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The neurocognitive basis of feature integration

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The Neurocognitive Basis of Feature Integration

André W. Keizer

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The Neurocognitive Basis of Feature Integration

Proefschrift

ter verkrijging van
de graad van Doctor aan de Universiteit Leiden,
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door

André Willem Keizer
geboren te Leeuwarden
in 1980

Promotiecommissie

Promotor	Prof. dr. B. Hommel
Overige leden	Prof. dr. P. Roelfsema (<i>University of Amsterdam</i>) Prof. dr. E. Crone Prof. dr. N. O. Schiller Dr. S. Nieuwenhuis Dr. G. P. H. Band

“Zoals je met een lens de achtergrond onscherp kunt draaien, zo kun je ervoor zorgen dat de realiteit van de ander langzaam onscherp wordt, korreliger, steeds korreliger, tot die korrels beloftes worden.”

Arnon Grunberg – Fantoompijn

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Chapter 1

General Introduction

The brain is modular

One of the most striking features of the brain is that it is modular; it consists of often highly specialized areas. The brain can be broadly divided in distinct areas for processing sensory information, areas that are important for storing information and areas important for planning and executing actions. One of the best studied brain regions is the occipital cortex, which is known to be important for processing visual features of the environment. The visual cortex is subdivided in areas specialized for processing basic visual features such as color in V4 (Zeki et al., 1991), shape in the lateral occipital cortex (LOC; Kourtzi & Kanwisher, 2000) and motion in MT/MST (Tootell et al., 1995; Zeki et al., 1991), but also for higher order features, or feature compounds such as faces in the fusiform face area (FFA; Kanwisher, McDermott, Chun, 1997) and houses in the parahippocampal place area (PPA; Epstein & Kanwisher, 1998). Moreover, the processing of visual information can be subdivided into two pathways; a dorsal stream, which contains areas that are specialized in processing spatial and action-related features and a ventral stream, which contains areas that are specialized in non-spatial features (Milner & Goodale, 1995).

Behavioral investigations of feature integration

The modular organization of the brain requires effective communication in order to integrate the information that is represented in distinct brain areas. An example of the necessity to integrate is when the visual field consists of multiple objects. When these objects have different colors and shapes, there needs to be a mechanism that enables the system to associate the correct color with the correct shape. The need for a mechanism that is responsible for integration of information that is represented in distinct brain modules has been commonly referred to as the 'binding problem' (Treisman, 1996).

One way to investigate the binding problem is to study the possible behavioral consequences of integrated features. A method that has been used in many studies on the binding problem is the investigation of sequential effects. In a paradigm originally designed by Hommel (1998), subjects are subsequently confronted with two objects that consist of multiple features (for instance shape and location, Figure 1). When subjects have to make a discriminatory response to one of the features of the second object (S2), performance (RTs and error rates) is influenced by the preceding object (S1). More specifically, performance on S2 is generally good (fast RTs and low error rates), when both features are repeated, or when both features are alternated from S1

to S2. However, performance is impaired (slow RTs and high error rates) when one of the features is repeated, while the other is alternated.

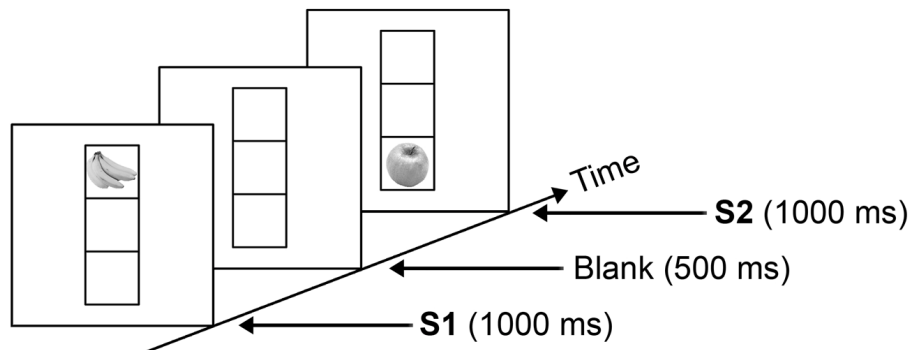


Figure 1. Example trial of the binding paradigm.

It has been proposed that this behavioral pattern can be explained as a signature of the integration that occurs on S1. If an association is established between two features, repeating one of these features automatically reactivates the previously associated feature in a kind of pattern-completion process. In the case of partial repetition of features, the reactivation of a feature that does not reflect the current sensory input, or ‘event’, and it therefore leads to conflict. The increased reaction times and error rates are thought to reflect this conflict, since additional processing is needed to suppress the erroneously activated feature and remove the association between the two features that were presented on S1, a process that has been called ‘unbinding’ (Colzato, van Wouwe, Lavender, & Hommel, 2006).

These ‘binding costs’ have not only been shown for arbitrary visual features of an object, but also for different sensory domains (Zmigrod & Hommel, 2009) and representations of actions (Colzato, Raffone & Hommel, 2006; Hommel, 1998). The term ‘event-files’ has been coined to describe bindings that involve these different representational domains (Hommel, 1998).

Importantly, integration of features in the above-described paradigm is not necessary for the task that subjects have to perform. Binding costs can thus be seen as a reflection of implicit, automatic integration of features. This does not imply that goal-directed, top-down processes cannot influence the maintenance of relational information between features. Indeed, it has been shown that the amount of attention

devoted to S1 influences binding costs (Colzato, Raffone & Hommel, 2006). Moreover, previous research has shown that binding costs are larger when visual feature conjunctions include images of real objects. The authors suggest that real objects elicit top-down priming due to a conceptual match in long-term memory (Hommel & Colzato, 2009; Colzato, Raffone, and Hommel, 2006).

How do brain modules communicate?

It has been proposed that neural synchrony is the underlying brain mechanism that enables feature binding to occur. Originally, it was the work of Engel and Singer on animals (for an overview, see: Engel & Singer, 2001) that spurred theories about the functional relevance of neural synchronization in feature integration. However, many findings have shown that neural synchronization can also be demonstrated in EEG-recordings of human subjects (for an overview, see: Jensen, Kaiser & Lachaux, 2007). Neural synchrony refers to the coherence of neural firing in distinct groups of neurons. When two features that are represented in distinct brain areas are bound together, the groups of neurons that represent these features fire in the same frequency in phase. In this way, an association between two representations can be formed and maintained, even though a physical distance separates the two representations. It has been suggested that neural synchrony reflects a communication window or channel that can overcome the noise of the neural firings that occur between the two groups of neurons (Fries, 2005). In concordance with this theory, it has been proposed that the firing frequency decreases when larger physical distances between neural representations have to be bridged (Varela, Lachaux, Rodriguez & Martinerie, 2001). It has been demonstrated that neural synchrony in the gamma range (~30-100 Hz) occurs when visual features are integrated (Engel & Singer, 2001). In contrast, neural synchronization in the beta range (~12-20Hz) has shown to be important for integration between visual and auditory information (von Stein, Rappelsberger, Sarnthein & Petsche, 1999) and between visual information and motor information (Roelfsema, Engel, Koenig & Singer, 1997).

