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# Alterations in the Relationship Between Hippocampal Volume and Episodic Memory Performance in Preterm Children

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This study examines the relationship between episodic memory and hippocampal volume (magnetic resonance imaging [MRI] volumetry) in preterm children with uncomplicated neonatal courses (<34 weeks of gestation, birth weight <2,000 g) and controls (7–11 years). To examine episodic memory performance and retrieval processes, neuropsychological tests and a recognition experiment were used. Although preterm children showed reduced hippocampal volumes relative to controls by 12%, episodic memory accuracy was not reduced. However, only in controls hippocampal volume correlated with some measures of episodic memory. Together, behavioral and MRI results indicate a minor functional specificity of the hippocampus regarding episodic memory functions in preterm children.

Preterm birth is associated with altered brain development and long-term memory impairments (e.g., Beauchamp et al., 2008; Caldú et al., 2006). Of interest here is the relationship between episodic memory (i.e., the memory of events) and hippocampal (Hc) volume in preterm children. Magnetic resonance imaging (MRI) studies have reported marked volume reductions in

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the Hc (e.g., Peterson et al., 2000), which is a key structure in episodic memory (Nadel, Ryan, Hayes, Gilboa, & Moscovitch, 2003). In line with this finding impairments in episodic memory have frequently been reported in preterms (e.g., Briscoe, Gathercole, & Marlow, 2001; Giménez et al., 2005). In some studies, however, preterms do not show episodic memory deficits despite reductions in Hc volume (Narberhaus et al., 2009). A preferred interpretation of these findings are compensatory mechanisms, that is, other brain structures functionally compensate for the reduced integrity of the Hc in order to reach levels of performance that are similar to those of full-term subjects. Probably preterm children are able to recruit alternative pathways for episodic memory due to neural plasticity in the developing preterm brain. This would be consistent with the idea of a minor functional specificity of brain regions in relation to cognitive functions in preterms. An alternative explanation for the fact that episodic memory deficits are not found in all studies is that prematurity might not affect episodic memory in general but only specific processes subserving episodic recognition memory (Rose, Feldman, Jankowski, & Van Rossem, 2011). According to dual-process models of recognition memory, two retrieval subprocesses can be dissociated: (1) familiarity, a fast assessment without retrieving contextual details and (2) recollection, which is slow and Hc-dependent recognition of contextual details. To date, these subprocesses have hardly been examined in preterms, but there is some evidence that prematurity selectively affects recollection and not familiarity (Rose et al., 2011).

The current study integrates episodic memory and its specific subprocesses into the question of a compromised Hc system associated with preterm birth. The mentioned studies have one problem in common: they assessed heterogeneous preterm samples comprising participants with a wide range of perinatal complications (e.g., intraventricular hemorrhage, periventricular lesions). Therefore, the results might be confounded by varying degrees of hypoxic-ischemic or inflammatory insults to the Hc. Therefore, we investigated only preterm children with uncomplicated neonatal courses (no intraventricular hemorrhage, hypoxic-ischemic injury up to the time of data collection, or any other complications). To test episodic memory performance, neuropsychological tests were used. Additionally, to disentangle familiarity- and recollection-based retrieval processes, a recognition memory experiment was conducted. By focusing on the different temporal dynamics of both processes (i.e., familiarity-based retrieval is faster than recollection-based retrieval), we chose a response deadline procedure to dissociate both processes (Mecklinger, Brunnemann, & Kipp, 2011). Accordingly, we tested recognition memory with a speeded condition in which recollection is diminished while familiarity-based retrieval is still above chance (Hintzman & Caulton, 1997). We compared this with a nonspeeded condition allowing familiarity-based and the slower Hc-dependent recollection-based recognition. We did not investigate familiarity and recollection with the classical remember/know procedure. In this procedure, participants have to indicate whether they recognize an item because of remembering contextual details of the study episode or on the basis of familiarity. However, children seem to be unable to distinguish between these two mental states. Therefore, we did not use this method. Finally, we estimated structural changes in the Hc of both groups by means of MR-based volumetry.

