejeune F, Berne-Audeoud F, Gentaz E, Debillon T. Tactile sensory capacity of the preterm infant: manual perception of shape from 28 gestational weeks. Pediatrics 2012;130(1):e88-94.

Marinovic V, Hoehl S, Pauen S. Neural correlates of human-animal distinction: an ERP-study on early categorical differentiation with 4- and 7-month-old infants and adults. Neuropsychologia 2014;60:60-76.

Matuz T, Govindan RB, Preissl H, Siegel ER, Muenssinger J, Murphy P, et al. Habituation of visual evoked responses in neonates and fetuses: a MEG study. Dev. Cogn. Neurosci. 2012;2(3):303-16.

McDiarmid TA, Bernardos AC, Rankin CH. Habituation is altered in neuropsychiatric disorders-A comprehensive review with recommendations for experimental design and analysis. Neurosci. Biobehav. Rev. 2017;80:286-305.

McIntosh AR, Kovacevic N, Itier RJ. Increased brain signal variability accompanies lower behavioral variability in development. PLoS Comput. Biol. 2008;4(7):e1000106.

McIsaac H, Polich J. Comparison of infant and adult P300 from auditory stimuli. J. Exp. Child Psychol. 1992;53(2):115-28.

Mecklinger A, Brunnemann N, Kipp K. Two processes for recognition memory in children of early school age: an event-related potential study. J. Cogn. Neurosci. 2011;23(2):435-46.

Millar WS, Weir CG, Supramaniam G. The relationship between encoding, discriminative capacities and perinatal risk status in 4-12-month old infants. J. Child Psychol. Psychiatry 1991;32(3):473-88.

Milligan JE, Feaster SJ, Hogan GR, Ourth LL. Retention of habituation of the Moro response in the newborn. Dev. Med. Child Neurol. 1970;12(1):6-15.

Miltner W, Johnson R, Braun C. Auditory and somatosensory event-related potentials: II. Effects of inter-stimulus interval. Journal of Psychophysiology 1991.

Missana M, Atkinson AP, Grossmann T. Tuning the developing brain to emotional body expressions. Dev Sci 2015;18(2):243-53.

Missana M, Grossmann T. Infants' emerging sensitivity to emotional body expressions: insights from asymmetrical frontal brain activity. Dev. Psychol. 2015;51(2):151-60.

Molina M, Sann C, David M, Toure Y, Guillois B, Jouen F. Active touch in late-preterm and early-term neonates. Dev. Psychobiol. 2015;57(3):322-35.

Moore JK, Linthicum FH, Jr. The human auditory system: a timeline of development. Int. J. Audiol. 2007;46(9):460-78.

Morokuma S, Doria V, Ierullo A, Kinukawa N, Fukushima K, Nakano H, et al. Developmental change in fetal response to repeated low-intensity sound. Dev Sci 2008;11(1):47-52.

Morokuma S, Fukushima K, Kawai N, Tomonaga M, Satoh S, Nakano H. Fetal habituation correlates with functional brain development. Behav. Brain Res. 2004;153(2):459-63.

Muenssinger J, Matuz T, Schleger F, Draganova R, Weiss M, Kiefer-Schmidt I, et al. Sensitivity to Auditory Spectral Width in the Fetus and Infant - An fMEG Study. Front. Hum. Neurosci. 2013a;7:917.

Muenssinger J, Matuz T, Schleger F, Kiefer-Schmidt I, Goelz R, Wacker-Gussmann A, et al. Auditory habituation in the fetus and neonate: an fMEG study. Dev Sci 2013b;16(2):287-95.

Muenssinger J, Stingl KT, Matuz T, Binder G, Ehehalt S, Preissl H. Auditory habituation to simple tones: reduced evidence for habituation in children compared to adults. Front. Hum. Neurosci. 2013c;7:377.

Netser S, Zahar Y, Gutfreund Y. Stimulus-specific adaptation: can it be a neural correlate of behavioral habituation? J. Neurosci. 2011;31(49):17811-20.

Oakes LM, Kovack-Lesh KA, Horst JS. Two are better than one: comparison influences infants' visual recognition memory. J. Exp. Child Psychol. 2009;104(1):124-31.

Ojima S, Matsuba-Kurita H, Nakamura N, Hagiwara H. The acceleration of spoken-word processing in children's native-language acquisition: an ERP cohort study. Neuropsychologia 2011;49(5):790-9.

Ornitz EM, Lane SJ, Sugiyama T, de Traversay J. Startle modulation studies in autism. J. Autism Dev. Disord. 1993;23(4):619-37.