Even though neural synchrony has been deemed important for many cognitive functions, such as (visual) awareness, short-term memory, long-term memory and attention, all of these functions rely on communication and integration of information represented in distinct brain areas. In the case of (visual) awareness, neural synchrony in the gamma range has been associated directly with binding processes. In other words, binding through neural synchrony has been proposed to be a necessary condition for awareness (Engel & Singer, 2001). Short-term memory and attention have also been associated with neural synchronization in the gamma range and can

be seen as the way frontal brain areas, which are associated with top-down control, influence local representations of for instance sensory information. It has also been shown that increases of synchronization in the gamma band reflect the 'bias-signal', which facilitates processing of attended sensory information (Fell, Fernández, Klaver, Elger & Fries, 2003). Moreover, increased synchronization in the gamma band reflects can reflect the retention of (sensory) information in short-term memory (Tallon-Baudry & Bertrand, 1999). Again, top-down control may be responsible for influencing local representations during short-term memory retention.

Finally, the role of neural synchronization in long-term episodic memory has also been demonstrated (Klimesch, 1999; Sederberg, Kahana, Howard, Donner & Madsen, 2003). It has been shown that synchronization in the both the gamma (~30-100 Hz) and theta range (4-8 Hz) are related to encoding and retrieval of episodic information in long-term memory. Multiple brain regions are involved in long-term memory processes. The most well-known brain area that is important for the formation of episodic memory traces is the medial temporal, which includes the hippocampus (Squire, Stark & Clark, 2004). Second, research has shown that (pre)frontal areas are important for top-down control of consolidation and retrieving of episodic information (Simons & Spiers, 2003). Finally, there is evidence that the posterior parietal cortex is involved in the attentional processing demands that accompany retrieval of episodic memory traces (Cabeza, Ciaramilli, Olson & Moscovitch, 2008). During encoding or retrieval of information in long-term memory, all these areas must communicate effectively with each other, but also with brain areas that represent the to-be-encoded or to-be-retrieved information; communication which may be supported by neural synchronization.

Beyond correlations, tools for investigating the functional relevance of neural synchronization

Even though many studies have demonstrated correlations between neural synchronization and feature integration, the functional relevance of neural synchronization in feature binding is still under heated debate, on a theoretical level (Ghose & Maunsell, 1999; Reynolds & Desimone, 1999; Shadlen & Movshon, 1999; Treisman, 1999) and due to empirical studies showing an absence of neural synchrony during integration demanding situations (Lamme & Spekreijse, 1998), contour grouping (Roelfsema, Lamme & Spekreijse, 2004) and motion coherence (Thiele & Stoner, 2003). One of the core arguments against the functional relevance of neural synchronization is based on the fact that many of the supporting empirical findings are correlational. This leaves the possibility that neural synchronization is epiphenomenal;

it may co-occur during feature integration, but it does not reflect the underlying mechanism that is responsible for feature integration.

In order to investigate the functional relevance of neural synchronization in feature binding and other cognitive processes, methods are required that enable experimental manipulation of neural synchronization itself. In this way, the effects of altered neural synchronization on feature integration and other cognitive processes can be measured, resulting in greater explanatory power than the demonstration of mere correlations.

There are several techniques, with which neural synchronization can be experimentally manipulated. First, neural synchronization can be manipulated indirectly using psychopharmacological substances that are known to influence neural synchronization via neurotransmitter systems. The muscarinic-cholinergic neurotransmitter system is known to be directly related to neural synchronization in the gamma range, especially in the visual cortex (Rodriguez-Bermudez, Kallenbach, Singer & Munk, 2004). Findings on human subjects have shown that psycho-active drugs that are known to manipulate the muscarinic-cholinergic neurotransmitter system, such as alcohol and caffeine have profound effects on feature integration (Colzato, Erasmus, & Hommel, 2004; Colzato, Fagioli, Erasmus, & Hommel, 2005). These effects have later been replicated with more specific muscarinic-cholinergic agonists and antagonists (Botly & De Rosa, 2007; Botly & De Rosa, 2008).

Promising methods that have been used to manipulate neural synchrony directly are repetitive transcranial magnetic stimulation (rTMS), the presentation of visual flicker stimuli and neurofeedback.

It has been shown that rTMS can influence neural synchronization in frequencies such as the alpha band (8-12 Hz) and beta band (14-30 Hz; for an overview, see Thut & Miniussi, 2009). However, much research on the use of rTMS is needed, since there currently does not seem to be a one-to-one relationship between the frequency of magnetic stimulation that is used and the frequency band that is influenced (Thut & Miniussi, 2009).

Presenting oscillating visual stimuli have shown to 'entrain' the firing frequency of neurons in the visual cortex (Herrmann, 2001). In other words, neural synchronization in particular frequency bands can be studied by presenting oscillating visual stimuli in the frequency that is under investigation. Indeed, a recent study by Bauer, Cheadle, Parton, Müller and Usher (2009) showed that subliminal visual flicker that oscillated in the gamma range (at 50 Hz) facilitated the processing of an upcoming target stimulus, possibly by mimicking the top-down bias-signal that is known to occur in the gamma range.

Finally, neurofeedback has been shown to be effective in increasing and decreasing neural synchronization directly in specific frequency bands (Bird, Newton, Sheer, & Ford, 1978; Vernon et al., 2003). Neurofeedback has mainly been studied as a possible treatment method for psychological and neurological disorders that are associated with impairments of neural synchrony, such as ADHD (Fuchs, Birbaumer, Lutzenberger, Gruzelier, & Kaiser, 2003), migraine (Kropp, Siniatchin, & Gerber, 2002), and epilepsy (Kotchoubey, Strehl, Holzapfel, Blankenhorn, Fröscher, & Birbaumer, 1999). However, recent studies by Egner & Gruzelier (2001, 2003, 2004) and Vernon et al. (2003) have shown that neurofeedback can be used to manipulate neural synchronization and study its effects on cognitive processes.

Outline of the thesis

Chapter 2 describes a study in which we investigated whether binding can occur between features that are processed in the dorsal stream and features that are processed in the ventral stream. It has been hypothesized that the dorsal stream of visual information processing operates exclusively online and has no access to memory (Cant, Westwood, Valyeara, & Goodale, 2005; Milner & Goodale, 1995). If this is indeed the case, sequential effects of binding, which reflect a memory trace of previous communication, should not be expected between dorsal and ventral features. Our results are inconsistent with this view; we showed that binding can occur between objects that are known to be processed in the ventral stream (faces and houses) and motion, which is known to be processed in the dorsal stream.

