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Modifications of Recognition Memory Processes in Preterm Children: An Event-Related Potential Study

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Prematurity may cause hippocampal compromise. Therefore, hippocampus-dependent memory processes (recollection-based retrieval) may be more impaired than hippocampus-independent processes (familiarity-based retrieval). The memory of 18 children born preterm with reduced hippocampal volumes, without neonatal complications (weeks of gestation < 34, weight < 1,600 g), and 15 controls (8–10 years) was tested using an item recognition task. While groups were equal in memory performance, dissociation was found: The event-related potential (ERP) correlate of familiarity was intact in the preterm group, whereas the correlate of recollection was attenuated. A follow-up experiment ruled out that this was due to general cognitive deficits. Furthermore, gestational age correlated with the ERP index of recollection. Thus, recognition memory in preterm children may be characterized by a compensation of attenuated recollection by familiarity.

Children born preterm are at high risk for later cognitive impairment (Vohr, 2010) due to brain injuries or uncompleted intrauterine brain maturation (Kinney, 2009). Studies examining declarative memory in preterm children have come to inconsistent results ranging from clear memory deficits (Isaacs et al., 2000; Narberhaus et al., 2007) to normal performance (Hoff Esbjørn, Hansen, Greisen, & Mortensen, 2006). Declarative memory is one of two types of long-term memory and refers to memories for facts and events that can be consciously experienced (Baddeley, Eysenck, & Anderson, 2009). In contrast to procedural memories, that is, not consciously assessable memories such as skills or priming, declarative memories critically depend on the integrity of the hippocampus (Hc) and surrounding medial temporal lobe (MTL) structures and by this are vulnerable to MTL damage (Brown & Aggleton, 2001; Squire & Zola, 1996). It is likely that specific memory processes rather than declarative memory per se are affected by prematurity and this may have led to the aforementioned mixed pattern of results. This assumption is in line with data showing that prematurity has adverse effects on some MTL regions, as for example, the Hc, to a disproportionate degree (Isaacs et al., 2000; Peterson et al., 2000). A consequence of these region-specific abnormalities could be that declarative memory processes that rely on the integrity of the Hc could be selectively impaired (cf. Rose, Feldman, Jankowski, & Van Rossem, 2011). In this study, we explored this assumption using event-related potential (ERP) measures of recognition memory subprocesses.

Recognition memory, the judgments of the prior occurrence of an event, is a subcategory of declara-

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tive memory. In a standard recognition memory test, participants are presented with previously studied items that are intermixed with new items and are required to classify these items as previously studied (old) or new. Dual-process models of recognition memory assume that recognition memory of items we have encountered before can be based on two different subprocesses: familiarity and recollection (see Yonelinas, 2002; Yonelinas, Aly, Wang, & Koen, 2010, for reviews). Familiarity reflects a fast-acting process that assesses the strength of a memory representation without retrieving contextual information. Recollection reflects the retrieval of detailed memories from a prior study episode. In an item recognition test, it is assumed that participants respond "old" when they can recollect specific information about a study event or when they judge the item to be sufficiently familiar.

Notably, several ERP studies with adults have shown that recollection and familiarity exhibit distinct electrophysiological correlates. Even though there is no one-to-one mapping between an ERP effect and an underlying memory process, ERPs are regarded as effective to dissociate both subprocesses of recognition memory as shown, for example, by Addante, Ranganath, Olichney, and Yonelinas (2012), Mecklinger (2006), and Rugg and Curran (2007). These studies indicate that an early ERP old/new effect at frontal and central recording sites, that is, more positive going ERPs for correctly classified old than new items, can be considered as the ERP correlate of familiarity. This effect is referred to as the *midfrontal old/new effect*. A later old/new effect at parietal recordings, referred to as the *parietal old/new effect*, can be taken as the correlate of recollection (Friedman & Johnson, 2000; Jäger, Mecklinger, & Kipp, 2006; Rugg & Curran, 2007; but see Paller, Voss, & Boehm, 2007, for a different view).

It is important to note, that spatially and temporally dissociable ERP measures for familiarity and recollection in the majority of the aforementioned studies have been reported for adults only. ERP studies with children of early school age reveal a mixed pattern of results regarding the ERP measures of familiarity and recollection. The parietal old/new effect can be reliably recorded from the age of 6–8 years (Cycowicz, Friedman, & Duff, 2003; Czernochowski, Mecklinger, Johansson, & Brinkmann, 2005) suggesting that recollection is available for recognition judgments at this age. Conversely, the midfrontal old/new effect is less consistently found in ERP studies on memory development (see Mecklinger, Sprondel, & Kipp, in press, for a review). Notably, ERP studies not reporting the midfrontal old/new effect in early school age did either not explicitly explore the development of familiarity and recollection from a dual-process point of view or used operational definitions that were not sensitive to explore ERP correlates of familiarity and recollection (Czernochowski, Mecklinger, & Johansson, 2009; van Strien, Glimmerveen, Martens, & de Bruin, 2009).

In a recent developmental ERP study, we took into account that familiarity is faster than recollection and explored ERP correlates of familiarity and recollection under speeded and nonspeeded test conditions (Mecklinger, Brunnemann, & Kipp, 2011). Supporting the view that under speeded test conditions, recognition decisions are mainly based on a fast familiarity process (Boldini, Russo, & Avons, 2004; Hintzman & Caulton, 1997), there was a reliable midfrontal old/new effect but no parietal old/new effect in the speeded condition. Conversely, if the time allowed to make a response was not limited, only the parietal old/new effect was present (Mecklinger et al., 2011). As both effects were reliably found for adults *and* children and also very similar across age groups, the results also imply that ERP measures of familiarity and recollection can be used to explore recognition memory processes in this age range.