Paquette N, Vannasing P, Lefrancois M, Lefebvre F, Roy MS, McKerral M, et al. Neurophysiological correlates of auditory and language development: a mismatch negativity study. Dev. Neuropsychol. 2013;38(6):386-401.

Pereira DR, Cardoso S, Ferreira-Santos F, Fernandes C, Cunha-Reis C, Paiva TO, et al. Effects of inter-stimulus interval (ISI) duration on the N1 and P2 components of the auditory event-related potential. Int. J. Psychophysiol. 2014;94(3):311-8.

Perez-Gonzalez D, Malmierca MS. Adaptation in the auditory system: an overview. Front. Integr. Neurosci. 2014;8:19.

Perone S, Madole KL, Ross-Sheehy S, Carey M, Oakes LM. The relation between infants' activity with objects and attention to object appearance. Dev. Psychol. 2008;44(5):1242-8.

Pihko E, Nevalainen P, Stephen J, Okada Y, Lauronen L. Maturation of somatosensory cortical processing from birth to adulthood revealed by magnetoencephalography. Clin. Neurophysiol. 2009;120(8):1552-61.

Pincham HL, Wu C, Killikelly C, Vuillier L, Fearon RM. Social provocation modulates decision making and feedback processing: Examining the trajectory of development in adolescent participants. Dev. Cogn. Neurosci. 2015;15:58-66.

Pinel JP. Development of the Nervous System. In: Pinel JP, editor Biopsychology. Boston: Allyn and Bacon; 2003, p. 221-39.

Polich J. Updating P300: An integrative theory of P3a and P3b. Clin. Neurophysiol. 2007;118(10):2128-48.

Ponce FP, Quintana GR, Philominraj AS, Vogel EH. Habituation of the eyeblink response in humans with stimuli presented in a sequence of incremental intensity. Biol. Res. 2011;44(3):295-9.

Pons F, Albareda-Castellot B, Sebastian-Galles N. The interplay between input and initial biases: asymmetries in vowel perception during the first year of life. Child Dev. 2012;83(3):965-76.

Potter SM, Zelazo PR, Stack DM, Papageorgiou AN. Adverse effects of fetal cocaine exposure on neonatal auditory information processing. Pediatrics 2000;105(3):E40.

Preissl H, Lowery CL, Eswaran H. Fetal magnetoencephalography: current progress and trends. Exp. Neurol. 2004;190 Suppl 1:S28-36.

Putkinen V, Tervaniemi M, Saarikivi K, de Vent N, Huotilainen M. Investigating the effects of musical training on functional brain development with a novel Melodic MMN paradigm. Neurobiol. Learn. Mem. 2014a;110:8-15.

Putkinen V, Tervaniemi M, Saarikivi K, Ojala P, Huotilainen M. Enhanced development of auditory change detection in musically trained school-aged children: a longitudinal event-related potential study. Dev Sci 2014b;17(2):282-97.

Querleu D, Renard X, Versyp F, Paris-Delrue L, Crepin G. Fetal hearing. Eur. J. Obstet. Gynecol. Reprod. Biol. 1988;28(3):191-212.

Rankin CH, Abrams T, Barry RJ, Bhatnagar S, Clayton DF, Colombo J, et al. Habituation revisited: an updated and revised description of the behavioral characteristics of habituation. Neurobiol. Learn. Mem. 2009;92(2):135-8.

Richards JE. Localizing the development of covert attention in infants with scalp event-related potentials. Dev. Psychol. 2000;36(1):91-108.

Richardson C, Anderson M, Reid CL, Fox AM. Neural indicators of error processing and intraindividual variability in reaction time in 7 and 9 year-olds. Dev. Psychobiol. 2011;53(3):256-65.

Roberts TP, Khan SY, Blaskey L, Dell J, Levy SE, Zarnow DM, et al. Developmental correlation of diffusion anisotropy with auditory-evoked response. Neuroreport 2009;20(18):1586-91.

Rojas DC, Walker JR, Sheeder JL, Teale PD, Reite ML. Developmental changes in refractoriness of the neuromagnetic M100 in children. Neuroreport 1998;9(7):1543-7.

Rojas-Benjumea MA, Sauque-Poggio AM, Barriga-Paulino CI, Rodriguez-Martinez EI, Gomez CM. Development of behavioral parameters and ERPs in a novel-target visual detection paradigm in children, adolescents and young adults. Behav. Brain Funct. 2015;11:22.

Rueda MR, Posner MI, Rothbart MK, Davis-Stober CP. Development of the time course for processing conflict: an event-related potentials study with 4 year olds and adults. BMC Neurosci. 2004;5:39.

