Building on Prior Knowledge: Schema-dependent Encoding Processes Relate to Academic Performance

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Abstract

■ The acquisition and retention of conceptual knowledge is more effective in well-structured curricula that provide an optimal conceptual framework for learning new material. However, the neural mechanisms by which pre-existing conceptual schemas facilitate learning are not yet well understood despite their fundamental importance. A pre-existing schema has been shown to enhance memory by influencing the balance between activity within the medial-temporal lobe and the medial pFC during mnemonic processes such as encoding, consolidation, and retrieval. Specifically, correctly encoding and retrieving information that is related to pre-existing schemas appears rather related to medial prefrontal processing, whereas information unrelated or inconsistent with pre-existing schemas rather relates to enhanced medial temporal processing and enhanced interaction between these structures. To further investigate interactions between these regions during conceptual encoding in a real-world university setting, we probed human brain activity and connectivity using fMRI during educationally relevant conceptual encoding carefully embedded within two course programs. Early second-year undergraduate biology and education students were scanned while encoding new facts that were either related or unrelated to the pre-existing conceptual knowledge they had acquired during their first year of study. Subsequently, they were tested on their knowledge of these facts 24 hr later. Memory scores were better for course-related information, and this enhancement was associated with larger medial-prefrontal, but smaller medial-temporal subsequent memory effects. These activity differences went along with decreased functional interactions between these regions. Furthermore, schema-related medial-prefrontal subsequent memory effects measured during this experiment were found to be predictive of second-year course performance. These results, obtained in a real-world university setting, reveal brain mechanisms underlying acquisition of new knowledge that can be integrated into pre-existing conceptual schemas and may indicate how relevant this process is for study success. ■

INTRODUCTION

How knowledge acquisition guides successful remembrance is of fundamental importance for education. The fact that prior conceptual knowledge—an activated schema—can facilitate new knowledge acquisition has been widely investigated behaviorally (Bransford, Brown, & Cocking, 2000; Bartlett, 1932). Additionally, recent research in both rodents (Tse et al., 2007, 2011) and humans (van Kesteren, Fernandez, Norris, & Hermans, 2010; van Kesteren, Rijpkema, Ruiter, & Fernandez, 2010) has provided essential insight into the underlying neuronal processes of schema-enhanced memory consolidation (van Kesteren, Rijpkema, et al., 2010; Tse et al., 2007) and encoding (van Kesteren, Beul, et al., 2013; Tse et al., 2011; van Kesteren, Fernandez, et al., 2010). However, to substantiate how a pre-existing schema facilitates successful encoding of new conceptual information in humans, specifically in situations relevant for long-term educational success, mechanistic evidence is required. Such an account might be critical for the nascent discipline of educational neuroscience (Carew & Magsamen, 2010; Goswami & Szucs, 2011) to develop a new science of learning (Meltzoff, Kuhl, Movellan, & Sejnowski, 2009).

A pre-existing schema is suggested to facilitate memory consolidation by enabling relevant new information to be more rapidly assimilated (Wang & Morris, 2010; Tse et al., 2007) into this activated schema (van Kesteren, Ruiter, Fernandez, & Henson, 2012; Wang & Morris, 2010). The acquisition of knowledge is thought to be mediated by an interplay between the medial-temporal lobe (MTL), the medial pFC (mPFC), and brain areas in occipital, parietal, and temporal cortices that represent elements of the to-be-learned information (Rasch & Born, 2007; Frankland & Bontempi, 2005). Newly learned information represented in these posterior brain areas is initially bound together by the MTL (Squire, 1992). With consolidation, this hippocampal dependence of a memory trace is thought to shift to neocortical areas, including specifically the mPFC (Frankland & Bontempi, 2006; Takashima et al., 2006), a process that is now known to accelerate with a relevant schema (van Kesteren, Rijpkema, et al., 2010; Tse et al.,

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2007). Next to consolidation, processing in both the MTL and mPFC, as well as interactions between these areas, contribute already to encoding (Benchenane et al., 2010; Siapas, Lubenov, & Wilson, 2005). The MTL–mPFC interaction seems to depend on pre-existing schema (van Kesteren, Beul, et al., 2013; Tse et al., 2011; van Kesteren, Fernandez, et al., 2010). For example, hippocampal-mPFC connectivity is reduced during encoding of new information related to a schema as compared with new information that is schema-unrelated (van Kesteren, Fernandez, et al., 2010). Additionally, successful encoding of schema consistent object–scene associations is associated with larger medial prefrontal contributions, whereas successful encoding of schema inconsistent object–scene associations shows stronger medial temporal contributions (van Kesteren, Beul, et al., 2013). These findings suggest that MTL–mPFC interactions and the balance of processing between these two regions are important already during initial stages of knowledge acquisition, possibly contributing to differences in long-term memory performance.

Here, we sought to clarify schema-related conceptual encoding processes using an educationally relevant fMRI paradigm (Figure 1) by probing memory formation for course material that was carefully integrated into a university curriculum. We predicted that new discipline-related information would be better remembered after a 24-hr interval, related to more mPFC involvement (Tse et al., 2011; van Kesteren, Rijpkema, et al., 2010), whereas non-discipline-related encoding, being more unfamiliar (or novel; van Kesteren et al., 2012), would show more MTL involvement along with greater interactions between the MTL and mPFC (van Kesteren, Fernandez, et al., 2010).