Chapter 3 investigates one of the core assumptions regarding the neural basis of the sequential effects of feature integration. As described above, partial repetition of features is thought to result in performance costs due to automatic reactivation of a previously associated, now inappropriate feature. Using an event-related fMRI study, we provided direct evidence for this mechanism. The results showed that perceiving a face moving in the same direction as a just-perceived house increased activation in the PPA.

Chapter 4 explores whether binding can occur in true absence of top-down signals and investigates the relationship between implicit, automatic binding and explicit binding. First, our results show that binding between visual features does occur in the absence of task-relevant information, but only between real objects and not between arbitrary features. This is in accordance of a previous study which showed that binding costs are larger when real objects are included (Colzato, Raffone, and Hommel, 2006; Hommel & Colzato, 2009), due to top-down priming resulting from a conceptual match in long-term memory. Our findings show that top-down priming

resulting from a match in long-term memory is sufficient to elicit binding costs (experiment 1a and 1b). Second, the results of experiment 2a and 3a showed that explicit storage of visual relations in short-term memory does not result in binding effects of arbitrary features in the absence of task-relevant information (Experiment 2a), suggesting that the absence of binding costs can be attributed to an absence of retrieval processes. Interestingly, binding effects disappeared between real objects as a result of explicit storage (Experiment 2b), which points to interference of top-down related retrieval processes by short-term memory processes.

Chapter 5 investigates neurofeedback as a possible method for studying the functional role of gamma band activity (GBA) in feature binding. The results showed that subjects are indeed able to enhance occipital GBA in the course of 8 neurofeedback sessions. Moreover, enhanced GBA resulted in a decrease of visual binding costs, but not of visuo-motor binding costs. We hypothesize that enhanced occipital GBA reflects increased top-down control, which leads to increased flexibility in the handling of event files. This conclusion is supported by the finding that the change in GBA correlated positively with the change of fluid intelligence, which is arguably related to control processes.

Chapter 6 replicates the findings of chapter 5 in that increased GBA causes a decrease in binding costs. The results of this study suggest that increased occipital GBA is caused by an increase of frontal GBA, which again points to enhanced top-down control as a result of GBA-enhancing neurofeedback. Moreover, the results of this study showed that increased GBA led to an increase of the ability to retrieve contextual information from long-term memory, which has also been associated with frontal control mechanisms.

Chapter 7 contains the summary and conclusions.

The following references correspond with chapters 2-6 of this thesis:

Keizer, A. W., Colzato, L. S., & Hommel, B. (2008). Integrating faces, houses, motion, and action: Spontaneous binding across ventral and dorsal processing streams. *Acta Psychologica*, 127, 177-185. (Chapter 2).

Keizer, A. W., Nieuwenhuis, S., Colzato, L. S., Theeuwisse, W., Rombouts, S. A. R. B., & Hommel, B. (2008). When moving faces activate the house area: an fMRI study of object file retrieval. *Behavioral and Brain Functions*, 4:50. (Chapter 3).

Keizer, A. W., & Hommel, B. The control of object-file retrieval. In preparation. (Chapter 4).

Keizer, A. W., Verschoor, M. Verment, R. S., & Hommel, B. (2010). Enhancing gamma band power (36-44Hz) improves feature-binding flexibility and intelligence. *International Journal of Psychophysiology*, 75, 25-32. (Chapter 5).

Keizer, A. W., Verment, R. S. & Hommel, B. (2010). Enhancing cognitive control through neurofeedback: A role of gamma-band activity in managing episodic retrieval. *NeuroImage*, 49, 3404-3413. (Chapter 6).

Chapter 2

Integrating Faces, Houses, Motion and Action: Spontaneous Binding Across Ventral and Dorsal Processing Streams

This chapter is published as: Keizer, A. W., Colzato, L. S., & Hommel, B. (2008). Integrating faces, houses, motion and actions: Spontaneous binding across ventral and dorsal processing streams. *Acta Psychologica*, 127, 177-185.

Abstract

Perceiving an event requires the integration of its features across numerous brain maps and modules. Visual object perception is thought to be mediated by a ventral processing stream running from occipital to inferotemporal cortex, whereas most spatial processing and action control is attributed to the dorsal stream connecting occipital, parietal, and frontal cortex. Here we show that integration operates not only on ventral features and objects, such as faces and houses, but also across ventral and dorsal pathways, binding faces and houses to motion and manual action. Furthermore, these bindings seem to persist over time, as they influenced performance on future task-relevant visual stimuli. This is reflected by longer reaction times for repeating one, but alternating other features in a sequence, compared to complete repetition or alternation of features. Our findings are inconsistent with the notion that the dorsal stream is operating exclusively online and has no access to memory.

Introduction

Processing a visual object in the human brain involves numerous functionally and spatially distinct cortical areas. For instance, the shape and color of an object are coded in dedicated feature maps in V1-4, the features of a face in motion are registered in the fusiform face area (FFA) (Kanwisher, McDermott, & Chun, 1997) and the motion-sensitive area MT/MST (Tootell et al., 1995; Zeki et al., 1991) while a house or landscape will be coded in the Parahippocampal Place Area (PPA) (Epstein & Kanwisher, 1998). This form of distributed processing creates multiple binding problems (Treisman & Gelade, 1980; Treisman & Schmidt, 1982) which call for some kind of integration.

A well established method to indicate what kind of information is integrated under what circumstances is the analysis of interactions between sequential effects. The logic is straightforward: if the codes of two given features or objects have been bound together they should from then on act as a pair. If so, reactivating one of the codes (through repeating the corresponding stimulus) should reactivate the other code as well, even if the two coded features are uncorrelated and co-occurred only once. An implication of this mechanism would also be that performance is impaired if one member of the pair is repeated but the other is not. Indeed, repeating the shape of an object but changing its color or location produces slower reaction times (RTs) and more errors than repeating both features or repeating none (Hommel, 1998; Hommel, Proctor, & Vu, 2004; Kahneman, Treisman, & Gibbs, 1992) suggesting that processing an object leads to the spontaneous binding of the neural codes of its features. Interestingly, this logic also seems to apply to perception-action associations: repeating an object feature but changing the action it accompanies produces worse performance than repeating both or neither (Hommel, 1998, 2004) suggesting that stimulus features get bound to the actions they “afford”.

The object features investigated so far in research on binding phenomena, such as shape, color, or allocentric location, can all be considered to be processed by ventral pathways in the human brain (Goodale & Milner, 1992; Milner & Goodale, 1995; Neggers, Van der Lubbe, Ramsey, & Postma, 2006). Ventral pathways are commonly distinguished from dorsal pathways in terms of the information they process. Whereas earlier approaches associated visual ventral and dorsal pathways with the processing of nonspatial (what) and spatial (where) information, respectively (Ungerleider & Mishkin, 1982) more recent accounts assume that ventral pathways process information necessary for object perception, whereas dorsal pathways process action-relevant information (Creem & Proffitt, 2001; Goodale & Milner, 1992; Milner & Goodale, 1995). Importantly, dorsal pathways are assumed to operate exclusively

online and, thus, to have no memory (beyond a few milliseconds, see Milner & Goodale, 1995). For instance, Cant, Westwood, Valyeara, and Goodale (2005) found that visually guided actions were not influenced by previewing the goal object, while memory guided actions were. They argue that visually guided actions are entirely fed by dorsal pathways, which because of their nonexisting short-term memory capacity cannot maintain information necessary to produce priming effects. In contrast, memory guided actions involve ventral pathways that do have sufficient short-term memory capacity.