Sandman CA, Wadhwa P, Hetrick W, Porto M, Peeke HV. Human fetal heart rate dishabituation between thirty and thirty-two weeks gestation. Child Dev. 1997;68(6):1031-40.

Sann C, Streri A. Inter-manual transfer of object texture and shape in human neonates. Neuropsychologia 2008;46(2):698-703.

Santesso DL, Segalowitz SJ, Schmidt LA. Error-related electrocortical responses in 10-year-old children and young adults. Dev Sci 2006;9(5):473-81.

Schexnider VY, Bell RQ, Shebilske WL, Quinn P. Habituation of visual attention in infants with minor physical anomalies. Child Dev. 1981;52(3):812-8.

Schipke CS, Friederici AD, Oberecker R. Brain responses to case-marking violations in German preschool children. Neuroreport 2011;22(16):850-4.

Schipke CS, Knoll LJ, Friederici AD, Oberecker R. Preschool children's interpretation of object-initial sentences: neural correlates of their behavioral performance. Dev Sci 2012;15(6):762-74.

Schneider U, Giessler F, Nowak H, Logemann T, Grimm B, Haueisen J, et al. Fetal MCG and fetal MEG measurements with a 3-channel SQUID system. Neurol. Clin. Neurophysiol. 2004;2004:65.

Schneider W, Lindenberger U. Entwicklungspsychologie*.* 7 ed. Basel: Beltz; 2012.

Shafer VL, Morr ML, Kreuzer JA, Kurtzberg D. Maturation of mismatch negativity in school-age children. Ear Hear. 2000;21(3):242-51.

Shalev E, Benett MJ, Megory E, Wallace RM, Zuckerman H. Fetal habituation to repeated sound stimulation. Isr. J. Med. Sci. 1989;25(2):77-80.

Sheridan CJ, Matuz T, Draganova R, Eswaran H, Preissl H. Fetal Magnetoencephalography - Achievements and Challenges in the Study of Prenatal and Early Postnatal Brain Responses: A Review. Infant Child Dev 2010;19(1):80-93.

Sheridan CJ, Preissl H, Siegel ER, Murphy P, Ware M, Lowery CL, et al. Neonatal and fetal response decrement of evoked responses: a MEG study. Clin. Neurophysiol. 2008;119(4):796-804.

Sinyaya MS, Pinchuk D, Shelyakin AM, Tobias TV, Bogdanov OV. Compensatory plasticity of the brain under conditions of its injury. Neurosci. Behav. Physiol. 1992;22(6):543-9.

Skoe E, Krizman J, Anderson S, Kraus N. Stability and plasticity of auditory brainstem function across the lifespan. Cereb. Cortex 2015;25(6):1415-26.

Slater A, Morison V, Rose D. Habituation in the Newborn. Infant Behav. Dev. 1984;7:183-200.

Slater A, Morison V, Somers M. Orientation discrimination and cortical function in the human newborn. Perception 1988;17(5):597-602.

Sokol S, Jones K. Implicit time of pattern evoked potentials in infants: an index of maturation of spatial vision. Vision Res. 1979;19(7):747-55.

Sokolov EN. Higher nervous functions: The orienting reflex. Annu. Rev. Physiol. 1963a;25(1):545-80.

Sokolov EN. Perception and the conditioned reflex. 1963b.

Sommerville JA, Woodward AL. Pulling out the intentional structure of action: the relation between action processing and action production in infancy. Cognition 2005;95(1):1-30.

Sommerville JA, Woodward AL, Needham A. Action experience alters 3-month-old infants' perception of others' actions. Cognition 2005;96(1):B1-11.

Sörös P, Knecht S, Manemann E, Teismann I, Imai T, B. L, et al. Hemispheric asymmetries for auditory short-term habituation of tones? In: Nenonen J, Ilmoniemi RJ, Katila T, editors. Biomag 2000, Proceedings 12th International Conference on Biomagnetism. Espoo: Helsinki University of Technology; 2001, p. 47-9.

Streri A, Lemoine C, Devouche E. Development of inter-manual transfer of shape information in infancy. Dev. Psychobiol. 2008;50(1):70-6.

Streri A, Pecheux MG. Tactual habituation and discrimination of form in infancy: a comparison with vision. Child Dev. 1986;57(1):100-4.

Sussman E, Steinschneider M, Gumenyuk V, Grushko J, Lawson K. The maturation of human evoked brain potentials to sounds presented at different stimulus rates. Hear. Res. 2008;236(1-2):61-79.