Based on previous studies showing that episodic memory impairments may be limited to children who are most medically compromised (Briscoe et al., 2001), we expected our preterms with uncomplicated neonatal courses to show no or only marginal impairments in episodic memory performance relative to controls. Regarding the two processes of recognition memory, the following predictions were made: Preterms were expected to show the same performance as the controls

under the speeded condition because familiarity, which seems to be intact in preterm individuals (Rose et al., 2011), is fostered in this condition. As Hc-dependent recollection is assumed to be impaired in preterms (Rose et al., 2011), performance in the nonspeeded condition should be lower relative to controls. Due to the disproportionate vulnerability of the Hc in the developing preterm brain (Peterson et al., 2000), we hypothesized reduced Hc volumes in preterms relative to controls. With respect to the association between episodic memory performance and Hc volume, we expected positive correlations for the control group (i.e., children with larger Hc volumes should reach higher memory performance). For preterms, reduced correlations would be consistent with the idea of a minor specificity of brain regions in relation to cognitive functions after preterm birth.

## METHODS

### Participants

Twenty-five preterm children were recruited from archives of a Department of Pediatrics and Neonatology of a University Hospital with a level 3 neonatal unit. Exclusion criteria were: (a) small for gestational age (i.e., birth weight (BW) $\leq$ 10th percentile according to Voigt's National Growth Charts; Voigt, Schneider, & Jährig, 1996), (b) major surgeries during the first year of life, (c) intracranial hemorrhage or hypoxic-ischemic injury up to the time of data collection, and (d) craniofacial malformations, cerebral palsy, or other neurological diseases up to the time of data collection. The MR images of four children could not be analyzed due to movement artifacts and technical failures. The mean gestational age (GA) of the remaining 21 children (mean age: 9;00, range: 7;06–11;02) was 30.57 weeks (range: 26–34) and the mean BW was 1,360 g (range: 880-1920). Since one child reached insufficient memory performance in the recognition experiment (memory performance did not exceed chance performance) possibly due to a non-understanding of the task, we excluded it from further analyses. Two subjects were left-handed. The control group consisted of 24 age-matched full-term children, all of whom had had a normal neonatal course according to hospital records. The MR images of five children could not be analyzed due to movement artifacts and technical failures. The mean GA of the remaining 19 controls (mean age: 9;06, range: 7;06–11;01) was 40.21 weeks (range: 38–43) and the mean BW was 3435 g (range: 2,000–4,400). All subjects were right-handed. All children were judged to have brain scans that were entirely normal (i.e., no focal, central, or generalized atrophy and abnormalities in the whole brain) on visual inspection by two pediatric neuroradiologists blind to the group membership of the children. Their native language was German. Further details of both groups are shown in Table 1. All children were paid for participation. The study was approved by the Ethics Committee of the Saarland Medical Association (ID No. 151/07).

### Procedure

Episodic memory performance was measured in two modalities: (1) To measure verbal memory, the Verbaler Lern- und Merkfähigkeitstest (VLMT; Helmstaedter, Lendt, & Lux, 2001)—the German version of the Auditory Verbal Learning Test (AVLT)—was used, measuring memory performance with respect to a list of 15 words. (2) To measure visual memory, the Rey-Osterrieth

TABLE 1
Neonatal and Demographic Data of the Control and Preterm Group

| | *Control Group (n = 19)* | *Preterm Group (n = 21)* | *Statistics* |
|---|---|---|---|
| *Neonatal characteristics* | | | |
| Gestation at birth (weeks) | 40.21 (0.30; 38.0–43.0) | 30.57 (0.46; 26.0–34.0) | $t(38) = 17.11, p < .001$ |
| Birth weight (g) | 3435 (127.32; 2000–4400) | 1360 (67.28; 880–1920) | $t(38) = 14.80, p < .001$ |
| 1-Minute Apgar score, median | 10; (range, 8–10) | 7; (range, 1–9) | $t(38) = 6.39, p < .001$ |
| 5-Minute Apgar score, median | 10; (range, 9–10) | 8; (range, 2–10) | $t(38) = 5.36, p < .001$ |
| Days on ventilator, median | NA | 4; (range, 1–12) | |
| Postnatal steroids (Solu-Decortin) | NA | 7 | |
| Gender (female/male) | 8/11 | 14/7 | $\chi^2(1) = 2.43, p = .12$ |
| Socioeconomic status (SES)[a] | 65 (3.01; 37–88) | 54 (3.70; 31–84) | $t(38) = 2.30, p < .05$ |
| *Anthropometric data at assessment* | | | |
| Age in years | 9.00 (0.23; 7–11) | 8.91 (0.22; 7–11) | $t(38) = 0.30, p = .77$ |
| Height (cm)* | 144.34 (1.97; 131.0–160.0) | 135.74 (1.75; 126.0–158.0) | $F = 11.20, p < .01$ |
| Weight (kg)* | 36.29 (1.56; 27.0–55.5) | 30.95 (1.45; 23.0–46.0) | $F = 6.41, p < .05$ |
| Occipito-frontal head circumference* | 54.16 (0.40; 50.0–57.0) | 52.71 (0.35; 50.0–56.0) | $F = 4.67, p < .05$ |