Studies with neurological patients and neuroimaging studies with healthy adults have demonstrated that distinctive MTL regions contribute to both subprocesses of recognition memory (Quamme, Yonelinas, & Norman, 2007; Vargha-Khadem et al., 1997). Familiarity seems to depend largely on anterior MTL regions, centered around perirhinal and entorhinal cortices. Recollection is more reliant on the Hc and parahippocampal cortices (Bowles et al., 2007; Brown & Aggleton, 2001; Yonelinas et al., 2010). In accordance with the dual-process framework, patients suffering from an isolated Hc injury show an attenuated ERP correlate of recollection while the ERP correlate of familiarity-based retrieval remains intact (Addante et al., 2012; Düzel, Vargha-Khadem, Heinze, & Mishkin, 2001). The high relevance of hippocampal integrity for the ERP correlate of recollection is also revealed by a recent memory study with elderly participants (Schiltz et al., 2006). Recognition memory performance was lower for elderly than for young subjects and the magnitude of the left parietal old/new effects of the elderly subjects was correlated with hippocampal diffusion, a regionally selective measure of structural integrity of the Hc. In contrast, no correlations between structural measures of the Hc and the ERP correlate of familiarity were obtained in the aforementioned study.

The finding that structural abnormalities of the Hc might lead to deficits in recollection-based retrieval while leaving familiarity intact has important implications for children born preterm. In fact, several MRI studies have reported reduced Hc volumes in preterm children even when controlling for total brain volume (e.g., Giménez et al., 2005; Isaacs et al., 2000; Nosarti et al., 2002). The cause of this injury is usually seen in hypoxic-ischemic or inflammatory insults that often co-occur with premature birth. However, there is some evidence that Hc volume reductions are not confined to acute, hemorrhagic, or hypoxic lesions but perhaps of subtler, not measurable and more chronic disturbances in regional perfusion (Peterson et al., 2000). Notably, if prematurity bears the risk of compromising the structural integrity of the Hc to a larger extent than other brain regions, then preterm children should show selective impairments in recollection-based retrieval and preserved familiarity-based retrieval (cf. Rose et al., 2011).

This study aimed at directly testing the hypothesis of selectively impaired recollective processing in preterm children by examining ERP measures of familiarity and recollection in a recognition memory task. ERP measures have two major advantages over neuropsychological or behavioral measures of memory processes in clinical populations. First, as objective physiological measures of familiarity and recollection, ERP measures do not depend on the subjects' reports of memory as, for example, the Remember/Know procedure (e.g., Tulving, 1985) or confidence judgments (e.g., Yonelinas, 2002). Second, in situations in which memory decisions are supported by both recollection and familiarity as in item recognition memory tasks, a selective impairment of one specific subprocess might be compensable by another subprocess. It is conceivable that in these situations, recollection impairments can occur without direct behavioral manifestations of memory impairments and that purely behavioral measures would not be sensitive enough to detect impairments of either process. To illustrate this point, Addante et al. (2012) used ERPs and behavioral measures to explore item and source memory impairments in amnesic patients with circumscribed Hc lesions. Even though the patients did not show a parietal old/new effect, the ERP correlate of recollection, their item memory was well above chance, suggesting that preserved familiarity was used for recognition judgments (see Mecklinger, von Cramon, & Matthes-von Cramon, 1998, for a similar finding).

The children born preterm and the control children of this study were 8–10 years old. Both groups (preterms: n = 18; controls: n = 15) were subgroups of the children examined in the volumetric study by Brunnemann et al. (2013). The overlap of subjects tested in both studies was 14 children born preterm and 13 control children. Brunnemann et al. explored school-age children born preterm without hypoxic-ischemic injury and found their Hc volumes to be reduced by 12% relative to age-matched controls while neuropsychological tests of declarative memory did not differ between groups (Brunnemann et al., 2013). In addition, Hc volumes of the control group were positively correlated with recognition memory performance and neuropsychological tests of visual long-term memory. Consistent with the view that posterior parts of the Hc are highly relevant for memory retrieval (Daselaar, Fleck, Dobbins, Madden, & Cabeza, 2006; Greicius et al., 2003), the latter correlations were significant only when the posterior two thirds of the Hc volumes were taken into account. A possible explanation for the intact memory performance in the preterm children could be that they used an altered memory network with reduced reliance on hippocampal structures and a stronger recruitment of extrahippocampal MTL structures that may have compensated for impaired Hc processing.

In this study, we used a response deadline procedure to explore the ERP correlates of familiarity and recollection as in the Mecklinger et al. (2011) study. The control group presented here consists of a subgroup of the children in the Mecklinger et al. study (15 of 18; 3 children were excluded because they were born small for gestational age [GA], see the Method section for details). As described above, in the speeded condition in which familiarity is fostered, the children in the latter study showed a reliable midfrontal old/new effect but no parietal old/new effect. In the nonspeeded condition, in which recollective processing is fostered, a parietal but no midfrontal effect was obtained for the control children. To the extent to which Hc volumes are significantly reduced in the preterm group, we expected their ERP correlate of recollection to be attenuated relative to the control group. The early midfrontal old/new effects should not differ between the preterm and the control groups.

Study 1

Method

Participants

Twenty-five preterm children born at Saarland University Hospital in Homburg, Germany, were tested. One child was excluded from our analyses because it was born small for GA (i.e., birth weight [BW] ≤ 10th percentile according to Voigt's National Growth Charts; Voigt, Schneider, & Jährig, 1996). Due to movement artifacts in the electroencephalography (EEG) session, 6 additional children had to be excluded from analyses. The remaining group consisted of 18 children (age = 8;01–10;10 years, *M* = 9.17 years) with a GA of 26 to 33 weeks (*M* = 30.03) and a BW of 880 to 1,540 g (*M* = 1,252 g). For determining the socioeconomic status (SES), we used the International Socio-Economic Index of Occupational Status (Ganzeboom, de Graaf, Treiman, & de Leeuw, 1992), which involves a weighting of the standardized education and income on basis of occupations scoring between 10 and 90. The SES of the preterm children varied between 31 and 77 (*M* = 54.56). Exclusion criteria were diabetes of the mother, serious neonatal complications like hypoxic-ischemic insults, inflammation, or cerebral hemorrhage of degree 2 or higher. One child had an insufficient number of trials (< 17) in the nonspeeded response condition due to EEG artifacts. Therefore, we excluded this child from the ERP analyses of the nonspeeded condition (*N* = 17) but included the child for the speeded condition and the analyses of behavioral results (*N* = 18). The MR images of 4 children who took part in the ERP session could not be analyzed because of movement artifacts or technical failures. Hence, the Hc volumetric analyses reported here are based on the data of 14 preterm children.