Thompson RF, Spencer WA. Habituation: a model phenomenon for the study of neuronal substrates of behavior. Psychol. Rev. 1966;73(1):16-43.

Tremblay E, Vannasing P, Roy MS, Lefebvre F, Kombate D, Lassonde M, et al. Delayed early primary visual pathway development in premature infants: high density electrophysiological evidence. PLoS One 2014;9(9):e107992.

Uppal N, Foxe JJ, Butler JS, Acluche F, Molholm S. The neural dynamics of somatosensory processing and adaptation across childhood: a high-density electrical mapping study. J. Neurophysiol. 2016;115(3):1605-19.

van den Boomen C, Lamme VA, Kemner C. Parallel development of ERP and behavioural measurements of visual segmentation. Dev Sci 2014;17(1):1-10.

van der Meer AL, Svantesson M, van der Weel FR. Longitudinal study of looming in infants with high-density EEG. Dev. Neurosci. 2012;34(6):488-501.

van Heteren CF, Boekkooi PF, Jongsma HW, Nijhuis JG. Fetal learning and memory. Lancet 2000;356(9236):1169-70.

van Heteren CF, Boekkooi PF, Jongsma HW, Nijhuis JG. Fetal habituation to vibroacoustic stimulation in relation to fetal states and fetal heart rate parameters. Early Hum. Dev. 2001;61(2):135-45.

Vanvooren S, Hofmann M, Poelmans H, Ghesquiere P, Wouters J. Theta, beta and gamma rate modulations in the developing auditory system. Hear. Res. 2015;327:153-62.

Verbaten MN, Roelofs JW, Sjouw W, Slangen JL. Habituation of early and late visual ERP components and the orienting reaction: the effect of stimulus information. Int. J. Psychophysiol. 1986;3(4):287-98.

Vuillier L, Bryce D, Szucs D, Whitebread D. The Maturation of Interference Suppression and Response Inhibition: ERP Analysis of a Cued Go/Nogo Task. PLoS One 2016;11(11):e0165697.

Wakai RT, Lutter WJ, Chen M, Maier MM. On and Off magnetic auditory evoked responses in early infancy: a possible marker of brain immaturity. Clin. Neurophysiol. 2007;118(7):1480-7.

Waxer M, Morton JB. The development of future-oriented control: an electrophysiological investigation. Neuroimage 2011a;56(3):1648-54.

Waxer M, Morton JB. Multiple processes underlying dimensional change card sort performance: a developmental electrophysiological investigation. J. Cogn. Neurosci. 2011b;23(11):3267-79.

Weber P, Depoorter A, Hetzel P, Lemola S. Habituation as Parameter for Prediction of Mental Development in Healthy Preterm Infants: An Electrophysiological Pilot Study. J. Child Neurol. 2016;31(14):1591-7.

Weitzman L, Graziani L, Duhamel L. Maturation and topography of the auditory evoked response of the prematurely born infant. Electroencephalogr. Clin. Neurophysiol. 1967;23(1):82-3.

Woods DL, Elmasian R. The habituation of event-related potentials to speech sounds and tones. Electroencephalogr. Clin. Neurophysiol. 1986;65(6):447-59.

Yordanova JY, Kolev VN. Developmental changes in the alpha response system. Electroencephalogr. Clin. Neurophysiol. 1996;99(6):527-38.

Yoshimura Y, Kikuchi M, Ueno S, Shitamichi K, Remijn GB, Hiraishi H, et al. A longitudinal study of auditory evoked field and language development in young children. Neuroimage 2014;101:440-7.

Yrttiaho S, Forssman L, Kaatiala J, Leppanen JM. Developmental precursors of social brain networks: the emergence of attentional and cortical sensitivity to facial expressions in 5 to 7 months old infants. PLoS One 2014;9(6):e100811.

Zemon V, Hartmann EE, Gordon J, Prunte-Glowazki A. An electrophysiological technique for assessment of the development of spatial vision. Optom. Vis. Sci. 1997;74(9):708-16.

Tables

Table 1: Age-group classification of study populations

Age category	Age in years	Developmental stage
1	< 0	Fetal
2	0-2	Earliest childhood
3	2-6	Early childhood
4	6-12	Childhood (6-8: middle childhood; 9-12: late childhood)
5	12-18	Adolescence
6	> 18	Adulthood

Table 2: Age-related changes in event-related brain responses

Columns represent number of subjects (N), method of event-related brain response evaluation, the respective age groups and whether or not a developmental trend could be observed. Asterisks (*) indicate studies that used a longitudinal design; EEG = electroencephalography; MEG = magnetoencephalography; DTI = diffusion tensor imaging; MRI = magnetic resonance imaging; n.a. = not applicable.