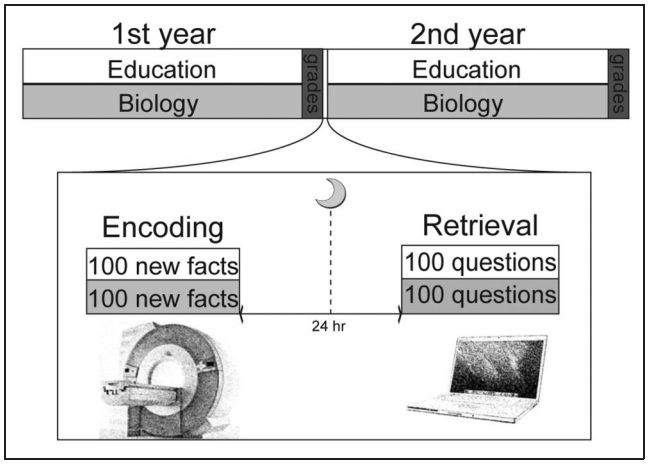

Figure 1. Study design, embedded in educational curricula (education and biology). The experiment was performed after one study year (on average around the time the second year started), and participants' grades were obtained for Study Year 1 and Study Year 2. During the experiment, participants started on Day 1 with a pretest where they answered 40 questions (20 for each discipline). They then learned 200 factual sentences (100 for each discipline) in the MRI scanner. The next day (24 hr later), they returned for the test, where they answered 200 questions, one for each fact they learned the day before.

Lastly, we wondered whether a facilitated shift to mPFC processing of task-related new information might be related to subsequent course performance. Such results would further support the view that schema-related knowledge processing shifts the MTL–mPFC balance during encoding in a way that is relevant for effective knowledge acquisition and thus academic success.

METHODS

Participants

Thirty-nine native Dutch female right-handed undergraduate students participated in this experiment. Twenty were education (pedagogy, developmental psychology, and education) students, and 19 were biology students, all at the Radboud University Nijmegen. All students were in their second year, thus going through the same curriculum when tested, and were tested on average in the second month of the second study year (mean = 1.74, *SD* = 1.37). None of the students had studied anything related to the other discipline before (i.e., education for the biology students or biology for the education students), except for studying biology in high school. All participants were healthy and had normal or corrected-to-normal vision. They were paid to participate and were told that they could earn extra money for better performance. Eight participants were excluded after data acquisition because they did not have enough confident trials (<10) for analysis, which left 31 participants for analysis (19 biology and 12 education students). This sample covered an age range of 18–21 years, with a mean age of 19.16 years. They self-reported to have slept on average 7.9 hr in between both examination days (ranging from 6 to 10 hr). No group differences were found for age, sleep, first-year grades, and intelligence (as measured by four different intelligence tests: Wordlist and Matrices from the Groninger Intelligentie Test [GIT-2; Luteijn & Van Der Ploeg, 1983] to test for verbal comprehension and logical reasoning and Symbol search and Digit Span from the WAIS [official Dutch translation; Kaufman & Lichtenberger, 2006] to test for processing speed and working memory performance). Ethical approval was obtained from the institutional review board (CMO Region Arnhem-Nijmegen, The Netherlands), and all participants gave written informed consent.

Stimuli

Participants learned sentences containing factual information that was either related to their discipline (schema-related) or not (schema-unrelated). In total, 240 sentences were constructed (120 for biology, 120 for education), of which 40 (20 per discipline) were used to test pretest performance before learning. The sentences were constructed by two student assistants, one was finishing his study biology and the other just finished studying education, both at the Radboud University Nijmegen. All

sentences were constructed so they contained at least one term or concept that was learned in the first year of study and one new term or concept taken from courses starting in the second half of the second year until the end of the curriculum (e.g., Glutamate is an excitatory neurotransmitter, in which students knew the term excitatory neurotransmitter, but not glutamate yet). Participants thus learned new information either fitting to the knowledge obtained in their first year of study or hardly fitting any prior knowledge (e.g., for education students, both excitatory neurotransmitter and glutamate are new concepts). For each fact, a multiple-choice question with three options was constructed, in which the wrong options were intermixed with information from other facts to reduce effects of familiarity (for the example above: *What is a neurotransmitter? 1. glutamate. 2. colchicine. 3. alpha-actine*; where the remaining two answers are taken from the facts *Colchicine blocks the growth of microtubuli* and *Alpha-actines are often found in muscles*; see for more example sentences Table 1).

The sentences and the experimental setup were piloted in an independent sample of biology and education students ($n = 10$). The sentences and questions that were indicated to be already known, and sentences that turned out to be too easy (as determined by memory performance and confidence measures) were discarded or adjusted. Subsequently, the sentences were carefully counterbalanced for number of words, number of syllables, and lemma frequencies (as tested using the CELEX database; Baaijen, Piepenbrock, & van Rijn, 1993). Numbers and abbreviations were avoided unless directly related to the prior knowledge. None of the sentences were longer than 10 words or 60 syllables, so reading times would not be extensive and the facts could easily be read within the 6-sec presentation time.

Design and General Procedure

In this experiment, we used a 2 × 2 design of Schema × Memory (confident correct vs. incorrect items) as within-subject factors (see Figure 1). Participants were invited to come to the imaging center on two consecutive days with 24 hr between the two visits.

Pretest

On Day 1, participants completed initially a self-paced pretest on a computer using Presentation 10.2 (Neurobehavioral Systems, Albany, CA), in which they answered 40 questions (20 of either discipline) of which they did not learn the corresponding sentences before, to assess pretest knowledge. These 40 questions were randomly drawn from the entire sample of 240 questions and were presented in pseudorandom order (i.e., no more than three consecutive facts of the same field of study). The questions were presented for 20 sec maximally, and participants could only answer after 5 sec of presentation to make sure they would not answer without reading the question and answers, using three different buttons (1, 2, or 3). After answering the question, participants were asked to indicate how certain they were of the answer given (1 = *Sure*, 2 = *Somewhat sure*, 3 = *Guess*), within 5 sec. They were furthermore instructed that they would have to answer the same sort of questions on the day after about the sentences they were going to learn in the MRI scanner. In total, this pretest lasted on average approximately 10 min.