The control group was composed of 26 full-term children. Three children had to be excluded because they were born small for GA (BW ≤ 10th percentile; Voigt et al., 1996). Another 8 children had to be excluded from our analyses due to movement artifacts. All statistical analyses are based on 15 control children (age = 8;00–10;11, *M* = 8.98) with GAs of 39 to 42 weeks (*M* = 40.00) and BWs of 3,050–4,400 g (*M* = 3,545). The SES varied between 37 and 88 (*M* = 65.80). None of the control children had a diabetic mother or experienced prenatal or postnatal health problems. The ERP results of this control group have been reported elsewhere with an extended sample (*n* = 18; Mecklinger et al., 2011). The MR images of two children of the control group who took part in the ERP session could not be analyzed due to movement artifacts or technical failures. Therefore, the following Hc volumetric analyses are based on the data of 13 children.

Both groups were matched with respect to age, $t(31) = 0.69$, $p = .50$. No child was on regular medication, suffered from neurodevelopmental abnormalities, had developed epilepsy, or showed noticeable abnormalities in the EEG. Their native language was German. Both groups did not differ with regard to working memory measured with the forward and backward digit span test, a subtest of HAWIK–R (Hamburg-Wechsler-Intelligenztest für Kinder-Revision [German version of the Wechsler Intelligence Scale for Children], Tewes, 1985), preterm group = 9.39, control group = 10.53, $t(31) = 1.17$, $p = .25$. However, both groups differed in SES: preterm group = 54.56, control group = 65.80, $t(31) = 2.25$, $p < .05$.

All children were paid for participation. Informed consent was obtained from the parents. Further details about both groups are given in Table 1. The overlap of children also tested by Brunnemann et al. (2013) consisted of 13 control children and 14 preterm children. This study had been approved by the Ethics Committee of the Saarland Medical Association (ID No. 151/07).

Procedure

The children performed two sessions: (a) structural MR imaging (duration ½ hr) and (b) a recognition memory experiment with a *speeded* and a *nonspeeded condition* with EEG recording (2½ hr, including setting up the EEG cap).

MR imaging and Hc volumetry. Structural MR imaging was performed on a 1.5-T Siemens Sonata scanner (A3DMP-RAGE sequence with a repetition time of 1,900 ms; echotime, 3.93 ms; inversion time, 1,100 ms). Cerebral volume (CV) and Hc volumes were measured manually. Detailed information about the magnetic resonance protocol and volumetric analyses can be found in Brunnemann et al. (2013). Each Hc volume was normalized for individual variation in total intracranial volume. Total intracranial volume is most frequently used to correct for intersubject variation in head size (Geuze, Vermetten, & Bremner, 2004). For normalization, we used the covariance method described by Jack et al. (1989) that adjusts the observed volume of a region of interest by an amount proportional to the difference between an individual's observed total CV and the mean CV volume for all subjects of the observed group. The method is known to reduce

Table 1
Demographic Data for Preterm and Control Group

	Preterm group	Control group	Statistics (*p*)
N	18	15	
Male/female	9/9	8/7	.73
Right/left-handed	16/2	15/0	.49
Age at assessment	9.17 (8;01–10;10)	8.98 (8;00–10;11)	.50
Gestational age (in weeks)	30.03 (26–33)	40.00 (39–42)	< .001
Birth weight (in g)	1,252.22 (880–1,540)	3,545.33 (3,050–4,400)	< .001
Apgar score			
At 1 min	6.28 (2–9)	9.53 (8–10)	< .001
At 5 min	7.33 (2–10)	9.93 (9–10)	< .001
Days of mechanical ventilation	4.94 (0–12)	—	
N	15	13	
Hc volume (in cm^3)			
Left Hc	2.51 (2.07–3.12)	2.76 (2.11–3.11)	< .05
Right Hc	2.70 (2.32–2.98)	2.93 (2.29–3.57)	.06
M	2.60 (2.29–2.97)	2.84 (2.20–3.27)	< .05
Left posterior part Hc	1.52 (1.14–2.00)	1.69 (1.28–1.93)	< .05
Right posterior part Hc	1.69 (1.47–2.05)	1.86 (1.48–2.44)	.06
M	1.60 (1.42–1.89)	1.78 (1.54–2.17)	< .05

Note. The *p* values refer to χ^2 (gender and handedness) and *t* tests for independent samples (all other variables). Hc = hippocampus.

variance compared to just dividing Hc volume by CV (Jack et al., 1989).

As memory retrieval seems to be subserved mainly by the posterior two thirds of the Hc (Greicius et al., 2003), the total slice number of each Hc was divided into thirds along the anterior–posterior axis. The middle and posterior parts of each Hc were summed (for left and right Hc, respectively) to allow additional analyses of correlations between posterior Hc volumes and memory performance (see Greicius et al., 2003, for a similar procedure).