Study	N	Method	Age fetal	Age 0-2	Age 2-6	Age 6-12	Age 12-18	Adults	Development trend	Kind of component investigated
(Atchley et al., 2006)	29	EEG				x	x	x	yes	endogenous
(Brinkman and Stauder, 2007)	112	EEG			x	x		x	yes	exogenous
(Brinkman and Stauder, 2008)	122	EEG			x	x		x	yes	exogenous
(Butler and Trainor, 2013)	60	EEG		x					yes	exogenous
(Byrne et al., 1999)	56	EEG			x	x	x		yes	endogenous
(Chen et al., 2010)	80	MEG/ MRI				x	x	x	yes	exogenous
(Clery et al., 2012)	24	EEG				x	x	x	yes	exogenous
(Cody and Townsend, 1973)	179	EEG		x	x			x	no	exogenous/endogenous
(Cragg et al., 2009)	56	EEG				x			yes	endogenous
(Cummings et al., 2008)	28	EEG				x	x		yes	endogenous
(Davies et al., 2004a)	124	EEG				x	x	x	yes	endogenous
(Davies et al., 2004b)	153	EEG				x	x	x	yes	endogenous
(Eswaran et al., 2004)	12	fMEG	x						yes	endogenous
(Eswaran et al., 2005)	11	fMEG	x						n.a.	Unclear
(Fabrizi et al., 2011)	46	EEG		x					yes	exogenous/endogenous

(Fox et al., 2010)	43	EEG				x	x	x	yes	exogenous
(Friedrich and Friederici, 2005)	113	EEG		x				x	yes	endogenous
(Fuchigami et al., 2009)	99	EEG			x	x	x	x	yes	endogenous
(Fujioka et al., 2006)*	12	MEG			x	x			yes	exogenous/endogenous
(Gebuis et al., 2009)	51	EEG			x	x		x	yes	endogenous
(Gorga et al., 1989)	535	EEG			x	x			yes	exogenous
(Hirai et al., 2009)	60	EEG				x	x		yes	exogenous/endogenous
(Jansen-Osmann and Heil, 2007)	72	EEG				x	x	x	yes	endogenous
(Jeng et al., 2010)	18	EEG		x				x	no	not relevant (frequency)
(Johnstone et al., 2007)	24	EEG				x	x		yes	exogenous/endogenous
(Jonkman et al., 2003)	25	EEG					x	x	yes	endogenous
(Kihara et al., 2010)	178	EEG			x	x			yes	exogenous/endogenous
(Kimura et al., 2004)	24	MEG/EEG				x	x	x	yes	exogenous
(Kushnerenko et al., 2001)	18	EEG		x				x	n.a.	endogenous
(Lamm and Lewis, 2010)	49	EEG				x	x	x	no	endogenous
(Lasky, 1984)	40	EEG		x				x	yes	exogenous
(Lauronen et al., 2006)	41	MEG		x				x	yes	exogenous
(Lee et al., 2012)	218	EEG		x	x	x		x	yes	exogenous
(Lippe et al., 2009)	40	EEG		x	x		x		yes	exogenous/endogenous
(Lippe et al., 2007)	79	EEG		x	x			x	yes	exogenous/endogenous
(Lo et al., 2013)	50	EEG			x	x			yes	endogenous
(Mahajan and McArthur, 2013)	100	EEG				x	x	x	yes	exogenous
(McIntosh et al., 2008)	79	EEG				x	x	x	yes (in PCA)	exogenous
(Mecklinger et al., 2011)	52	EEG				x		x	yes	endogenous
(Muenssinger et al., 2013a)*	62	fMEG	x	x					n.a.	unclear
(Ojima et al., 2011)*	80	EEG				x	x	x	yes	endogenous
(Paquette et al., 2013)	40	EEG			x	x	x	x	yes	exogenous
(Pihko et al., 2009)	51	MEG		x	x	x		x	yes	exogenous
(Richards, 2000)	35	EEG		x					yes	exogenous
(Richardson et al., 2011)	77	EEG				x			no	exogenous/endogenous
(Roberts et al., 2009)	26	MEG, DTI				x	x		yes	exogenous