Encoding

After the pretest, participants were taken into the MRI scanner. Participants lay supine in the scanner and responded with their right hand using a button box. They viewed the screen through a mirror positioned on top of the head coil. Lights in the MRI scanner room were switched off during the task to allow better contrast for reading the sentences. After instruction on the task, preparatory, and weighting scans (necessary for weighting

Table 1. Example Sentences (Translated from Dutch)

Biology	*Education*
Clay is a sedimentary rock.	Selective attention is acquired.
Darwin's finches belong to the microevolution.	Iconic memory is visual short-term memory.
Light puts a brake on the growth of hypotocyls.	A non sequitur is a classical fallacy.
A tundra is one of the primary biomes.	Piaget sees the child in principle as a small adult.
Plants send out a lot of biophotons.	Sex segregation is a universal phenomenon.
Histones are part of the nucleosome.	Nativists state that intelligence is inborn.
Alpha-actins are present in muscles.	The Wada test measures language lateralization.
Lipoma are benign tumors.	Duchenne and mental retardation are comorbid.
Trehalose is an important disaccharide.	Sleepwalking is a parasomnia.
Methanobacteria are autotrophic organisms.	Vygotsky is a representative of contextualism.

optimal echo times [TEs] for different brain regions, see MRI scanning parameters), they were scanned while encoding the 200 remaining sentences, presented in pseudorandom order (applying the same rules as during the pretest) using Presentation 10.2 in the middle of the screen for 6 sec. During presentation, participants were instructed to encode the sentence and indicate after the 6-sec presentation time whether (1) they already knew the fact, (2) thought they would remember it the next day, or (3) did not think they would remember it the next day, within 3 sec. This orientation task was chosen to provide an easy way to extract previously known facts and to provide a deep learning procedure for the participants rather than understanding meta-memory processes. After responding, the trials were interleaved with a fixation cross presented for 2–4 sec. After the encoding session, which lasted for 40 min, a structural MRI scan was acquired. Then, the participants went home and were asked to keep track of how many hours they slept that night.

Retrieval

On Day 2 (24 hr later), participants were tested on their knowledge of the facts by answering 200 three-choice questions, each related to a sentence they encoded the day before. This test was presented in the same way as the pretest. After they finished the questions, participants were asked to fill out questionnaires, consisting of intelligence tests and a study-related self-report questionnaire. This part of the experiment lasted on average around 1 hr.

Memory Tests and Analyses

Behavioral measures were analyzed using PASW Statistics Data Editor 18.0.0 (Polar Engineering and Consulting, Nikiski, AK) by calculating the percentage correct and incorrect items for schema-related and schema-unrelated questions. The questions belonging to a fact that was not responded to within 3 sec during the encoding session and were indicated to be already known were discarded. Also the questions that were not responded to in time during the test session were discarded. For the behavioral analyses, correct items were thus defined as all new, correctly answered questions, and incorrect items were defined as all new, incorrectly answered questions that were responded to during encoding and retrieval. For the MRI analyses, questions that were correctly answered but were indicated to be a guess were additionally discarded. Correct items were here thus defined as facts that were not missed during encoding, were not known in advance, and were confidently answered correctly on the retrieval test. Incorrect items were similarly defined, with the difference that also unconfident answers (guesses) were incorporated in the analyses. On the basis of these analyses, only participants with 10 or more trials for either factor (schema-related hits, schema-related misses, schema-unrelated hit, and schema-unrelated misses) were used for subsequent analyses. A further distinction between confidence levels was not possible because of low trial numbers in some bins.

These measures were tested in paired-samples t tests probing the behavioral effects of schema on memory during the pretest and the retrieval test. Furthermore, one-sample t tests were used to test differences from chance level (33%), and relations between group and schema-relatedness were examined using a repeated-measures ANOVA. RTs were analyzed using the same tests. Alpha was set at .05 throughout.

Grades

Participants were asked to provide us with their first-year grades of all courses when coming to the imaging center. Both first and repeated exams were used to calculate the average grade for each participant, and grades that were not denoted in numbers (such as "good" or "fair") were not used in the calculation. After the end of the study year, the participants were again asked for their grades, now of their second-year subjects. Of the 31 participants included in the final analyses, 25 responded. The amount of grades obtained per participant ranged from 11 to 19 in the first year and from 5 to 18 in the second year, because of differences in the amount of exams taken or repeated. The average of their grades was again calculated using the same method as mentioned above, and average second-year grades were normalized individually by dividing with the average of the first-year grades. This measure was then used to correlate with brain activity for schema subsequent memory effects during the experiment using Pearson bivariate two-tailed correlation tests. Alpha was again set at .05.

MRI Scanning Parameters

Participants were scanned using a 1.5-Tesla Siemens Magnetom Avanto system equipped with a 32-channel phased array head coil (Siemens). For BOLD fMRI images, we used a T2* weighted gradient-echo multiecho EPI sequence (Poser, Versluis, Hoogduin, & Norris, 2006) with the following parameters: repetition time = 2.64 sec, TE1 = 6.9 msec, TE2 = 24.2 msec, TE3 = 33 msec, TE4 = 43 msec, TE5 = 52 msec, 34 slices, ascending slice order, 3 mm slice thickness, 0.51 mm slice gap, matrix size = 64 × 64, field of view = 224 × 224 × 119 mm, flip angle = 80°, voxel size = 3.5 × 3.5 × 3.0 mm. Slices were angulated in an oblique axial manner to reach whole-brain coverage. To ensure reaching a steady state condition, the first seven scans were discarded. Additionally, T1 weighted anatomical scans at 1 mm isotropic resolution were acquired using an MP-RAGE scan with repetition time of 2250 msec,

inversion time of 850 msec, flip angle of 15°, and field of view of 350 × 263 × 350 mm.

fMRI Data Preprocessing and Analyses

Raw, multiecho fMRI data were first combined into single-echo scans using in-house software written in Matlab 7.5, which used 29 separately acquired weighting scans to calculate the most optimal echo time for each voxel and performed motion correction on the first echo by using iterative rigid body realignment to minimize the residual sum of squares between the first and all further functional scans. The combined scans were further preprocessed using SPM5. Rigid body coregistration to corresponding individual T1 images was performed using mutual information optimization. Then, data were spatially normalized into a common space, defined by the Montreal Neurological Institute (MNI) 152 T1 image (voxel size = 2 × 2 × 2 mm), and smoothed by convolving the data with an 8-mm FWHM 3D kernel. Because the first seven scans were excluded, 914 scans were left for analysis.