Design of the recognition memory experiment. The experiment consisted of two study-test blocks, the first with a *speeded* and the second with a *nonspeeded* response condition. As revealed by extensive pretesting, it was more difficult for participants to switch from nonspeeded to speeded response requirements than the other way round. Therefore, the study-test cycle for the speeded condition was always performed first. In both study phases the children saw 60 colored pictures of everyday objects (Rossion & Pourtois, 2004) sequentially on a computer screen. The children had to memorize the items and make an indoor/outdoor decision by pressing a corresponding key. Each study trial was composed of a fixation cross (400 ms), the picture (1,000 ms), and an intertrial interval (1,400 ms). During a 1-min retention interval, the children had to perform an easy arithmetic task. In the following test phase, the children saw 60 old items mixed with 60 new items and had to make an old/new judgment for each item by pressing a corresponding key (the assignment of keys to old/new status was balanced across subjects). Each trial started with a fixation cross (500 ms) and the picture presentation (1,050 ms). In the speeded block, the children had to give their old/new responses during the 1,050-ms picture presentation period. This particular deadline was selected on the basis of prior studies showing that for adults the contribution of recollection to recognition judgments can be substantially reduced with deadlines between 500 and 1,000 ms. The current control group data were collected in a group design in which the memory performance of children and adults was contrasted (Mecklinger et al., 2011). For adults, a deadline of 750 ms was selected. Since pilot studies revealed that children in this age range take about 300 ms longer than adults to give recognition judgments, the deadline for all children groups was setup 750 + 300 = 1,050 ms. Too slow responses were notified by a brief sound. In the nonspeeded block, the children had unlimited response time. In both blocks, the children received visual feedback about response accuracy after each old/new decision. After an intertrial interval of 2,000 ms, the next trial started. Each experimental block was preceded by a short practice block. To control the effects of fatigue, the duration of both study-test blocks was around 16 min, and a break (duration = 5 min) was given after the first block.

EEG Recording

EEG was recorded with 27 Ag/AgCl-electrodes embedded in a cap based on an extended version of the international 10–20 system (Jasper, 1985). The sampling rate was 250 Hz. AFz was the ground electrode. Electroencephalography was referenced to the left mastoid and re-referenced offline to linked mastoids. Electrooculogram was recorded from electrodes placed above and below the right eye and at the outer canthi of both eyes. Electrode impedance was kept below 5 kΩ. A low-pass filter at 30 Hz and a high-pass filter at 0.2 Hz were engaged.

Statistical Analyses

Behavioral data. Trials with response times below 200 ms and with time-out responses in the speeded block were discarded. Memory accuracy was analyzed by means of the discrimination index (Pr; Hits − False Alarms; Snodgrass & Corwin, 1988). Response bias (Br), which indicates the probability of saying "old" when in an uncertain state, was defined as False Alarms/(1 − Pr) (Snodgrass & Corwin, 1988). Between-group differences were assessed by means of analyses of variance (ANOVAs) with the factors group (preterm vs. control) and block (speeded vs. nonspeeded).

ERP data. The EEG was segmented into epochs of 1,200 ms including a 200-ms prestimulus baseline, respectively. Before averaging, trials with excessive artifacts were rejected and eye movement artifacts were corrected (Gratton, Coles, & Donchin, 1983). ERP averages were calculated for hits and correct rejection (CR) at nine electrodes along the anterior–posterior and laterality axis (F3, FZ, F4, C3, CZ, C4, P3, PZ, P4). For preterm children, the mean trial numbers (range) in the speeded condition were as follows: hits = 26 (19–35), CR = 25 (19–36); and in the nonspeeded condition: hits = 27 (17–38), CR = 28 (18–40). The equivalent values for the control children in the speeded condition were as follows: hits = 29 (19–40), CR = 29 (19–45); and in the nonspeeded condition: hits = 29 (18–37), CR = 29 (20–42). As in the Mecklinger et al. (2011) study, the midfrontal and parietal old/new effects were measured as mean amplitudes in an early (300–450 ms) and late time window (600–750 ms), respectively. Initial ANOVAs were calculated separately for each block (speeded vs. nonspeeded) with the factors group (preterms, controls), time window (early, late), item status (hits, CR), anterior–posterior (frontal, central, parietal), and laterality (left, middle, right). Interactions involving one of the factors group or time window were then analyzed with specific follow-up tests. Whenever appropriate, Greenhouse–Geisser corrections for nonsphericity were used, and corrected p values are reported together with uncorrected degrees of freedom. For the ERP data, only effects that include the factor item status are reported. As both child groups differed with respect to the SES, we controlled for confounding influences of this factor on memory performance and ERP old/new effects by calculating additional analyses of covariance (ANCOVAs) with SES as a covariate in case of group differences in any of the analyses. Since in all the analyses, the ANCOVA results did not differ from the ANOVA results, we report the initial ANOVAs only.

Correlational analyses. Based on the assumption that the risk of brain damage increases with decreasing GA (e.g., white matter damage, Dammann, Leviton, Gappa, & Dammann, 2005; metabolic changes like absolute metabolite concentrations or Creatine and myo-inositol, Giménez et al., 2008), we first tested whether the ERP correlates of familiarity and recollection are also modulated by the degree of prematurity. We correlated GA (in days) with both ERP measures (bivariate Spearman's correlation): familiarity—magnitude of the early old/new (old minus new difference) effect at Cz (where the effect was largest) in the speeded condition; recollection—magnitude of the late old/new effect (old minus new difference) at Pz in the nonspeeded condition. As the range of GA in the control group was too small to allow adequate correlation analyses, (preterm group = 187–234 days, control group = 273–294 days), these correlation analyses were conducted for the preterm group only. Second, we tested correlations between posterior Hc volumes (mean of the right and left posterior two thirds of the Hc volumes) and the just defined ERP indices of familiarity and recollection for both child groups, separately. We controlled for confounding influences of age and SES on the size of these correlations by calculating additional partial correlations with age and SES as covariates. Since the partial correlation results did not differ from the initial correlations, only the results of the initial analyses will be reported.

Results

Hc Volumetry

As expected and consistent with the analysis conducted with the larger sample in the Brunnemann et al. (2013) study, the preterm group showed a smaller normalized volume than the control group for the left Hc, $t(26) = 2.36$, $p < .05$; preterm group = 2.51 cm^3; control group = 2.76 cm^3; and a marginally significant smaller volume for the right Hc, $t(26) = 1.95$, $p = .06$; preterm group = 2.70 cm^3; control group = 2.93 cm^3. Highly similar results were obtained for the posterior two thirds of the Hc volumes: left posterior Hc, $t(26) = 2.29$, $p < .05$; preterm group = 1.52 cm^3; control group = 1.69 cm^3; and for the right posterior Hc, $t(26) = 2.00$, $p = .06$; preterm group = 1.69 cm^3; control group = 1.86 cm^3.