Considering that binding stimulus (and/or response) features can only affect later performance if the binding is maintained, the apparently different memory characteristics of ventral and dorsal pathways raise the question whether binding takes place across dorsal and ventral pathways at all and/or whether such bindings can be maintained long enough to affect performance a second or more (the typical interval between prime and probe in binding studies) later. We investigated this issue by testing whether binding effects can be demonstrated between visual object features (or even whole objects) that are presumably processed in different pathways. In particular, we tested whether motion (a dorsal feature) can be bound to faces and houses (ventral features), and to manual responses. We carried out four experiments using the standard paradigm introduced by Hommel (1998). Given that our crucial experiments, 3 and 4, used faces and houses as “ventral” stimuli, and given that these stimuli were never used in sequential studies before, we first ran two more experiments (1–2) to make sure that the previous demonstrations of spontaneous binding between shape, color, and location extend to these more complex stimuli.

Experiments 1 and 2

We used two modified versions of the S1–S2 paradigm introduced by Hommel (1998; for an overview, see Hommel, 2004). In the task employed in Experiment 1, subjects are confronted with two objects, separated in time by a short interval, and they respond to one feature of the second object (S2) while ignoring the first (S1). As discussed before, such setups create (typically binary) interactions that are indicative of feature integration processes: repeating one of two features but not the other yields worse performance than repeating both or none (Hommel, 1998). In Experiment 1, we presented blended face-house compounds as S1 and S2, and S2 could repeat or alternate the picture of the face and the picture of the house to create an orthogonal 2 X 2 design.

As already discussed, integration can also include the response, leading to interactions between stimulus (feature) repetition and response repetition (i.e., better

performance if stimulus and response are both repeated or both alternated). To investigate whether this pattern extends to faces and houses, participants in Experiment 2 were to respond to S1 by means of a precued manual reaction (R1; see Hommel, 1998 and Figure 2). This design creates temporal overlap between S1 and R1 (which is known to be a sufficient condition for integration: Hommel, 2004) without making R1 contingent on S1, which allows for the orthogonal manipulation of stimulus and response repetition.

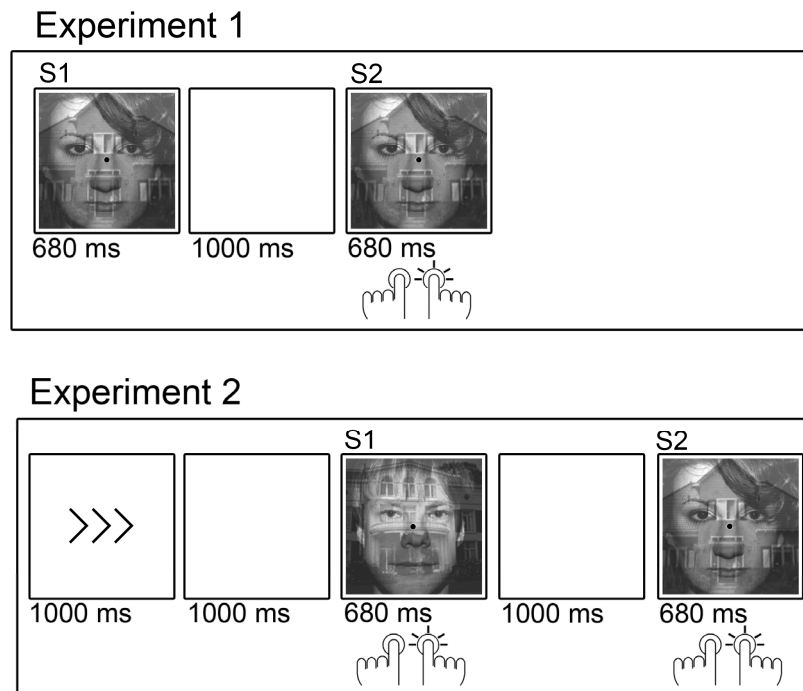


Figure 2. Overview of the display and timing of events in Experiments 1 and 2.

Methods

Participants

22 and 20 healthy, young undergraduates participated in Experiment 1 and Experiment 2, respectively. All subjects participated in exchange for course credit or money.

Stimuli and task

Following O'Craven, Downing, and Kanwisher (1999) each stimulus was composed by transparently superimposing one of eight grayscale front-view photographs of male (4) and female (4) faces on one of eight grayscale photographs of houses. The images were cropped to fit a square size (10° by 10°). All images were adjusted to assure the same average luminance. The house-face combinations of the 128 trials of Experiment 1 were constructed by randomly drawing from the eight possible houses and faces, except that the stimuli were chosen to result in equal proportions (32 trials) in the four cells of the 2 X 2 analytical design (house repetition vs. alternation X face repetition vs. alternation). The trials of Experiment 2 were composed the same way, except that adding the response-repetition manipulation increased the design cells to eight (house repetition vs. alternation X face repetition vs. alternation X response repetition vs. alternation) and the number of trials to 256.

In Experiment 1 (see Figure 2a), subjects were presented with a picture of a face transparently superimposed on a house, twice within a single trial and they were instructed to make a discriminative response (R2) to the gender of the second stimulus (S2). Half of the participants responded to the male and the female face by pressing the left and right key of a computer keyboard, respectively, while the other half received the opposite mapping. S1 appeared for 680 ms, followed by a blank interval of 1000 ms. S2 appeared and stayed until the response was given or 2000 ms had passed. S2 was followed by a fixation circle (diameter: 0.5°), which stayed for a randomly chosen duration of between 1000 and 2500 ms (varied in 100-ms steps). If the response was incorrect, auditory feedback was presented.

The procedure of Experiment 2 was the same, with the following exceptions. Participants carried out two responses per trial. R1 was a simple reaction with the left or right key, as indicated by a 1000-ms response cue (three arrows pointing either leftward or rightward) appearing 2000 ms before S1. R1 was to be carried out as soon as S1 appeared, disregarding S1's attributes. As in Experiment 1, R2 was a binary-choice reaction to the gender of S2.