After preprocessing, statistical parametric maps were generated by modeling the evoked BOLD response for each factor (schema-related hits, schema-related misses, schema-unrelated hits, and schema-unrelated-misses) as a delta function convolved with a hemodynamic response function during the onset of the fact presentation trial. Furthermore, the derivative of the hemodynamic response function for each factor and the individual movement regressors were added as regressors of no interest to each first-level model. All contrasts and interactions of interest were created in these first-level models and subsequently random effects one-sample t tests were performed to test them at the group level. These analyses were performed as whole-brain analysis with an initial uncorrected threshold of $p < .001$, masked with the AAL template. Results were considered significant ($p < .05$) after correcting for multiple comparisons within the entire brain or within specific a priori defined ROIs. ROI results were assessed using small volume correction (SVC) at $p < .05$ cluster-level corrected and ROIs were defined as follows: (a) left and right MTL (hippocampus and parahippocampal gyrus combined) for main analyses, where we had a less specific hypothesis on where in the MTL we found find differential activation; (b) left and right hippocampus, all taken from the AAL template (Tzourio-Mazoyer et al., 2002) for connectivity analyses, where we were specifically interested in hippocampal connectivity; and (c) a mask of activity patterns in the mPFC as observed in a memory retrieval task related to schema (van Dongen, Takashima, Barth, & Fernandez, 2011; peak MNI [14,42,4], encompassing 28 voxels and stretching through anterior cingulate and frontal superior medial structures). Additionally, peak beta values of the significant activity differences within these ROIs were extracted and were used to correlate measures of brain activity (subsequent memory effect [schema correct–schema incorrect within both mPFC and MTL) with measures of study performance (baseline-corrected second-year grades).

Psychophysiological interactions (PPIs) were calculated to assess functional connectivity between brain regions. These were executed using SPM5 (www.fil.ion.ucl.ac.uk/spm) in combination with in-house software, written in Matlab 7.5 (The Mathworks, Inc., Natick, MA). PPI analyses probe differences in coactivation of a certain seed region (physiological factor) with the rest of the brain modulated by an external factor (psychological factor). Here, we examined coactivation differences that were significantly larger for schema-related hits than for schema-unrelated hits and vice versa from a sphere around the mPFC and MTL peaks we found in the interaction effect. Specifically, these seed regions were defined by taking the peak voxels obtained from the Schema × Memory interaction, surrounded by a 6-mm sphere. Only voxels that were significantly active in an effect of interest analyses were used for this analysis. The single-subject general linear model constructed for the previously described analyses was extended with two regressors: the general deconvolved signal from the seed region and the deconvolved signal from the seed region for the contrast schema-related hits versus schema-unrelated hits. For each subject, contrast estimates of this second regressor were used as input for the second-level random effects analysis. Similar to the previously described significance values, connectivity was considered significant at $p < .001$ uncorrected at voxel-level and $p < .05$ corrected at cluster-level SVC (Hayasaka, Phan, Liberzon, Worsley, & Nichols, 2004) with left and right hippocampus as an independently determined ROI, taken from the AAL template (Tzourio-Mazoyer et al., 2002).

RESULTS

Memory Performance

During encoding, there was a small but reliable difference in participants expectancy to remember schema-related and schema-unrelated facts (2.33 for schema-related and 2.70 for schema-unrelated items; $t(30) = 8.87$, $p < .001$).

Performance on the pretest showed a congruency effect with better performance for schema-related information ($t(30) = 6.71$, $p < .001$, schema-related = 50.41% [SD = 13%] average correct, schema-unrelated = 34.15% [SD = 9%] average correct). At this test, performance for the schema-related information was significantly different from chance ($t(30) = 7.15$, $p < .001$), whereas performance for the schema-unrelated information was not ($t(30) = .51$, ns). For biology students, performance was on average better than for education students ($F(1, 29) = 41.46$, $p < .001$; biology schema-related = 53.93% [SD = 11%] and schema-unrelated = 33.73% [SD = 11%]; education schema-related = 44.85% [SD = 15%] and schema-unrelated = 34.82% [SD = 5%], and a Schema Relatedness × Group interaction was found ($F(1, 29) = 4.70$, $p < .05$).

Critically for the hypothesis at hand, retrieval test performance after learning new facts inside the scanner showed a substantial effect of prior knowledge on learning new information ($t(30) = 10.04$, $p < .001$, schema-related = 67.4% [SD = 11%] correct, schema-unrelated = 50.2% [SD = 9%] correct). Performance was significantly different from chance for both conditions (33%, schema-related: $t(30) = 18.01$, $p < .001$; schema-unrelated: $t(30) = 10.19$, $p < .001$). For biology students, performance was on average better than for education students ($F(1, 29) = 104.50$, $p < .001$; biology schema-related = 70.05% [SD = 11%] and schema-unrelated = 54.72%