Recognition Memory

Behavioral results. An overview of the behavioral results is given in Table 2. The number of time-out responses in the speeded block was low and did not differ between groups (preterm group = .89, range = 0–4; control group = .80, range = 0–3). Memory accuracy (Pr) was higher in the nonspeeded than in the speeded block, main effect of block $F(1, 31) = 24.70$, $p < .001$, $\eta_p^2 = .443$. No effects involving the factor group were found for Pr, indicating that memory accuracy did not differ between the two groups in either response condition. For response bias no effects of group and block were obtained. Analyzing response times with a three-factor ANOVA (group, block, and item status) revealed only the expected main effect of block, $F(1, 31) = 64.62$, $p < .001$, $\eta_p^2 = .676$, indicating that both groups took more time to make their decisions in the nonspeeded than in the speeded block. In sum, both child groups did not differ with respect to recognition accuracy and speed.

Table 2
Mean Reaction Times (ms) and Standard Deviations for Correctly Recognized Old and New Pictures, Probabilities of Hits and CRs, Pr and Br for Each Group

	Preterm group		Control group	
	Speeded	Nonspeeded	Speeded	Nonspeeded
Proportion hits	0.72 (0.02)	0.80 (0.03)	0.72 (0.03)	0.84 (0.03)
Proportion CRs	0.73 (0.03)	0.83 (0.03)	0.81 (0.02)	0.88 (0.02)
Pr	0.45 (0.05)	0.63 (0.06)	0.53 (0.04)	0.71 (0.04)
Br	0.46 (0.03)	0.45 (0.03)	0.43 (0.04)	0.37 (0.04)
RT hits	716 (11)	1,128 (72)	737 (16)	1,202 (114)
RT CR	724 (14)	1,185 (79)	740 (11)	1,248 (73)

Note. M = mean; SD = standard deviation; CRs = correct rejections; Pr = discrimination index; Br = Bias.

ERP results. Figure 1 shows (A) the grand mean ERP waveforms and (B) the scalp topographies of the mean amplitude measures for the early and late ERP effects separately for each child group and response condition.

For the *speeded condition* an overall ANOVA with the factors group, time window, item status, anterior–posterior, and laterality revealed a main effect of item status, $F(1, 31) = 6.17$, $p < .05$, $\eta_p^2 = .166$; interactions between item status and time window, $F(1, 31) = 8.43$, $p < .01$, $\eta_p^2 = .214$; item status and laterality, $F(2, 62) = 3.93$, $p < .05$, $\eta_p^2 = .112$; and item status, anterior–posterior and laterality, $F(4, 124) = 2.45$, $p = .05$, $\eta_p^2 = .073$. No interactions involving the group and item status factors were found. This pattern of results indicates that old/new effects (item status) were similar in both child groups but differed as a function of time window and recording site. To further explore these effects, time–window–specific analyses were conducted. In the early time window, we found a main effect of item status, $F(1, 31) = 14.49$, $p < .01$, $\eta_p^2 = .319$, and an interaction between item status and laterality, $F(2, 62) = 4.28$, $p < .05$, $\eta_p^2 = .121$. The interaction reflects the fact that the early old/new effect was larger at midline electrodes ($\eta_p^2 = .39$) than at left- ($\eta_p^2 = .31$) and right-sided ($\eta_p^2 = .14$) electrodes. Consistent with our predictions, in the late time window, tapping into the ERP correlate of recollection, neither an item status effect nor any interaction with this factor occurred. These results suggest that both child groups mainly relied on familiarity and much less so on recollection when making recognition decisions in the speeded condition.

In the *nonspeeded condition,* the five-way ANOVA revealed a two-way interaction between item status and anterior–posterior, $F(2, 60) = 4.62$, $p < .05$, $\eta_p^2 = .133$, and a four-way interaction between item status, group, time window, and anterior–posterior, $F(2, 60) = 3.99$, $p < .05$, $\eta_p^2 = .117$. This indicates that old/new effects and their topographic distributions differed as a function of group and time window. Thus, both time windows were analyzed separately, for the preterm and for the control group, respectively. The preterm group did not show a significant item status effect or any interactions involving this factor in neither time window