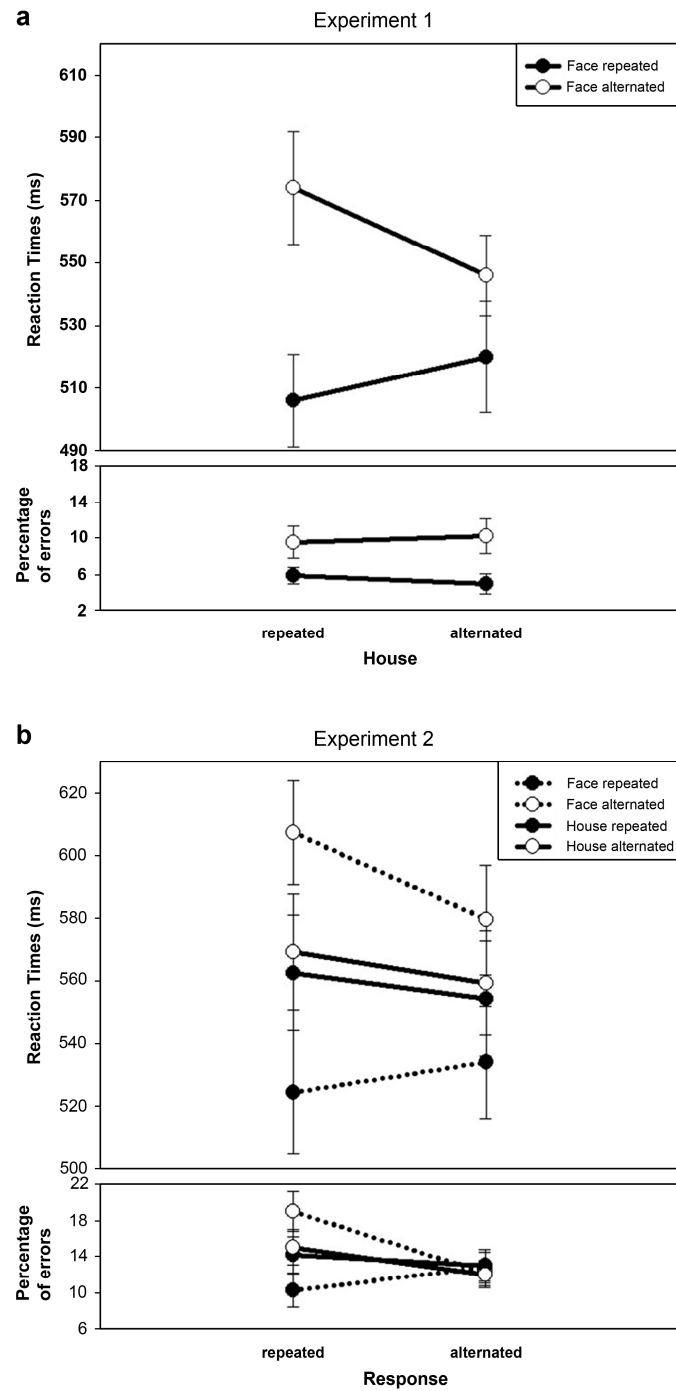
Results and discussion

RTs and error rates were analyzed by means of repeated-measures ANOVAs with the factors face repetition (vs. alternation) and house repetition in Experiment 1, and with face repetition, house repetition, and response repetition in Experiment 2. The RTs revealed a main effect of face repetition in Experiment 2, $F(1,19) = 73.918$, $p < .001$. More importantly, there were significant interactions between face repetition and house repetition in Experiment 1 (Figure 3a), $F(1,21) = 13.373$, $p < .01$ and in

Experiment 2 (Figure 3b), $F(1,19) = 6.831$, $p < .05$, indicating significantly faster RTs when both features were repeated or alternated, as compared to when only one was repeated but the other alternated. Moreover, Experiment 2 provides evidence for binding between faces and responses, as indicated by the significant interaction between face repetition and response repetition, $F(1,19) = 30.184$, $p < .001$.

Error rates showed comparable results: a main effect of face repetition was obtained in Experiment 1, $F(1,19) = 20.958$, $p < .001$, and in Experiment 2, $F(1,21) = 11.059$, $p < .01$, a response repetition effect in Experiment 2, $F(1,19) = 5.208$, $p < .05$, and a significant interaction between face and response repetition in Experiment 2, $F(1,19) = 47.805$, $p < .001$.

Experiments 1 and 2 provided evidence for the spontaneous integration of blended faces and houses: repeating a face was beneficial if the house was also repeated, but turned into a cost if the house changed. Hence, the mere co-occurrence of a face and house was sufficient to create a binding between their representations. Furthermore, Experiment 2 provides evidence for a binding between the task-relevant stimulus feature (face) and the response, even though the latter was not determined, but only triggered by the former. This extends previous findings of stimulus-response integration obtained with simpler stimuli, but it also shows that face-house compounds were not treated as a single stimulus. If they were, the hint to the integration of faces and houses would be of less theoretical interest—even though this would fail to explain why “complete alternations” were not associated with the worst performance. Also in line with previous findings (Hommel, 1998), sensorimotor integration was restricted to the task-relevant stimulus information (faces), suggesting that the creation and/or the retrieval of bindings is under attentional control (Hommel, 2007).



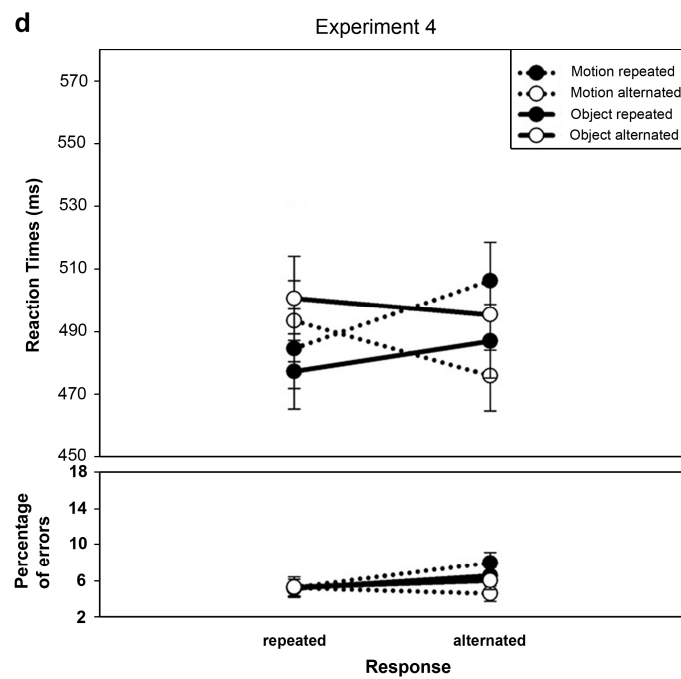
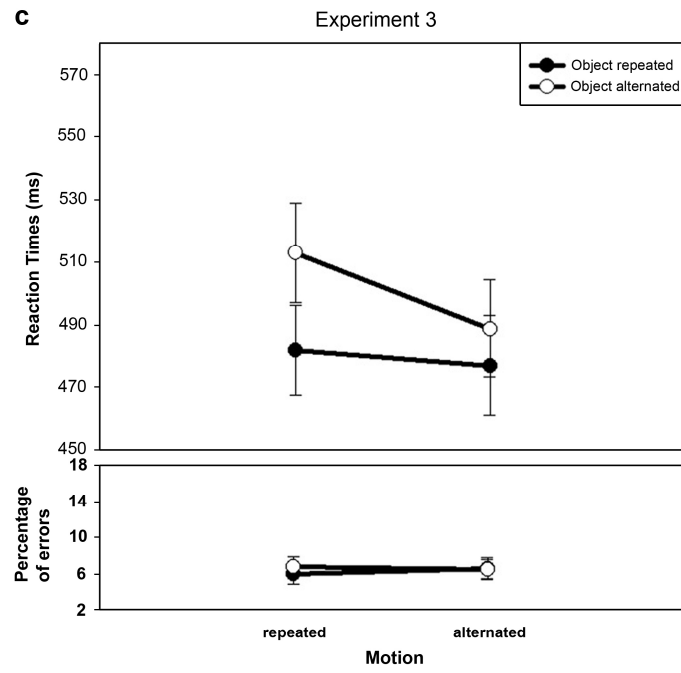