(Rojas et al., 1998)	22	MEG				x	x		yes	exogenous
(Rueda et al., 2004)	40	EEG			x			x	yes	exogenous/endogenous
(Santesso et al., 2006)	67	EEG				x		x	yes	endogenous
(Schipke et al., 2011)	87	EEG			x	x			yes	endogenous
(Schipke et al., 2012)	109	EEG			x	x		x	yes	endogenous
(Shafer et al., 2000)	78	EEG			x	x		x	yes	endogenous
(Sussman et al., 2008)	61	EEG				x	x	x	yes	exogenous/endogenous
(van der Meer et al., 2012)*	10	EEG		x					yes	endogenous
(Wakai et al., 2007)*	17	MEG		x					yes	endogenous
(Waxer and Morton, 2011a)	80	EEG				x	x	x	yes	exogenous/endogenous
(Weitzman et al., 1967)*	25	EEG		x					yes	exogenous/endogenous
(Yordanova and Kolev, 1996)	80	EEG				x		x	yes	not relevant (frequency)
(Yoshimura et al., 2014)*	20	MEG			x	x			yes	exogenous
(Zemon et al., 1997)	40	EEG		x	x	x	x	x	yes	not relevant (frequency)
(Fuchigami et al., 1993)	175	EEG			x	x	x	x	yes	endogenous
(van den Boomen et al., 2014)	111	EEG				x	x		yes	exogenous/endogenous
(Putkinen et al., 2014b)*	133	EEG				x	x		yes	endogenous
(Cho et al., 2015)	188	EEG				x	x	x	yes	not relevant (frequency)
(Skoe et al., 2015)	586	EEG		x	x	x	x	x	yes	exogenous (brainstem)
(Putkinen et al., 2014a)	117	EEG				x	x		yes	endogenous
(Marinovic et al., 2014)	66	EEG		x				x	yes	endogenous
(Yrttiaho et al., 2014)*	125	EEG		x					n.a.	endogenous
(Missana et al., 2015)	40	EEG		x					yes	endogenous
(Tremblay et al., 2014)	72	EEG		x					yes	exogenous/endogenous (N1)
(Kujawa et al., 2015)*	559	EEG			x	x			n.a.	endogenous
(Babkirk et al., 2015)*	32	EEG			x	x			n.a. (prediction)	endogenous
(Hadley et al., 2015)*	70	EEG		x	x				n.a. (training and follow up)	exogenous/endogenous
(Cho et al., 2015)	30	MEG			x			x	yes	(M100, M170) exogenous/endogenous
(Missana and Grossmann, 2015)	40	EEG		x					yes	not relevant (frequency domain)

(Chevalier et al., 2015)	64	EEG			x	x			yes	endogenous
(Anderson et al., 2015)	28	EEG		x					yes	exogenous (brainstem)
(Vanvooren et al., 2015)	67	EEG			x			x	yes	not relevant (frequency domain)
(Chan et al., 2015)	44	EEG				x		x	yes	exogenous/endogenous (NF, P1, N1)
(Rojas-Benjumea et al., 2015)	176	EEG				x	x	x	yes	endogenous
(Pincham et al., 2015)	60	EEG				x	x		yes	endogenous
(Uppal et al., 2016)	53	EEG				x	x		yes	exogenous/endogenous
(Agyei et al., 2016)*	20	EEG		x					yes	endogenous
(Brusini et al., 2016)	45	EEG			x			x	n.a.	endogenous
(Vuillier et al., 2016)	37	EEG				x		x	yes	endogenous

Table 3: Habituation studies during child development
Columns represent number of subjects (N), method and objective of response evaluation, method of stimulation, the habituation criteria used and the respective age groups. EEG = electroencephalography; MEG = magnetoencephalography; fMEG = fetal magnetoencephalography; EMG = electromyography; EKG = electrocardiogram. (Y) = habituation criterion was met; (P) = habituation criterion was partially met; (X) = habituation criterion was not met; (n.a.) = not applicable.

Study	N	Method	Objective	Stimulation	Tested habituation criteria	Age fetal	Age 0-2	Age 2-6	Age 6-12	Age 12-18	Adults
(Muenssinger et al., 2013c)	51	MEG	brain activity	auditory	response decrement (X), stimulus specificity (X), dishabituation (X)				x		x
(Hepper et al., 2012)	78	ultrasound	behavioural	auditory	response decrement (Y)	x					
(Matuz et al., 2012)*	63	fMEG	brain activity	visual/ auditory	response decrement (P), stimulus specificity (P)	x	x				
(Pons et al., 2012)	144	visual observation	behavioural	auditory/visual	response decrement (Y), stimulus specificity (P)		x				
(Streri et al., 2008)	72	visual observation	behavioural	tactile	response decrement (Y), stimulus specificity (P)		x				
(Sann and Streri, 2008)	24	visual observation	behavioural	tactile	response decrement (Y), stimulus specificity (P)		x				
(Lejeune et al., 2012)	24	visual observation	behavioural	tactile	response decrement (Y), stimulus specificity (Y)		x				
(Lejeune et al., 2010)	24	visual observation	behavioural	tactile	response decrement (Y), stimulus specificity (Y)		x				
(Kirkham et al., 2007)	96	visual observation	behavioural	visual	response decrement (P), stimulus specificity (P)		x				
(Horst et al., 2005)	78	visual observation (videotaped)	behavioural	visual/ auditory	response decrement (P), stimulus specificity		x				
(Perone et al., 2008)	41	visual observation	behavioural	visual/ auditory	response decrement (Y), stimulus specificity (Y)		x				
(Morokuma et al., 2008)	21	ultrasound	heartrate characteristics	auditory	response decrement (Y), stimulus specificity (Y)	x					