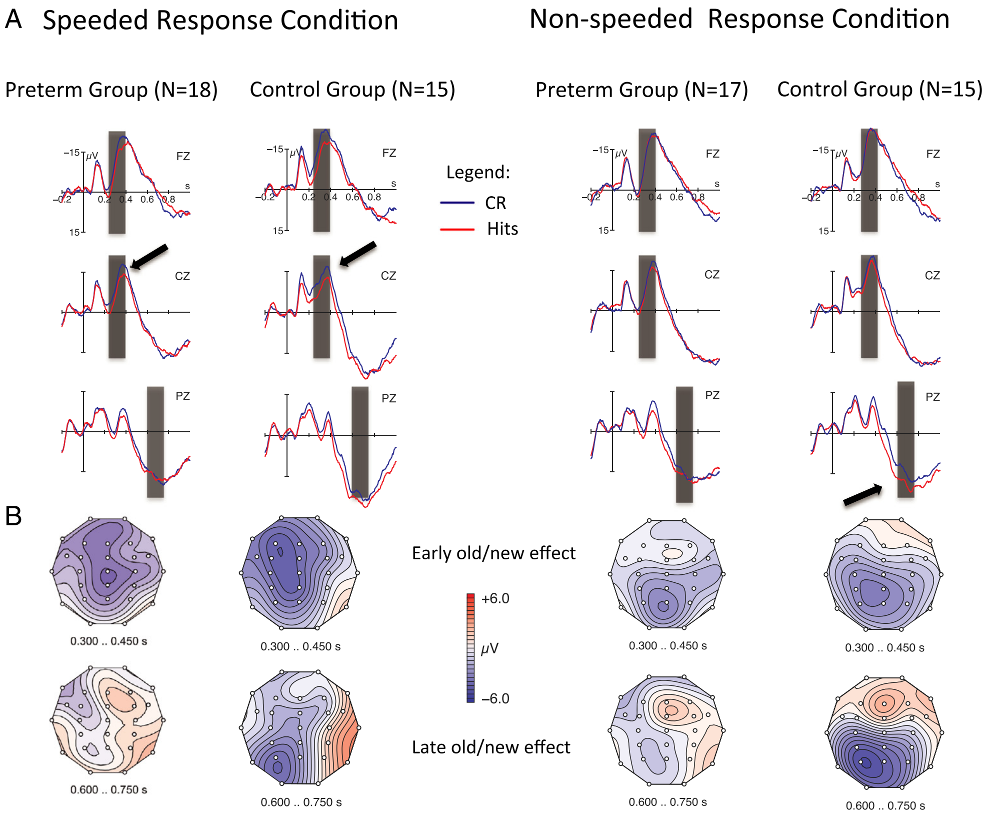

Figure 1. (A) Grand mean event-related potential (ERP) waveforms and (B) scalp topographies of the mean amplitude measures for early and late ERP effects separately for each response condition and child group. The arrows denote the early (familiarity) effects in both groups in the speeded condition and the late (recollection) effect in the nonspeeded condition which was present for the control group only. CR = correct rejection.

(all *ps* > .25). The control group revealed neither a main effect of item status nor any effects involving this factor in the early time window (all *ps* > .22), but there was a significant interaction between item status and anterior–posterior, $F(2, 28) = 6.30$, $p < .01$, $\eta_p^2 = .310$, in the late time window. This interaction is due to an item status effect that was significant only at parietal locations, $F(1, 14) = 9.50$, $p < .01$, $\eta_p^2 = .404$.

To summarize, in the speeded condition both child groups showed highly similar ERP correlates of familiarity and no ERP correlate of recollection. A group difference occurred in the nonspeeded condition: While the control group showed the putative ERP correlate of recollection, no effects of item status were obtained for the preterm group.

Correlational Analyses

The results of the correlation analyses between GA and the ERP indices of familiarity and recollection are illustrated in Figure 2. Notably, there was a positive correlation between GA and the ERP estimate of recollection (Spearman-Rho: $r = .64$, $p < .01$); that is, the greater the GA, the larger the late parietal old/new effect (see Figure 2). The corresponding correlation between GA and the ERP estimate of familiarity was negative and marginally significant (Spearman-Rho: $r = -.46$, $p = .06$); that is, the smaller the GA, the larger the early old/new effect tended to be.

For preterms, the correlations between the posterior part of the Hc and the ERP measures of recollection and familiarity revealed a correlation neither with recollection measure ($r = -.02$, $p = .95$) nor with the familiarity measure ($r = .35$, $p = .21$). For controls, the corresponding correlations between the posterior Hc and both ERP measures were also not significant (recollection: $r = .10$, $p = .73$; familiarity: $r = -.20$, $p = .51$).

Discussion

The aim of the study was to test whether preterm children show a selective impairment of memory processes that rely on the integrity of

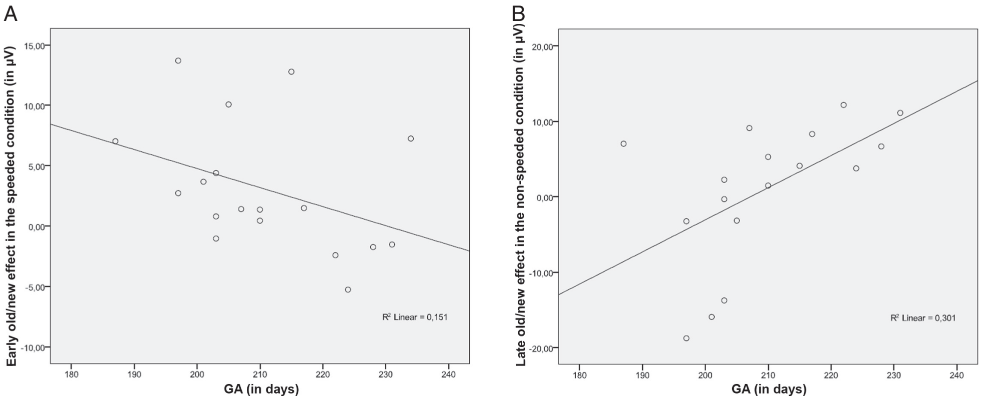

Figure 2. Correlation of gestational age (GA) in days with (A) the size of the event-related potential (ERP) estimate of familiarity (early old/new effect [correct old minus new responses] at Cz in the speeded condition) and with (B) the size of the ERP estimate of recollection (late old/new effect [correct old minus new responses] at Pz in the nonspeeded condition) for the preterm group. Note that this analysis was based on N = 18 (speeded, familiarity analysis) and N = 17 (nonspeeded, recollection analysis). See the Method section for details.

the Hc due to an increased risk of Hc compromise. In support of this view, the parietal old/new effect, the ERP correlate of recollection-based retrieval that has been shown to rely on the integrity of the Hc (Addante et al., 2012; Düzel et al., 2001) was attenuated in the preterm group compared to the control group. In contrast, the ERP correlate of familiarity-based retrieval, presumably generated by extrahippocampal, medial temporal regions was intact. In addition, we could verify a double-sided reduction in the Hc volume in the current group of preterm children relative to controls. Both child groups were subgroups of the sample examined in the larger volumetric analysis of Brunnemann et al. (2013).