Figure 3. Error bars represent standard errors in all graphs. (a) and (b) Mean reaction times and error percentages for Experiments 1–2, as a function of repetition vs. alternation of stimulus face and stimulus house (Experiment 1), or of stimulus face, stimulus house, and response (Experiment 2). (c) and (d) Mean reaction times and error percentages for Experiments 3–4, as a function of repetition vs. alternation of stimulus motion and the moving object (face or house; Experiment 3), or of stimulus motion, moving object, and response (Experiment 4).

Experiment 3 and 4

Experiments 3 and 4 studied whether bindings can link information processed in ventral pathways with motion, which is processed in the dorsal system MT/MST (Tootell et al., 1995). We still presented face-house compounds, but now faces and houses were always identical in S1 and S2 and either one or the other was continuously oscillating on a diagonal path. In Experiment 3, participants responded to the motion direction of S2 but were to ignore S1 altogether. In S1 and S2 the moving object could be the face or the house, and it could move on one or the other diagonal, so that the moving object and the direction of the motion could repeat or alternate. If encountering S1 would lead to the spontaneous integration of object and motion, repeating the object but not the motion, or repeating the motion but not the object, should lead to worse performance than complete repetitions or alternations. Experiment 4 added a precued response (R1) to the onset of S1, analogous to the design of Experiment 2. Here we expected the integration of the task-relevant stimulus feature (motion) and the response, as indicated by an interaction between motion repetition and response repetition.

Methods

Participants

19 and 20 young, healthy undergraduates participated in Experiments 3 and 4, respectively.

Stimuli and task

The procedure of Experiment 3 was as in Experiment 1, with the following exceptions. Faces and houses were always the same for S1 and S2. Either the face or the house oscillated in a straight path on one of two possible non-cardinal directions (left-up/right-down vs. right-up/left-down), while the total size of the combined images remained the same (10° by 10°). The maximal displacement caused by the motion was less than 10% of the size of the image. The moving image oscillated 2.5 cycles with a constant speed of 9° per second. Subjects performed left-right key presses (R2) to the

direction of the motion of S2, disregarding the moving object of S2 and the object and motion of S1. After every seven trials, a fixation circle was presented for 10 s. This rest period was included to allow for a later transfer of exactly the same task to a planned fMRI-study (Keizer, Nieuwenhuis, Colzato, Teeuwisse, Rombouts, & Hommel, 2009) where such rest periods are needed to prevent non-linearity effects of the BOLD-signal. The procedure of Experiment 4 was the same, except that they performed a precued, simple response to the onset of S1, just like in Experiment 2. Experiment 3 comprised 182 trials, which were randomly drawn from all combinations of the eight possible houses and faces (the particular combination was identical for S1 and S2), the two possible motions for S1 and S2, and the two possible objects that could move (either face or house); however, the stimuli were chosen to result in roughly equal proportions (averages ranging between 45 and 46) in the four cells of the 2 X 2 analytical design (repetition vs. alternation of motion X repetition vs. alternation of moving object). Experiment 4 comprised 378 trials, randomly drawn from all combinations used in Experiment 3 plus the repetition vs. alternation of the response. The stimuli were chosen to result in roughly equal proportions (averages ranging between 45 and 49) in the eight cells of the 2 X 2 X 2 analytical design.

Results and discussion

Main effects on RTs were obtained for motion repetition in Experiment 3, $F(1,18) = 9.709$, $p < .01$, and Experiment 4, $F(1,19) = 10.956$, $p < .01$, and for (moving-) object repetition in Experiment 3, $F(1,18) = 49.901$, $p < .001$, and Experiment 4, $F(1,19) = 52.122$, $p < .001$. More importantly, reliable interactions between motion repetition and object repetition provided evidence for visual integration in Experiment 3, $F(1,18) = 5.752$, $p < .05$, and in Experiment 4, $F(1,19) = 12.779$, $p < .01$. Separate analyses showed that it did not matter whether a face or a house was integrated with motion on S1, as indicated by an absence of a three-way interaction between the object that moved on S1 (face or house), repetition or alteration of the object that moved on S2 and repetition or alteration of the direction of motion on S2 in Experiment 3, $F(1,18) < 1$, and in Experiment 4, $F(1,19) < 1$. Experiment 4 points to the binding of motion and response, as indicated by the interaction between motion repetition and response repetition, $F(1,19) = 34.637$, $p < .001$. Even though less pronounced, the interaction between object repetition and response repetition was also significant, $F(1,19) = 6.553$, $p < .05$. Error rates of Experiment 3 did not yield reliable results and the errors of Experiment 4 showed a significant interaction between motion and response $F(1,19) = 9.844$, $p < .01$.

The results show significant binding between motion and the object that moved. This demonstrates that bindings between ventral and dorsal features can be created in principle and, what is more, that such bindings actually are spontaneously created even if integration is not required by the task. Experiment 4 included a response to the first stimulus, following the same logic as Experiment 2. Apart from replicating the face-motion and house-motion interactions, we found evidence for bindings between motion and response and between the moving object (be it face or house) and the response.

Interestingly, the results suggest that faces were integrated with motion in the same way as houses were. Considering that both houses and faces were not task-relevant, this outcome pattern is in line with the findings of O'Craven et al. (1999) and their claim that visual attention spreads from task-relevant features of an attended object (motion in our case) to the task-irrelevant features of that object. Apparently, then, this object-specific attentional spreading does not only affect online processing, as studied by O'Craven et al. (1999) but also affect the creation and maintenance of feature bindings. The observation that faces and houses were comparable in this respect is particularly relevant in view of claims that face information may be processed differently than house information. Even though it is clear that cortical face- and house-related areas (FFA and PPA) are both located in the ventral stream (Ishai, Ungerleider, Martin, Schouten, & Haxby, 1999) it has been argued that especially faces may be processed more holistically than places or objects are (Farah, 1996). This raises the question whether faces are integrated with other features just like house features are—a question to which our observations provide an affirmative answer.