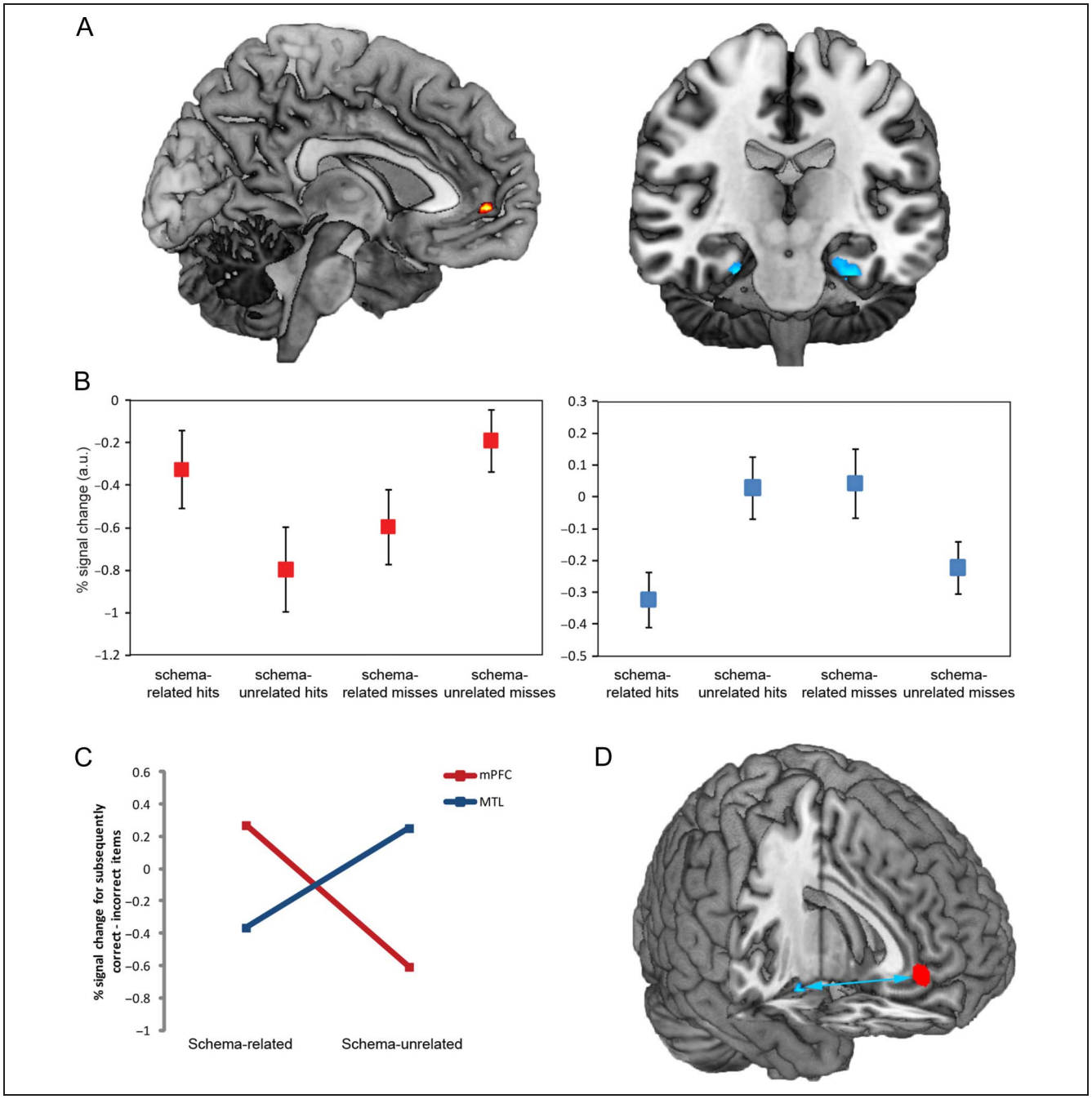

Figure 2. (A) Schema × Subsequent Memory interaction of brain activity during encoding revealed an interaction between mPFC and MTL regions, where mPFC (in red/yellow) was more active for congruent (subsequent correct items > subsequent incorrect items) > incongruent (subsequent correct items > subsequent incorrect items), and bilateral MTL (in blue/green) was more active for incongruent (subsequent correct items > subsequent incorrect items) > congruent (subsequent correct items > subsequent incorrect items). (B) The graphs show the beta values at peak level for the separate conditions and (C) visualizes the relation between the regions (mPFC and MTL) and schema. Note that these graphs are purely for visualization purposes, statistically significant effects are reported for each of these regions in the text, and these graphs just show the interactions that are not statistically tested because of possible inflated results because of circularity. (D) Psychophysiological interaction revealed larger differential functional connectivity from the mPFC to the right hippocampus for schema-unrelated correct items > schema correct items.