Notably, even though the preterm group showed an attenuated ERP correlate of recollection in the nonspeeded condition, memory performance in this group was equivalent to the control group. Similar dissociations between attenuated ERP measures and unimpaired memory performance have been reported in other patient studies (Addante et al., 2012; Mecklinger et al., 1998), suggesting that behavioral measures of memory performance are not sensitive enough to detect the highly specific and subtle memory modifications in preterm children (cf. Kipp, Mecklinger, Becker, Reith, & Gortner, 2010). Alternatively, this dissociation between relatively high item recognition memory and an attenuated ERP measure of recollection could indicate the presence of a “repair” mechanism that may have compensated for impaired recollection. In fact, a second correlation analysis revealed that with decreasing GA the ERP correlate of familiarity in the speeded condition tends to increase. It is tempting to speculate that children with low GA give more weight to a strength-like and context-free familiarity signal when making recognition judgments. By this, enhanced familiarity in early-born children may compensate for reduced recollection. Notably, the view that familiarity compensates for deficits in Hc-based recollection, tentatively supported by a marginally significant correlation in this study, has recently also been proposed for old adults on the basis of behavioral (Bastin & Van der Linden, 2003) and brain imaging (Daselaar et al., 2006) data. Taken together, this interpretation is preliminary and needs to be supported by further studies that provide more direct evidence for compensation, as, for example, by showing that the compensatory activity is positively correlated with memory performance (Friedman, 2013).

An objection against the view that the preterm group showed a selectively reduced ERP correlate of recollection while the correlate of familiarity remained intact could be that both memory processes differ in difficulty and that by this the group differences in the more demanding recollection processes cannot unequivocally be related to a selective reduction in recollection. This objection was tested in a follow-up experiment.

Follow-Up Study

As recollection is more effortful and resource demanding than familiarity it could be argued that a task-resource artifact has produced the dissociation between impaired recollection and intact familiarity in preterm children. It is known that subtle impairments of brain functioning have larger effects on tasks or cognitive functions that are more difficult and require more cognitive resources than easy tasks or functions (Shallice, 1988). This means that a general but small cognitive deficit in the preterm group could have led to a measurable deficit in the more demanding (recollection-based) but not in the less demanding (familiarity-based) retrieval situation. To test this possibility, we conducted a follow-up continuous recognition memory experiment, in which the resource demands of memory retrieval were operationalized by means of a repetition lag manipulation. If the task-resource artifact account holds true, preterm children should perform worse than control children in the high-demanding condition (long repetition lag) and should show no, or a much smaller, impairment in the low-demanding condition (short lag).

Study 2

Method

Participants

This study was conducted several weeks after the ERP session of the first study and 14 of the initial 18 preterm children and 12 of the 15 control children of the ERP study could be recruited. For both groups, there were no significant differences regarding age, GA, BW, and SES compared to the initial samples. The children were paid for participation and informed consent was obtained from the parents.

Procedure

The experiment consisted of two runs with a 10-min break in between. The children were given a short practice phase (14 items) prior to each of the two runs. For this experiment, 140 pictures of everyday objects in black and white (Rossion & Pourtois, 2004) were selected. Of these, 20 pictures were used as practice items, 60 as filler items, and 60 as experimental items.

In the first run, the children saw 60 pictures sequentially on the computer screen, which were repeated once within the run with a lag varying between 10 and 15 intervening items. No more than 4 old or 4 new items were presented consecutively. Thirty filler items were included that were repeated at variable lags (in total 90 trials). The children had to give a "new" (first presentation) or "old" (repetition) response for each item by pressing a corresponding key (the key-response assignment was balanced across subjects). Each trial consisted of a fixation cross (300 ms), picture presentation (1,000 ms), and a blank screen (500 ms). Visual feedback was given for each response with a smiley face (correct) or a frowning face (incorrect) for 500 ms. The next trial started after an intertrial interval (1,000 ms). The second run was similar to the first run. Each of the 60 pictures from the first run was repeated two more times. Thirty new filler items were mixed in and repeated at variable lags. The children were asked to judge each item solely according to its within-run repetition status and to ignore across-run repetitions. Different distances between the repetition of items across the two runs were used: (a) long lag, items that were presented in the first half of the first run were shown in the second half of the second run (217–235 intervening items) and (b) short lag, items of the second half of the first run were presented in the first half of the second run (125–142 intervening items).

Statistical Analyses

Trials that were not responded to and trials with filler items were removed from behavioral analysis. Relevant for the current issue is the comparison of memory accuracy (Pr) between high-demanding (long-lag condition) and low-demanding trials (short-lag condition). For memory accuracy in the long-lag condition, the rate of false alarms to items presented for the first time in the long-lag condition were subtracted from the hit rates in the long-lag condition. Pr_long = Target hits_long − NonTarget false alarms_long. For memory accuracy in the short-lag condition, false alarms to items presented for the first time in the short-lag condition were subtracted from the short-lag hit rates: Pr_short = Target hits_short − NonTarget false alarms_short. Reaction times for targets and nontargets in the short- and long-lag condition were determined. Between-group differences were assessed by means of ANOVAs with the factors lag condition (short vs. long) and group (preterm vs. control).

Results

Table 3 gives an overview of the results. Regarding memory accuracy, an ANOVA with the factors lag condition and group showed only a significant effect of lag condition, $F(1, 24) = 11.62$, $p < .01$, $\eta_p^2 = .326$. This indicates that both groups showed poorer discrimination performance in the long-lag condition compared to the short-lag condition and that both groups did not differ from each other ($F < 1$, $p = .77$, $\eta_p^2 = .004$). The interaction between the factors lag condition and group was also not significant ($F < 1$, $p = .38$, $\eta_p^2 = .033$).

Table 3

Follow-Up Experiment: Proportion Hits and NonTarget FAs, Pr, and Standard Deviations for the Short- and Long-Lag Condition in the Second Run, and Mean Reaction Times (ms) for Each Group

	Preterm group		Control group	
	Short	Long	Short	Long
Proportion hits	0.83 (0.11)	0.84 (0.09)	0.87 (0.10)	0.87 (0.07)
Proportion FAs	0.12 (0.08)	0.22 (0.13)	0.15 (0.07)	0.20 (0.13)
Pr	0.72 (0.12)	0.63 (0.17)	0.72 (0.15)	0.67 (0.19)
RT hits	742 (73)	748 (88)	762 (85)	756 (69)
RT nontarget CRs	753 (71)	777 (70)	793 (96)	806 (70)

Note. FAs = false alarms; CRs = correct rejections; Pr = discrimination index.