General discussion

The first experiment extended previous demonstrations of bindings between simple features, such as shape, color, or relative location, to complex stimuli, such as faces and houses. These findings bear significance with regard to the scope of the concept of event files (Hommel, 1998, 2004) in particular, but also for the related Theory of Event Coding (TEC, Hommel, Müsseler, Aschersleben, & Prinz, 2001). The observations that motivated and supported the event-file concept were commonly related to simple features, such as line orientations and color patches, but the present findings show that the same logic applies to more complex stimulus configurations, such as faces and houses. One may ask whether stimuli like faces and houses can be still described as features, since these stimuli are composites of numerous simple features and may therefore be more accurately described as event files themselves. If so, we can conclude that event file logic seems to apply to several levels of stimulus

representation, ranging from individual features to composites. Hence, events can apparently enter new 'higher order' bindings with other event files. This possibility is also suggested by the findings of Waszak, Hommel, and Allport (2003). They found that when subjects were presented with pictures and overlapping words, they found it more difficult to switch from one task to another when the concrete stimulus had already appeared in the alternative task. It seems that stimuli and stimulus compounds can be bound to a specific task context, which is reactivated automatically when the stimulus material is repeated. Future research may determine if it is possible to distinguish between different hierarchies of bindings or even binding mechanisms.

Experiment 2 confirmed that complex stimuli also enter sensorimotor bindings, and our findings showed consistently that feature binding seems to cross border between ventral and dorsal processing pathways. Experiment 3 provided evidence that motion is automatically integrated into enduring object representations and, as confirmed by Experiment 4, into sensorimotor event representations. One may argue that at least some of our findings (Experiment 2) may not necessarily reflect binding across ventral and dorsal pathways but integration at earlier stages of visual processing (before the ventral–dorsal split), e.g., involving the thalamic nuclei and/or V1/V2. However, there are several reasons to discount this possibility. First, the results from Experiment 2 seem to suggest that face-house compounds were treated as consisting of two distinct objects, as faces selectively formed a persistent binding with action while houses did not. Second, a recent fMRI study of ours (Keizer et al., 2009) showed that encountering a face moving into a particular direction after having seen a house moving into the same direction leads to an increase in activation of the PPA—the area coding house information. This suggests that processing a particular motion direction automatically retrieved the stimulus that just moved in the same direction, which again implies that a binding between this motion and that previous stimulus has been created. Reactivating this binding reactivates PPA, but not earlier visual areas, which strongly suggests that the binding includes information from both dorsal and ventral pathways.

Taken altogether, our findings thus suggest that stimulus information coded in the ventral stream is automatically integrated with information coded in the dorsal stream, and both types of information can be integrated with temporarily overlapping actions. The integration process creates memory structures that survive at least one second (the time between the presentations of the two stimuli in our experiments), and there are reasons to believe that this is a conservative estimate (Hommel & Colzato, 2004). Primate studies have shown that the dorsal area MT/MST projects to the ventral area V4 (Maunsell & Van Essen, 1983; Ungerleider & Desimone, 1986) and it has been suggested that this projection allows for the recognition of the semantic

characteristics of biological motion (Oram & Perrett, 1994; Perret, Harries, Benson, Chitty, & Mistlin, 1990) or form defined by motion (Sary, Vogels, & Orban, 1993). Our findings suggest a far more extensive and reciprocal connectivity between dorsal and ventral processing, connectivity that apparently allows for the fast and automatic integration of information about ventral and dorsal aspects of perception and action. Thus, even though physiological findings suggest that visual information processing is distributed across two anatomically separable streams, our present observations show that this separation by no means implies poor communication between them.

Our observations also question the characterization of the dorsal stream as exclusively online and as lacking memory beyond a few milliseconds (Cant et al., 2005; Goodale & Milner, 1992; Milner & Goodale, 1995). This does not necessarily contradict the claim that the dorsal stream is particularly well-suited to inform ongoing action (Hommel et al., 2001), but it does show that dorsally coded information is involved in off-line processing and in the integration of perception and action. Our findings are in accordance with studies showing priming effects of visual motion (Campana, Cowey, & Walsh, 2002; Pinkus & Pantle, 1997) i.e., of a feature processed in the dorsal stream; (Tootell et al., 1995) suggesting that dorsally coded information can be retained for a nontrivial period of time. In addition, Chun and Jiang (1999) studied the effect of predictable, but irrelevant motion patterns of items in a search display (one target item among distractor items). They found that subjects were apparently able to use these consistencies, as target localization reaction times were faster when all items moved in a predictable manner versus an unpredictable manner. It seems that the subjects formed long-term associations between particular motion patterns and the items in the search display, which would require integration of form and motion. Our results show that these findings can be extended to online, single-trial integration of complex forms (faces and houses) and motion. A phenomenon called the 'McGurk aftereffect' can also be explained in a similar way. When subjects are presented with a sound and an incongruent mouth movement, the perception of the sound is modulated by this mouth movement to produce the well-known McGurk effect (McGurk & MacDonald, 1976). Bertelson, Vroomen, and de Gelder (2003) showed that the perception of a subsequent presentation of that same sound in isolation is still modulated by the mouth movement that accompanied the sound in the initial presentation; the McGurk aftereffect. Apparently, mouth movement and sound can form an enduring association, which results in retrieval of the mouth movement when its associated sound is presented in isolation.

Soto-Faraco, Spence, and Kingstone (2005) showed that the integration between sound and motion occurs automatically, which suggests that the McGurk

aftereffect found by Bertelson et al. (2003) is not due to top-down influences (see also Vatakis & Spence, 2008, for a related discussion).

This raises the question of why Cant et al. (2005) observed priming effects for memory guided, but not for visually guided actions. As the authors themselves acknowledge, the conclusions of Cant et al. (2005) are based on a null effect, which makes it difficult to exclude the possibility that memory guided actions are only more sensitive to priming effects than visually guided actions are—which, given the fact that continuous visual input can easily overwrite the contents of the visual short-term memory buffer, is not implausible. Also, it is theoretically possible that visual guided actions are processed via the dorsal stream, but that they are functionally distinct from the dorsal features that were used in the current study (motion and responses). This may be so for the motion-sensitive area MT, because of its previously discussed connections with ventral area V4. Moreover, the responses used in our study may be inherently different than the visual guided actions used by Cant et al. (2005) as the former may be based on a relatively more semantic judgment. If this is indeed the case and visual guided actions cannot be bound to ventral, or other dorsal features like motion and the actions used in our study, the conclusions of Cant et al. (2005) would need to be moderated accordingly.