*Note.* All values except for Apgar scores, days on ventilator, and postnatal steroids are means (SE; range). NA = not available.

[a]Determined according to Ganzeboom, de Graaf, Treiman, and de Leeuw (1992).

*After controlling for gender.

Complex Figure was used (Osterrieth, 1944), where a complicated geometric figure has to be reproduced from memory. The verbal and visual memory tests provide reliable measures of the integrity of the Hc (Lezak, 1995). Additionally, intellectual functioning (IF) was assessed using the Raven's Coloured Progressive Matrices Test (CPM), a multiple choice test of visual abstract reasoning which can be used as a short screening of general cognitive ability (Raven, Raven, & Court, 2002).[1]

The two episodic memory retrieval subprocesses (familiarity and recollection) were measured with an experiment consisting of two study-test cycles, the first with a speeded and the second with a nonspeeded response condition (see Mecklinger et al., 2011). In both study phases, 60 pictures from a colored version of the Snodgrass and Vanderwart line drawings (Rossion & Pourtois, 2004) were presented consecutively (fixation cross: 400 msec, picture presentation: 1,000 msec, intertrial interval: 1,400 msec). The subjects were instructed to make an indoor/outdoor judgment with reference to the pictures and to memorize them. During the subsequent retention interval, subjects had to perform an easy arithmetic task for one minute. In each of the two test phases, a total of 120 pictures (60 old and 60 new items in randomized order) were presented and the subjects were instructed to make old/new decisions by pressing a corresponding key. In the speeded condition, subjects were instructed to make old/new decisions during picture presentation (maximal response time: 1,050 msec). Subjects were informed about time out by means of a brief sound. In the nonspeeded condition, subjects had unlimited time to respond. In both conditions, a

[1]The test–retest reliabilities of the standardized neuropsychological tests were high: VLMT ($r$ = .68–.87), Rey-Osterrieth Complex Figure ($r$ = .76–.97), and CPM ($r$ = .80–.90).

feedback stimulus (smiley or frown face) was presented indicating whether a correct or incorrect response had been given.

MR scanning lasted 30 min and took place within a 1.5-Tesla Siemens Sonata scanner. A 3D MP-RAGE sequence was obtained with a repetition time of 1,900 msec; echo time, 3.93 msec; inversion time, 1,100 msec; flip angle, 15°; matrix size, 256 × 256; field of view, 256 mm; partition thickness, 1 mm; 176 sagittal partitions. The volumetric analysis comprised the measurement of Hc volumes and cerebral volume (CV), using MRIcron software. First, CV was manually outlined in the coronal view by tracing every tenth slice. By summing up the cross-sectional areas and then multiplying this with the slice distance (i.e., 10 mm) the final volume was estimated. Second, the Hc was manually segmented. The posterior limit of the Hc was determined two contiguous slices before the slice with the maximal visible length of the fornix. To exactly determine the anterior boundary, the alvear covering of the Hc was used, which was included in the measurements. The medial and inferior border was marked by the contrast between gray and white matter. While uncus and subiculum were included in the measurements, fimbria and choroid plexus were excluded. Tracing of all Hc was conducted by one operator, blind to the group membership of the children. To assess variation in the measurement of volumes by this operator, six randomly chosen Hc were measured a second time. Intra-observer reliability was high, with a correlation value of 0.97. To correct the measured Hc volume for CV, the covariance method as described by Jack et al. (1989) was used. As episodic 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 and the middle and posterior part of each Hc were summed (for left and right Hc, respectively) (see Greicius et al., 2003).