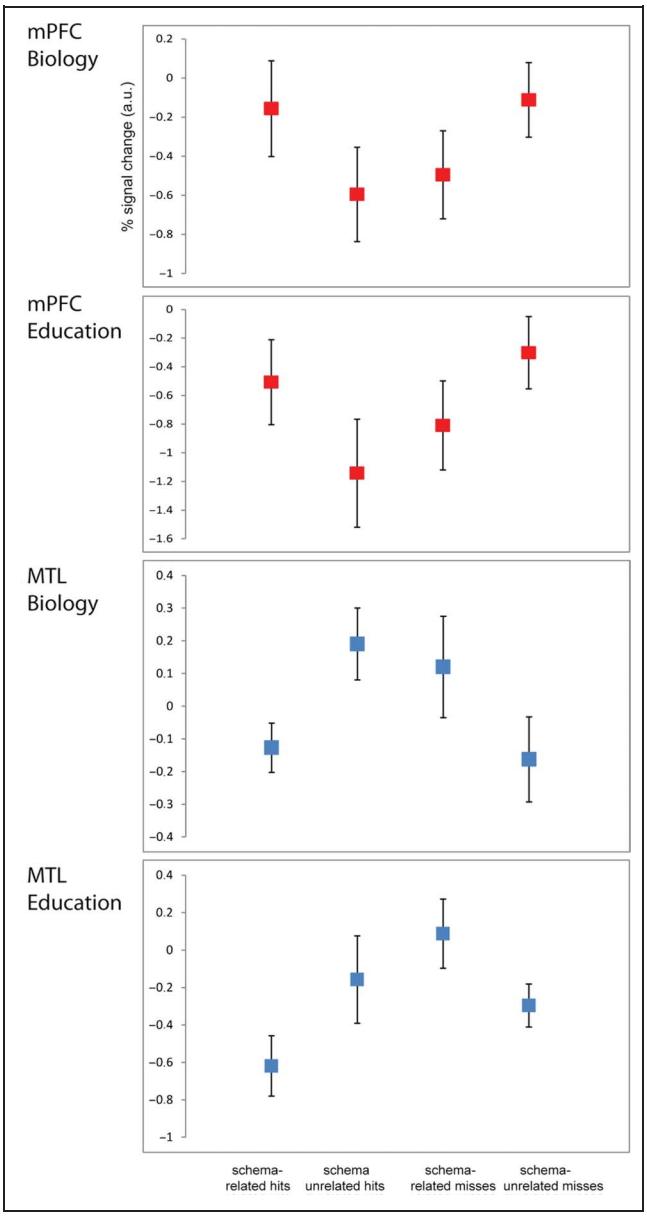

Figure 3. Group-specific depiction of the interaction effects shown in Figure 2B. These graphs are purely for visualization purposes; no statistical tests have been performed on these data.

[*SD* = 8%]; education schema-related = 63.18% [*SD* = 9%] and schema-unrelated = 43.13% [*SD* = 5%], but no Schema Relatedness × Group interaction was found ($F(1, 29) = 1.86$, $p = ns$). This pattern of results indicates that participants learned information for both the disciplines but showed better memory scores for schema-related information at the retrieval test. Importantly, RTs during encoding were not significantly different for schema-related versus schema-unrelated trials ($t(30) = .42$, *ns*, schema-related = 0.99 sec, schema-unrelated = 1.01 sec), indicating no differences in time on task and thus suggesting equal attentional processing when encoding schema-related and schema-unrelated information. Performance on the retrieval test for schema-related items showed a positive relation to the grades obtained in the first year ($r(30) = .57$, $p < .01$) but not for grades in the second year ($r(24) = .34$, $p < .1$). These relations show that the experimental design was related to information learned in the curriculum, which is important when relating it to course-related measures.

Neuroimaging Results: Differential Activity

The whole-brain analysis (Figure 2A) revealed a positive effect for the Congruency × Memory interaction in the mPFC (peak [MNI 2, 46, 0], $Z = 3.30$, 27 voxels, SVC for an mPFC mask taken from van Dongen et al., 2011, $p < .05$) for schema-related (correct > incorrect) > schema-unrelated (correct > incorrect). Furthermore, we found an opposite, negative effect for the Congruency × Memory interaction in a medial temporal cluster encompassing bilateral parahippocampal gyri and hippocampus (peaks [MNI −28,−20,−26], $Z = 3.64$, 33 voxels and [MNI 22, −16,−28], $Z = 3.67$, 40 voxels, SVC $p < .05$): for schema-unrelated (correct > incorrect) > schema-related (correct > incorrect). These findings indicate that the encoding signal corresponding to subsequently forgotten items subtracted from that for subsequently remembered items for the schema-related sentences and vice versa for the schema-unrelated sentences led to enhanced mPFC processing. The opposite comparison led to enhanced processing in MTL. These results reveal that brain activation shows a Schema × Memory interaction in both the mPFC and MTL, in which both factors contribute to the interaction (see Figure 2B and C, mPFC: schema-related hits > schema-related misses: $p = .06$, schema-unrelated misses > schema-unrelated hits: $p < .001$; schema-related hits > schema-unrelated hits: $p = .04$; schema-unrelated misses > schema-related misses: $p < .001$, MTL: schema-related misses > schema-related hits: $p < .001$; schema-unrelated hits > schema-unrelated misses: $p = .06$; schema-unrelated hits > schema-related hits: $p < .001$; schema-related misses > schema-unrelated misses: $p < .001$). Separate analyses on the two student groups indicated that both groups contributed to this interaction (see Figure 3 for a visualization of these separate group analyses).

Neuroimaging Results: Differential Connectivity

Next, we sought to examine the crosstalk between the MTL and mPFC with respect to the congruency of the new information (Figure 2D). Our hypothesis predicts that functional connectivity is greater for schema-unrelated information. This was assessed by PPI analyses with the mPFC as seed region (as determined by the peak voxel of the Schema × Memory interaction surrounded by a 6-mm sphere). This revealed a differential coactivation with the right hippocampus (peak [MNI 22,−12,−16],

11 voxels, $Z = 3.46$, SVC right hippocampus $p < .05$) stronger for schema-unrelated than for schema-related correct items. No significant effects were observed for the opposite contrast. We also investigated connectivity from the bilateral MTL activity in the same way but did not find any significant regions that functionally connected to this ROI in these analyses. Thus, functional coupling between the mPFC and the right hippocampus was larger for the schema-unrelated relative to schema-related correct items.

Relation to Course Performance

Testing memory in an experimental retrieval test is one thing, but our use of course-related material created the opportunity of additionally asking whether there was any long-term impact on course success. Our experiment might have, in part, mimicked gradual knowledge accumulation supposed to occur in education. If so, brain activation encoding patterns may be predictive of course success. Our analysis of this possibility revealed a positive relation between mPFC activity during learning of schema-related information and normalized grades (grades year 2/grades year 1) obtained in the subsequent course year ($r(24) = .43$, $p < .05$; Figure 4), suggesting that activity in the mPFC during encoding of schema-related information is related to subsequent course performance. Interestingly, given the emphasis upon the MTL with respect to learning, no such relation was observed for MTL activity ($r(24) = .09$, *ns*).