(Marcus et al., 2012)	48	visual observation (videotaped)	behavioural	tactile	response decrement (Y) stimulus specificity (Y), dishabituation (Y)		x				
(Oakes et al., 2009)	60	visual observation	behavioural	visual	response decrement (P), stimulus specificity (Y)		x				
(Groome et al., 1995)	56	ultrasound	behavioural/ heartrate	vibroacoustic	response decrement (Y)	x					
(Groome et al., 1993)	90	ultrasound	behavioural	vibroacoustic	response decrement (Y)	x					
(van Heteren et al., 2001)	37	ultrasound	behavioural	vibroacoustic	response decrement (Y)	x					
(van Heteren et al., 2000)	19	ultrasound	behavioural	vibroacoustic	response decrement (Y)	x					
(Lejeune et al., 2014)	40	visual observation	behavioural	tactile	response decrement (Y), stimulus specificity (Y), dishabituation (P)		x				
(Streri and Pecheux, 1986)	64	visual observation	behavioural	Tactile/ visual	response decrement (Y), stimulus specificity (Y)		x				
(Kuhlman et al., 1988)	174	ultrasound	behavioural	vibroacoustic	response decrement (P)	x					
(Leader et al., 1982b)	185	ultrasound	behavioural, maternal observation	vibroacoustic	response decrement (Y)	x					
(Leader et al., 1984)	167	ultrasound	behavioural, heartrate, maternal observation	vibrotactile	response decrement (Y)	x					
(Madison et al., 1986)	39	ultrasound	behavioural, heartrate	vibrotactile	response decrement (Y)	x					
(Morokuma et al., 2004)	26	ultrasound	behavioural	vibroacoustic	response decrement (P)	x					
(Shalev et al., 1989)	103	ultrasound	behavioural	auditory	response decrement (Y)	x					
(Sheridan et al., 2008)*	37	fMEG	brain activity	visual	response decrement (P)	x	x				
(Slater et al., 1984)	52	visual observation	behavioural	visual	response decrement (Y), stimulus specificity (Y)		x				
(Adams et al., 1991)	40	visual observation	behavioural/ fixation time	visual	response decrement (Y), stimulus specificity (P)		x				
(Fiser and Aslin, 2002)	24	visual observation	behavioural/fixation time	visual/ auditory	response decrement (Y), stimulus specificity (P)		x				
(Colombo et al., 2004)	70	EKG	changes in heart rate	visual	response decrement (Y), stimulus specificity (n.a.)		x				

(Kropp et al., 1999)	320	EEG	brain activity	auditory	response decrement (X)				x	x	x
(Laucht et al., 1994)	226	visual observation	behavioural/fixation time	visual	response decrement (Y), stimulus specificity (Y)			x	x		
(McIsaac and Polich, 1992)	20	EEG	brain activity	auditory	response decrement (X)			x			x
(Millar et al., 1991)	42	visual observation	behavioural/fixation time	visual	response decrement (P), stimulus specificity (P)		x	x			
(Ornitz et al., 1993)	72	EMG	muscle activity	auditory	response decrement (Y)			x			x
(Potter et al., 2000)	50	visual observation	behavioural/head turning	auditory	response decrement (P), stimulus specificity (P)		x				
(Adams and Courage, 1995)	140	visual observation	behavioural/fixation time	visual	response decrement (Y) , stimulus specificity (Y)		x				
(Sandman et al., 1997)	84	transabdominal transducers	fetal heart rate	visual	response decrement (Y), dishabituation (Y)	x					
(Schexnider et al., 1981)	20	visual observation	behavioural/fixation time	visual	response decrement (Y), stimulus specificity (Y)		x				
(Sinyaya et al., 1992)	72	bipolar electrodes	galvanic skin response	auditory/visual	response decrement (Y)			x			x
(Sommerville and Woodward, 2005)	80	visual observation	behavioural/fixation time	visual	response decrement (P), stimulus specificity (P)		x				
(Sommerville et al., 2005)	30	visual observation	behavioural/fixation time	visual	response decrement (P), stimulus specificity (P)		x				
(Slater et al., 1988)	16	visual observation	behavioural/fixation time	visual	response decrement (Y) stimulus specificity (Y)		x				
(Leader et al., 1982a)	67	ultrasound	fetal movement	vibro-acoustic	response decrement (Y)	x					
(Bellieni et al., 2005)	22	ultrasound	fetal movement	vibro-acoustic	response decrement (Y)	x					
(Milligan et al., 1970)	37	polygraph	behavioural/heart rate	tactile/sensation of falling	response decrement (Y), spontaneous recovery (P)		x				
(Clifton et al., 1968)	100	polygraph	heartrate, respiration	auditory	response decrement (P)		x				
(Hartkopf et al., 2016)*	58	fMEG	brain activity	auditory	response decrement (X), stimulus specificity (P), dishabituation (X)	x	x				