Discussion

Memory performance dropped in both groups from the short-lag to the long-lag retrieval condition. With a trial duration of 3.3 and a mean difference of 93 intervening items between the short- and long-lag conditions the mean difference in the repetition delay between both conditions was not larger than 5.1 min. With this small temporal delay, we feel safe to conclude that the two retrieval conditions differ merely in difficulty and not in the memory processes involved. This is important to note, as recent studies have shown that recollection is more affected by delay than familiarity when immediate memory performance is compared with memory performance at long delays of more than 24 hr (see Sadeh, Ozubko, Winocur, & Moscovitch, 2013, for a review). Notably, no interaction between delay and group was found, indicating that the delay effects were highly similar in both groups. By this, the preterm group did not show selectively lower memory scores in the high-resource condition, as would have been expected on the basis of the task-resource artifact account (Shallice, 1988). In sum, the outcome of this follow-up study provides further support for the view that recollection is selectively impaired in the preterm group.

General Discussion

This study examined ERP correlates of familiarity and recollection in an item recognition task to explore the role of both subprocesses in children of early school age, which were born preterm. The ERP correlate of recollection was selectively attenuated in the preterm group. As revealed by a follow-up study, this effect is not just a reflection of higher task difficulty in the sense that the more difficult memory process is more affected by brain injury. The outcome of the analyses of Hc volumes indicates that total and posterior left Hc volumes were reduced by 9% and by 10%, respectively, relative to controls and total and posterior right Hc volumes were reduced by 8% and by 9%, respectively. So altogether the present data support the view that prematurity can lead to ERP differences in Hc-mediated recollective processing.

We know of one other study that found that prematurity affects recollection but not familiarity (Rose et al., 2011). This study tested 1- to 3-year-old children and used structural equation modeling to examine the processes underlying recognition memory. Our study extends these results in several ways: We employed objective physiological estimates of recollection and familiarity and also demonstrated simultaneous reduced Hc volumes in preterms. Our study also shows that this selective deficit is not limited to early childhood but even persists in early school age (8–10 years.) Moreover, in extension of the aforementioned results we obtained correlations between GA and the ERP measures of recollection and of familiarity within the preterm group: With increasing GA the ERP correlate of recollection in the nonspeeded condition also increased. This suggests that the maturational state of the Hc at the time of birth might influence the maturation of memory functions in a way that these effects are still observable at an age of 8–10 years.

It has to be mentioned that in the current preterm sample the Hc volume did not correlate with the ERP index of recollection or the ERP index of familiarity. However, volume loss is only one indicator of structural Hc damage and it probably does not sufficiently map the degree of functional capability deficits (see Schiltz et al., 2006, for similar arguments). Another reason for the lack of a correlation could be that not only the Hc contributes to the scalp-recorded parietal old/new effect but also the inferior parietal cortex as suggested by recent brain imaging studies (Cabeza, Ciaramelli, Olson, & Moscovitch, 2008; Vilberg, Moosavi, & Rugg, 2006; Vilberg & Rugg, 2009). There is good evidence that the Hc has a large impact on recollection-based retrieval (Yonelinas et al., 2007) but that it is possibly not large enough to show clear correlations between Hc volume and electrophysiological measures. Finally, the outcome of preterm children is not just a result of immaturity but is significantly influenced by multiple factors like additional birth complications, SES of the family, nutrition, or individual support (Als et al., 2004; Cheatham, Sesma, Bauer, & Georgieff, 2010; Luciana, 2003) and these factors may have additionally clouded the relation between Hc volumes and memory measures in the preterm children.

The finding that both child groups did not show an ERP correlate of familiarity-based retrieval in the nonspeeded condition is in line with the literature. As in our nonspeeded test block the standard procedure in item recognition memory tasks does not explicitly constrain the response time. In such standard item recognition tasks children of early school age usually show a parietal old/new effect (Friedman, de Chastelaine, Nessler, & Malcom, 2010; Sprondel, Kipp, & Mecklinger, 2011; see Mecklinger et al., in press, for a review) but do not display a midfrontal old/new effect (Friedman, Nessler, Cycowicz, & Horton, 2009; van Strien et al., 2009). The reasons for the absence of the midfrontal old/new effect are unknown. Czernochowski et al. (2005) suggest that the childrens' conservative response bias is responsible for the missing effect. Others assume that the midfrontal old/new effect is masked by a negativity that reflects the allocation of attention to novel and unexpected events (de Haan, Johnson, & Halit, 2003). The current results, together with the data reported in Mecklinger et al. (2011), demonstrate that with operational definition of memory processes that take into account that familiarity is available earlier than recollection, children of early school age, even when born preterm, show a reliable midfrontal old/new effect.

A final issue to be addressed is that children born preterm in the nonspeeded condition achieved recognition memory scores comparable to the controls while nonreliable ERP effects were obtained. This issue cannot be solved conclusively. However, the absence of a statistically reliable ERP difference between two conditions does not mean the two conditions elicit the same ERPs (Picton et al., 2000). It is well conceivable that the small (nonsignificant) late old/new effect in the nonspeeded condition in the preterm group reflects a small and strongly attenuated recollection process that supported correct recognition judgments without giving rise to a significant parietal old/new effect. It must also be noted that ERP data are correlational in nature and it cannot necessarily be assumed that the absence of an ERP measure implies that the function with which it is assumed to correlate is absent as well.

In sum, our study suggests that ERP estimates of recollection and familiarity can disclose a subtle effect of prematurity on recognition memory processes that remains undiscovered by purely behavioral estimates of recognition memory performance. The earlier a child is born, the larger the adverse effect on recollection-based retrieval becomes. The current results provide electrophysiological evidence that prematurity can result in a deficit in recollection that leaves familiarity-based recognition intact. Though this result is preliminary and needs to be confirmed by behavioral evidence for a selective recollection impairment after prematurity, it is a potentially important finding, as it may imply that memory impairments in children born preterm can remain unnoticed in situations that make low demands on recollective processing and only become apparent in situations in which familiarity-based remembering is not sufficient. Further studies are required to better understand the functional implications of the Hc volume loss and the attenuated ERP correlate of recollection after prematurity.

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