DISCUSSION

These results support the view that a pre-existing schema in the neocortex facilitates mnemonic processing during the encoding of new, educationally relevant information forming the basis of long-term knowledge. Behavioral results show that newly learned schema-related information was better remembered than similar information unrelated to a schema. Additionally, the pattern of results revealed when depicting parameter estimates from the significant interaction effect suggests that successful encoding of schema-related information appeared associated with enhanced mPFC activity, whereas successful encoding of schema-unrelated information appeared associated with decreased mPFC activity. An opposite pattern, showing successful encoding of schema-unrelated information versus schema-related information was associated with enhanced MTL activity and enhanced mPFC–hippocampus connectivity. These results extend previous findings showing a memory-related shift in balance from the MTL to the mPFC in time (Frankland & Bontempi, 2006; Takashima et al., 2006), mediated by schema (Tse et al., 2011; van Kesteren, Fernandez, et al., 2010; van Kesteren, Rijpkema, et al., 2010), such that this shift in balance can be present already at encoding when new information is related to prior knowledge (van Kesteren, Beul, et al., 2013). Here, we replicate this process for conceptual encoding that is relevant in educational settings. Moreover, schema-related encoding activity in the mPFC was found to be predictive of grades obtained subsequently. Thus, these results show that a schema enhances conceptual encoding of new, educationally relevant information through facilitation of the shift in MTL–mPFC balance, leading to long-term learning benefits. These findings are consistent with the idea of parallel encoding in mPFC and MTL (Tse et al., 2011) and increased efficiency of information processing (Friston & Kiebel, 2009) as a function of prior knowledge.

The mPFC is a brain region that has been attributed to diverse cognitive processes, including many with a

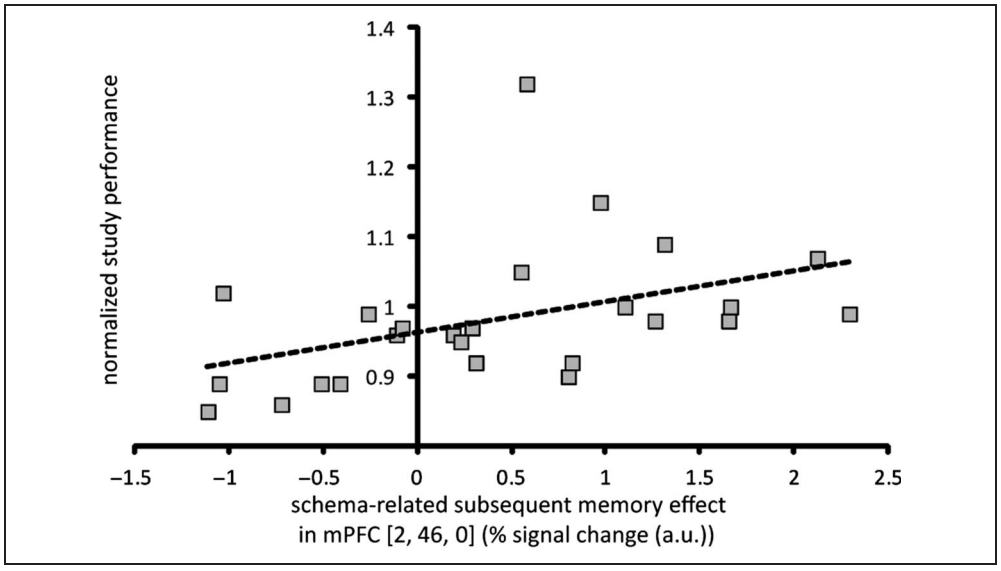

Figure 4. Correlation between mPFC activity for the schema subsequent memory contrast (schema correct items > schema incorrect items) and progress in study performance (normalized grades; $r(24) = .431$, $p < .05$).

mnemonic nature (Nieuwenhuis & Takashima, 2011; Frankland & Bontempi, 2006; Maguire, 2001), but its exact role in these processes remains unclear. Although the exact homologue of the mPFC in rodents and humans is still a matter of debate (Ongur & Price, 2000) and functional structure of the mPFC is still unclear, studies in both species consistently support its role in memory. Regarding conceptual learning, the mPFC is thought to be related to conceptual knowledge integration (Kumaran, Summerfield, Hassabis, & Maguire, 2009) and conceptual comprehension (van Kesteren, Fernandez, et al., 2010; Mar, 2004; Maguire, Frith, & Morris, 1999). More generally, the mPFC is also related to parallel encoding processes (Tse et al., 2011), remote associative memory retrieval (van Dongen et al., 2011; Takashima et al., 2007; Bontempi, Laurent-Demir, Destrade, & Jaffard, 1999) and retrieval of self-knowledge (Macrae, Moran, Heatherton, Banfield, & Kelley, 2004) and has been shown to actively replay learning-related neuronal spiking patterns during sleep in rodents (Peyrache, Khamassi, Benchenane, Wiener, & Battaglia, 2009; Takehara-Nishiuchi & McNaughton, 2008). Of specific relevance is that mPFC lesions lead to an absence of memory enhancement based on semantic congruency (Kan, Alexander, & Verfaellie, 2009), suggesting its importance in integrating or assimilating new information. In that way, its proposed contribution is to lay the foundations for enhanced future learning, both by detecting activated schemas and by assimilating novel, related information into these activated schemas (van Kesteren et al., 2012).

Schema theory has been described as knowledge organized into an elaborate network of abstract mental structures, which represent one's understanding of the world (Bartlett, 1932). Optimal construction and usage of a schema is thus recommended to lead to better structured learning (Ruiter, van Kesteren, & Fernandez, 2012; Bransford et al., 2000), until and if one's existing schema no longer maps onto the known world. Until now, research on schema theory has primarily focused on theoretical models aimed at explaining strictly behavioral findings. Now, using neurobiological techniques in animals and brain imaging techniques in humans, we can pave the way to better understand the neural mechanisms underlying the previously hypothesized different subprocesses of schema-related learning (i.e., selection, abstraction, interpretation, and integration; Alba & Hasher, 1983). Our findings focus on the interpretation and integration steps, indicating that distinct brain regions are differentially activated during conceptual learning but do not yet tap into selection and abstraction processes presumably represented in posterior, perceptual brain regions (Friston & Kiebel, 2009). Future research should investigate these different subprocesses more explicitly.