## Statistical Analyses

Trials with response times (RTs) faster than 200 msec and with time-out responses in the speeded condition of the recognition experiment were discarded. Memory performance was analyzed by means of the discrimination index Pr (Hits – False Alarms). In cases of group differences (*t*-tests) in any of the measured variables, ANCOVAs with the factors Gender, Socioeconomic Status (SES), and Age as covariates were carried out to control either for confounding influences of these factors on episodic memory differences between groups or for generalized scaling effects within the brain[2] with regard to volumetric differences between groups (cf. Peterson et al., 2000). As the entire Hc is involved in episodic memory performance in general (Nadel et al., 2003), within both groups, we examined the relationships of mean (left and right) total Hc volume with episodic memory measures of the neuropsychological tests by means of partial correlations (controlling for Gender, SES, and Age). As the posterior part of the Hc is more involved in retrieval processes than its anterior part (Greicius et al., 2003), within both groups, we examined the relationships of mean (left and right) Hc volume of the posterior two-thirds with the discrimination index Pr of the speeded and nonspeeded condition of the recognition experiment by means of partial correlations (controlling for Gender, SES, and Age). Two-tailed tests were used for all analyses.

[2]Since additional controlling for height, weight, and occipito-frontal head circumference can be regarded as an overcorrection because gender itself includes stature and body weight (Rushton & Ankney, 1996), we only used Gender, SES, and Age as covariates.

## RESULTS

An overview of the results is given in Table 2. IF differed between the preterm and control group even after controlling for Gender, SES, and Age, $F(1, 35) = 7.05$, $p < .05$, $n_p^2 = .168$. Regarding episodic memory performance in the neuropsychological tests no group differences were obtained. The mean number of time-out responses in the speeded condition was low and did not differ between groups (preterm group: .95, range: 0–5; control group: .79, range: 0–3). The mean number of trials with RTs below 200 msec in the speeded condition was also highly similar across groups (preterm group: .20, range = 0–2; control group: .16, range = 0–2). An ANOVA with the factors Response Condition (speeded, nonspeeded) and Group for the memory performance (Pr) yielded only a main effect of Response Condition, $F(1, 37) = 60.55$, $p < .001$, $n_p^2 = .621$, indicating that both groups responded more accurately in the nonspeeded than in the speeded condition. For mean RTs, an ANOVA with the factors Response Condition, Item Type (hits, correct rejections), and Group revealed reliable main effects of Response Condition, $F(1, 37) = 98.85$, $p < .001$, and Item Type, $F(1, 37) = 4.44$, $p < .05$, indicating that both groups took more time for responding in the nonspeeded than in the speeded condition and also for responding for correct rejections than for hits.

CV differed significantly between the two groups, $t(38) = 2.62$, $p < .05$; showing a 8.1% decrease in the preterm compared to the control group. This difference persisted after controlling for Gender, SES, and Age in an ANCOVA, $F(1, 35) = 4.84$, $p < .05$, $n_p^2 = .121$. As the group comparisons of absolute Hc volumes and of Hc volumes corrected for CV revealed the same results only outcomes of corrected Hc volumes will be reported below (see Table 2). An ANCOVA with the factors Hemisphere (left vs. right) and Group, and the covariates Gender, SES, and Age performed for Hc volumes yielded a main effect of Hemisphere, $F(1,35) = 4.55$, $p < .05$, $n_p^2 = .115$, and Group, $F(1, 35) = 17.60$, $p < .001$, $n_p^2 = .335$. The interaction of Hemisphere and Group was not significant ($F < 1$, $p = .91$), indicating that preterms had smaller Hc volumes compared to controls and that both groups had larger right versus left Hc volumes. For the posterior two-thirds of Hc volumes, an ANCOVA with the factors Hemisphere, Group, and the covariates Gender, SES, and Age yielded a main effect of Group, $F(1, 35) = 13.78$, $p < .01$, $n_p^2 = .282$. The interaction of Hemisphere and Group was not significant ($F < 1$, $p = .62$), indicating that preterm children had smaller Hc volumes of the posterior two-thirds relative to controls, irrespective of hemisphere.