(Weber et al., 2016)	33	EEG	brain activity	auditory	response decrement (Y), stimulus specificity (Y)		x				
(Molina et al., 2015)	64	visual observation/measurement of hand pressure	behavioural/grasp time/hand pressure frequency	tactile	response decrement (Y), stimulus specificity (P)		x				
(Muenssinger et al., 2013b)	62	fMEG	brain activity	auditory	response decrement (P), stimulus specificity (Y), dishabituation (X)	x	x				

Table 4: Neurophysiological habituation studies

Study	**Method**	**Investigated component**	**Kind of stimulation**	**Tested habituation criteria and results (fetuses and infants only)**	**Study population**
(McIsaac and Polich, 1992)	EEG	P300	auditory (blocks consisting of 10-tone sequences)	response decrement (X)	10 infants, (mean age 6.6 months, SD=0.49), 10 adults (mean age 19.8 years, SD=0.98)
(Kropp et al., 1999)	EEG	contingent negative variation (CNV)	auditory (two-stimulus reaction time go/no-go task)	response decrement (X)	86 children 8-14 years old, 27 youths 15-19 years old, 207 adults
(Sheridan et al., 2008)*	fMEG	visual event-related response	visual (light flashes)	response decrement (P)	12 newborns (age: 6-22 days), 25 fetuses (GA 29-37 weeks)
(Matuz et al., 2012)*	fMEG	visual event-related response	visual /auditory (light-flashes with tone)	response decrement (P), stimulus specificity (P)	40 fetuses (GA 30-38 weeks, 26 newborns (age 6-35 days)
(Muenssinger et al., 2013b)	fMEG	auditory event-related response	auditory (pure tones)	response decrement (P), stimulus specificity (Y), dishabituation (X)	41 fetuses (gestational age 30-39 weeks) and 22 newborns or babies (age 6-89 days)
(Muenssinger et al., 2013c)	MEG	M1 component	auditory (tones)	response decrement (P), stimulus specificity (X), dishabituation (X)	29 children (mean age 9.69 years, SD ± 0.47), 14 adults, (mean age 29.29, SD ± 3.47)
(Hartkopf et al., 2016)*	fMEG	auditory event-related response	auditory (syllables)	response decrement (X), stimulus specificity (P), dishabituation (X)	30 fetuses (GA 28-39 weeks), 28 infants (age 0-3 months)
(Weber et al., 2016)	EEG	mismatch negativity (MMN)	auditory (passive oddball paradigm)	response decrement (P), stimulus specificity (P)	17 healthy preterm infants (mean GA 27.4 weeks, range 25.0-31.3), 16 term infants (mean GA 40.3 weeks, range 37.9-41.7), assessed at term equivalent age (around 40.8 weeks of GA)

Figures

Figure 1: Typical cortical auditory-evoked potential (CAEP) with the most prominent components P1, N1, P2, N2 and P300.

Figure 2: Typical cortical visual-evoked potential (CVEP) with the most prominent components N1, P1, N2 and P300.

Figure 3: Example for an auditory habituation paradigm. The paradigm enables testing for response decrement, stimulus specificity and dishabituation by presenting spoken syllables (Hartkopf et al., 2016).

Figure 4: Flow chart of literature review process and strategy of selection of relevant publications for search *“age-related changes in event-related brain responses”.*

Figure 5: Flow chart of literature review process and strategy of selection of relevant publications for search *“habituation studies during child development”.*

Figure 6: Overview on studies from the search *“age-related changes in event-related brain responses”*. Applied methods and the investigated components of the event-related responses are displayed. *including brain-stem responses