Besides schema effects on memory, also novelty, or mismatches to a schema can show enhancing memory effects in specific cases (Tulving & Kroll, 1995). This mismatching process has been consistently attributed to processing in the MTL (Kumaran & Maguire, 2007; Strange & Dolan, 2001). We believe these findings are consistent with the model described above, when considering that newly learned information always either matches or mismatches to some extent with prior information. On the basis of earlier findings (Tse et al., 2007, 2011; van Kesteren, Fernandez, et al., 2010; van Kesteren, Rijpkema, et al., 2010; Maguire et al., 1999) and theories (van Kesteren et al., 2012) and the results described here, we thus hypothesize that mPFC serves to assimilate new information into a schema by activating (or retrieving) the schema enabling integration of novel information, whereas MTL detects mismatches with a schema and serves to bind directly different parts of the memory trace into a specific episodic memory (for further explanation, see Ruiter et al., 2012). Additional to encoding, differential effects of encoding on consolidation of schema-related and schema-unrelated memories are conceivable (see e.g., van Kesteren, Rijpkema, Ruiter, & Fernandez, 2013; Tse et al., 2007). Because we only tested memory after 24 hr, we cannot dissociate encoding from consolidation effects. Regardless, our fMRI data obtained during study suggest that already encoding processes are affected by schema, which in turn might modulate subsequent consolidation effects.

The current experimental design allowed us to correlate brain findings with real-world performance in the form of university grades. Yet, assessing the effect of a certain brain process on study success is far from straightforward. Student grades may reflect any of a host of influences, not just the brain process of interest. A large-scale educational study has shown that correcting for previous scores does a good job of capturing the various external influences students are exposed to (Chetty, Friedmann, & Rockoff, 2013). Thus, we correlated medial prefrontal activity during successful encoding of new, schema-related information to the mean second-year grades corrected by mean first-year grades. We think that these measures provide the most valid correlation between brain activity and real-world behavior given that both are related to schema learning, once in the scanner and once at university. However, we acknowledge that these measures are not optimally specific, because we cannot derive for the normalized grades an interaction-based measure providing optimal specificity for schema-related knowledge acquisition at university. Therefore, this correlation needs to be interpreted cautiously. The positive relationship found may suggest that greater neural processes of schema-related encoding are associated with greater ability to acquire new, related information also in the real world. We are well aware of the limitations this correlation bears, but we believe that our finding allows formulating a working hypothesis for future research probing the role of the mPFC in academic performance.

The interactions we depict are based on the maximum interaction effect in both mPFC and MTL. They also

show enhanced activity for schema-unrelated and schema-related misses, respectively (Figure 2B). These observations are difficult to reconcile given the way we extracted the data that is biased to find the maximal interaction effect and thus also differences in misses between the schema conditions. In functional terms, one may speculate that they may be related to inappropriate classification of schema-unrelated information (schema-unrelated misses) leading to medial prefrontal processes underlying assimilation of this information into a falsely related schema. On the contrary, when schema-related information is encoded via the MTL instead of being directly assimilated by the mPFC (schema-related misses), this might result in more misses as well. However, these explanations are mere speculations at this stage; further studies will be needed to investigate these ideas. Also, we acknowledge that the mask used for SVC reducing our search space for our statistical analysis in the mPFC might not be optimal as it is linked to activity measured during a retrieval task. As functional differentiation within the mPFC is still a largely unresolved issue in terms of mnemonic operations, future experiments are necessary to better understand medial prefrontal contributions to schema-related encoding, consolidation, and retrieval processes.

Experiments that are more closely related to real-life situations are impossible to perform without taking into account inherent confounds. Therefore, we spent special caution to control for potential confounds related to the ecological validity of the design. First, we were particularly careful when constructing the sentences that were used as stimuli in this experiment. We extensively piloted the sentences, subsequently reconstructed them, made sure there were no differences in length and word frequency of the sentences, and corrected for sentences that were already known by the participants in the encoding stage of the experiment. In doing so, we counterbalanced the sentences across the two disciplines to our maximum capability. Furthermore, because the participants from the two different disciplines were analyzed together as one group, possible group differences beyond the traits we controlled for are not likely to have an effect on our results. Moreover, analyses were performed using a delta function model of brain activity, taking into account differences because of attention toward the end of the trial. Also, RT differences were not found to be significantly different for the different conditions. Thus, controlling for all these factors, we strongly believe that potential confounding differential effects on schema-related versus schema-unrelated memory encoding did not influence our results. Nevertheless, we acknowledge that there might be differences in confidence and motivation between the conditions, which may be inherently related to the type of knowledge that the participants were acquiring. Such difference in expectancy is however likely the case for all studies contrasting two encoding conditions with higher and lower probability of subsequent memory, for instance, in deep versus shallow study tasks, but participants are usually not instructed to think about it. These factors can be better controlled in future experiments, when using, for example, artificially induced schemas or motivationally equal schema knowledge (see, e.g., van Kesteren, Beul, et al., 2013).

In summary, the results reported here show that a schema, represented as prior conceptual knowledge in the brain, facilitates encoding of new conceptual information related to this schema in a university setting. This facilitation leads to enhanced memory, altered activity in mPFC as opposed to MTL in comparison with schema-unrelated memories, and less connectivity between these regions. Moreover, schema-related mPFC activity is predictive of future performance. These results are of great importance for further understanding the fundamental neural principles of conceptual memory encoding and consolidation. Furthermore, as the acquisition and long-term retention of conceptual knowledge is one of the main objectives of (academic) education, these and future endeavors investigating the role of prior knowledge in conceptual knowledge acquisition could be of crucial significance for bridging the gap between neuroscience and education (Ruiter et al., 2012; Goswami & Szucs, 2011; Ansari & Coch, 2006). Next to investigating the schema effect in general, future research might focus on schema formation or adjustment according to newly learned information.

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