## RELATIONS BETWEEN MEMORY VARIABLES AND VOLUMETRIC DATA

For controls, partial correlations controlling for Gender, SES, and Age revealed a marginally significant positive correlation between mean Hc volume and delayed recall performance in the Rey-Osterrieth Complex Figure ($r = .48$, $p = .06$). The investigation of the mean posterior two-thirds of Hc volume in relation to the discrimination index Pr revealed a positive correlation in the nonspeeded condition ($r = .53$, $p < .05$) but no correlation in the speeded condition. The correlations remained stable even after controlling for outliers (i.e., > 2 SD from the group mean in any of the measured variables). No statistically significant correlations were detected between volumetric measurements and other episodic memory variables. For preterms, no significant correlations were found in either of the analyses.

TABLE 2
Neuropsychological, Recognition Memory, and Volumetric Assessment of the Control and Preterm Group. The Standard Errors of the Means Are Given in Parentheses

| *Cognitive Ability* | *Control Group (n = 19)* | *Preterm Group (n = 21)* | *p Values (t-Tests)* | *p Values of the ANCOVA: Gender, SES, and Age as Covariates* |
|---|---|---|---|---|
| *Intelligence Functioning (CPM)*[a] | 32.58 (0.50) | 29.33 (0.99) | <.01 | <.05 |
| *Verbal Episodic Memory (VLMT)*[b] | | | | |
| - immediate recall | 7.53 (0.34) | 7.10 (0.37) | .40 | — |
| - learning gains | 54.37 (2.15) | 49.81 (2.47) | .18 | — |
| - delayed recall | 11.95 (0.44) | 11.05 (0.48) | .18 | — |
| - loss after delay | 1.21 (0.29) | 0.52 (0.39) | .17 | — |
| - recognition | 14.47 (0.16) | 14.52 (0.18) | .84 | — |
| *Visual Episodic Memory (Rey-Osterrieth Complex Figure)* | | | | |
| - copy | 29.58 (1.18) | 26.02 (1.00) | <.05 | <.05 |
| - immediate recall[c] | 64.30 (3.59) | 64.01 (2.76) | .95 | — |
| - delayed recall[c] | 61.92 (3.75) | 58.44 (2.94) | .47 | — |
| *Recognition Memory* | | | | |
| speeded condition | | | | |
| - memory performance (Pr) | 0.47 (0.04) | 0.45 (0.04) | .68 | — |
| - RT Hits | 734 (15) | 735 (11) | .95 | — |
| - RT Correct rejections | 737 (11) | 744 (13) | .67 | — |
| nonspeeded condition | | | | |
| - memory performance (Pr) | 0.73 (0.03) | 0.65 (0.04) | .13 | — |
| - RT Hits | 1282 (97) | 1194 (73) | .47 | — |
| - RT Correct rejections | 1310 (61) | 1300 (91) | .93 | — |
| *Brain Region ($cm^3$)* | | | | |
| CV | 1283.39 (27.43; 1026.7–1479.2) | 1179.42 (28.36; 952.4–1442.2) | <.05 | <.05 |
| Left Hc (whole Hc) | 2.83 (0.08; 2.32–3.42) | 2.50 (0.07; 1.87–3.19) | <.01 | <.01 |
| Left Hc (whole Hc[d]) | 2.83 (0.06; 2.10–3.43) | 2.51 (0.06; 2.11–3.12) | <.01 | <.001 |
| Left Hc (posterior two-thirds[d]) | 1.75 (0.04; 1.29–2.03) | 1.53 (0.05; 1.16–2.02) | <.01 | <.01 |
| Right Hc (whole Hc) | 3.02 (0.10; 2.16–3.70) | 2.63 (0.06; 2.00–3.06) | <.01 | <.05 |
| Right Hc (whole Hc[d]) | 3.02 (0.09; 2.29–3.57) | 2.64 (0.05; 2.22–2.98) | <.001 | <.01 |
| Right Hc (posterior two-thirds[d]) | 1.92 (0.06; 1.54–2.48) | 1.67 (0.04; 1.43–2.04) | <.01 | <.05 |
| Mean of left and right Hc (whole Hc[d]) | 2.93 (0.07; 2.20–3.42) | 2.57 (0.05; 2.21–2.97) | <.001 | <.001 |
| Mean of left and right Hc (posterior two- thirds[d]) | 1.83 (0.05; 1.52–2.20) | 1.60 (0.03; 1.41–1.91) | <.001 | <.01 |

*Note.* All scores except for Rey-Osterrieth Complex Figure immediate and delayed recall scores as well as memory performance and reactions times (RT) in the recognition experiment are raw scores. In case of group differences in the initial *t*-test, an ANCOVA with Gender, Socioeconomic Status (SES), and Age as covariates was carried out.
[a]CPM = Coloured Progressive Matrices (Raven et al., 2002). [b]VLMT (Helmstaedter et al., 2001) is the German version of the Auditory Verbal Learning Test (AVLT). [c]Immediate and delayed recall performance is the percent immediate/delayed recall score (immediate/delayed raw score divided by the copy raw score multiplied with 100; Lezak, 1995). [d]Hippocampal volumes corrected for cerebral volumes (Jack et al., 1989).

## DISCUSSION

This study systematically examined episodic memory, Hc volume, and their relationship in 7- to 11-year-old preterm children with uncomplicated neonatal courses relative to controls. Consistent with previous findings that episodic memory impairments may be limited to children who are most medically compromised (Briscoe et al., 2001), we found similar performance in preterms with uncomplicated neonatal courses and controls. This suggests that episodic memory impairments are not a general feature of preterms, but that the degree of brain insult might play an important role in the development of memory problems. An alternative explanation for the lack of deficits in tests that presuppose Hc-dependent recollection (here nonspeeded condition) could be that preterms are able to utilize additional cognitive control processes in order to boost the initially weak recollection-based retrieval mechanism. Controlled memory processes include strategic search operations for task-relevant contextual details as well as evaluative processing of the retrieved memory contents.

We are aware of the fact that the current sample size was relatively small and heterogeneous in terms of GA and BW, so that an existing but small impairment in the preterm group might not have been detected. It is desirable that future studies add support to the current results with larger and more homogeneous samples. Notably, however, there are studies with the same or even smaller sample size and heterogeneity in terms of GA and BW showing behavioral differences with regard to episodic memory measures between preterms and controls (Briscoe et al., 2001; Giménez et al., 2005). Moreover, we found that although the sample size was small, the mean values of IF differed across groups and showed significant discrepancies. Such a general cognitive deficit is a common finding among preterms. It is noteworthy that in contrast to episodic memory a more distributed brain network seems to be involved in IF. Possibly, disturbances in this distributed brain network cannot be compensated as easily as impairments in the more spatially limited memory network. However, it cannot be ruled out that the lower IF scores of the preterm group are co-determined by the nature of the chosen test, the CPM. This test involves visual perceptual abilities that are known to be weak in preterms. Future studies should consider this aspect.

The view that prematurity entails risk of Hc compromise (e.g., Peterson et al., 2000) is supported by our finding of reduced Hc volumes in the preterm group. Despite this volume reduction, we did not find impairments in episodic memory performance. A possible explanation is an altered neurocognitive memory network in preterms (Narberhaus et al., 2009). This assumption may be further substantiated by the fact that Hc volume was positively correlated with delayed recall performance of the Rey Osterrieth Complex Figure and with memory performance in the nonspeeded condition of the recognition experiment only in controls. This might suggest a reduced specificity of the Hc for episodic memory functions in preterms and possibly the ability to recruit alternative pathways. As a matter of course, correlations between measures of Hc volume and memory performance do not allow to directly make conclusions regarding functional processes. Additionally, the heterogeneity of the preterm group in terms of GA and BW could have masked an existing relationship between Hc volume and test performance. Finally, the performance in episodic memory tests is based on encoding as well as retrieval processes. How much the Hc is involved in either process is controversial. However, our assessment of memory performance with standardized memory tests does not clearly separate encoding and retrieval processes. Therefore, an existing relationship between Hc volume and one of the two processes may not have been accurately captured. Specifically, a possible correlation in the preterm group

may have been underestimated. Not differentiating between memory processes in memory tests may be one reason for the heterogeneous results of earlier studies. By separating the two memory processes, functional neuroimaging studies could help to understand the exact mechanisms underlying the observed modifications in the memory network in preterms.

Taken together, our findings provide further evidence for disproportionate adverse effects of prematurity on Hc volumes that do not necessarily lead to impairments in episodic memory performance. In combination with the missing relationship between Hc volume and episodic memory performance in the present preterm sample this could suggests that in school-aged preterm children with uncomplicated neonatal courses other brain structures may compensate for the reduced Hc integrity. An improved understanding of a possible functional reorganization in preterm children remains an important endeavor for future research.

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