Chapter 3

When Moving Faces Activate the House Area: An fMRI Study of Object-file Retrieval

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Abstract

The visual cortex of the human brain contains specialized modules for processing different visual features of an object. Confronted with multiple objects, the system needs to attribute the correct features to each object (often referred to as ‘the binding problem’). The brain is assumed to integrate the features of perceived objects into object files—pointers to the neural representations of these features, which outlive the event they represent in order to maintain stable percepts of objects over time. It has been hypothesized that a new encounter with one of the previously bound features will reactivate the other features in the associated object file according to a kind of pattern-completion process. Fourteen healthy volunteers participated in an fMRI experiment and performed a task designed to measure the aftereffects of binding visual features (houses, faces, motion direction). On each trial, participants viewed a particular combination of features (S1) before carrying out a speeded choice response to a second combination of features (S2). Repetition and alternation of all three features was varied orthogonally. The behavioral results showed the standard partial repetition costs: a reaction time increase when one feature was repeated and the other feature alternated between S1 and S2, as compared to complete repetitions or alternations of these features. Importantly, the fMRI results provided evidence that repeating motion direction reactivated the object that previously moved in the same direction. More specifically, perceiving a face moving in the same direction as a just-perceived house increased activation in the parahippocampal place area (PPA). A similar reactivation effect was not observed for faces in the fusiform face area (FFA). Individual differences in the size of the reactivation effects in the PPA and FFA showed a positive correlation with the corresponding partial repetition costs. Our study provides the first neural evidence that features are bound together on a single presentation and that reviewing one feature automatically reactivates the features that previously accompanied it.

Introduction

The human visual cortex is divided into specialized modules that code a variety of different visual features, like motion in area MT/MST (Tootell et al., 1995; Zeki et al., 1995) faces in the fusiform face area (FFA; Kanwisher, McDermott & Chun, 1991) and houses in the parahippocampal place area (PPA; Epstein & Kanwisher, 1998). This division of labor entails a well-known problem: When confronted with multiple objects, how does the visual system 'know' which features belong together in one object?

This so-called 'binding problem' (Treisman & Gelade, 1980) calls for the integration of information into object representations or 'object files' (Kahneman, Treisman & Gibbs, 1992). The immediate consequences of such integration have been demonstrated in an elegant study by O'Craven et al. (O'Craven, Downing & Kanwisher, 1999). Their subjects saw overlapping pictures of a house and a face, with either the house or the face moving. When subjects were asked to respond to the direction of the motion, attention spread from the motion to the object, regardless of which object was moving: Functional magnetic resonance imaging (fMRI) results showed that the PPA was activated more strongly when the house moved, and the FFA was activated more strongly when the face moved. This suggests that attending to an event creates some sort of functional link between the representations of its features, whether they are relevant (like the direction of the motion in this example) or irrelevant (like the faces or houses). Further support for this notion comes from a recent fMRI study by Yi et al. (2008) who found that face-selective regions in the FFA and lateral occipital cortex exhibited significantly less activation when (task-relevant) faces were repeated in (task-irrelevant) continuous versus discontinuous trajectories. Again, this suggests that attending to a moving object creates an object file in which object identity and spatiotemporal parameters are closely integrated.

To ensure stable percepts of objects (e.g., tolerating small changes in viewpoint or lighting), the functional links or object files need to be persistent over time. Indeed, behavioral research suggests that object files outlive the events they represent by several seconds and that they affect subsequent behavior in a systematic fashion (Yi et al., 2008; Hommel, 2004). For example, if subjects respond to one feature (e.g., shape) of a two-dimensional stimulus (e.g., varying in shape and location), they respond faster and more accurately if the two stimulus features both repeat or both alternate, than if one feature repeats while the other alternates (Colzato, Erasmus & Hommel, 2004; Colzato, van Wouwe, Lavender & Hommel, 2006; Hommel, 1998; Hommel, 2004; Hommel & Colzato, 2004; Hommel, Müsseler, Ascherleben & Prinz, 2001). Consistent with the notion of object files, this finding suggests that processing

an object binds its features such that if one or all of these features are encountered again, the whole object file is retrieved. If this involves reactivation of a feature that mismatches with features of the present object (which happens when one feature repeats and another alternates), performance is impaired because of the conflict between retrieved and perceptually available features and/or because the old associations need to be deconstructed (Colzato, van Wouwe, Lavender & Hommel, 2006). Note that the task described here did not require participants to integrate features; therefore the obtained effects provide a relatively pure measure of automatic, implicit integration processes, free of particular task-dependent strategies (O'Reilly & Rudy, 2001).

Automatic retrieval of object files has the theoretically interesting property of mimicking several effects that are often attributed to executive control processes. For example, there is evidence that at least substantial portions of the flanker-compatibility effect (Mayr, Awh & Laurey, 2003), the Simon effect (Hommel, Proctor & Vu, 2004), inhibition of return (Lupianez, Milleken, Solano, Weaver & Tipper, 2001) and negative priming (Huang, Holcombe & Pashler, 2004) are actually produced by the impact of object files formed in the previous trial. However, the neural mechanisms underlying the hypothesized object-file retrieval are unknown and direct demonstrations that feature repetition actually induces the retrieval of corresponding object files are lacking. Accordingly, the present fMRI study was designed to test whether reviewing a particular stimulus feature reactivates the features of the object it previously accompanied. The features/objects that we used to address this question were motion, faces, and houses, which, as noted above, activate distinguishable regions of the occipitotemporal cortex (O'Craven et al., 1999). These stimuli have been shown to integrate in a similar way as more basic features such as location and color (Keizer, Colzato & Hommel, 2008). As in previous studies (Hommel, 2001), participants were presented with two stimuli: A task-irrelevant prime (S1) and a probe (S2). Both stimuli consisted of blended pictures of a face and a house. On each trial, either the face or the house moved in one of two possible directions and participants were instructed to respond as quickly as possible to the direction of the moving object in S2. Thus, each stimulus consisted of two features (motion direction and moving object) that were orthogonally repeated or alternated between S1 and S2 (Figure 4).

We expected to obtain the standard behavioral result: Repeating the motion direction and the moving object, or alternating both, should yield better performance than repeating one feature and alternating the other. The fMRI measures were used to test whether this pattern actually reflects object-file retrieval. In particular, our approach was to use activity in the FFA and PPA as an effective index of the degree to which the task-relevant stimulus feature (motion direction in S2) reactivated the task-irrelevant

feature (moving object) it accompanied in S1. Thus, we examined whether repeating the motion direction reactivated the object (face or house) that moved in this direction in S1. Diagnostic for this reactivation effect are conditions in which the moving object changes (e.g., if a house moved in S1 but a face moved in S2): Repeating the motion direction in S2 should tend to reactivate the representation of the house that moved in this direction in S1, which should lead to a greater activation of the PPA than if motion direction alternates.

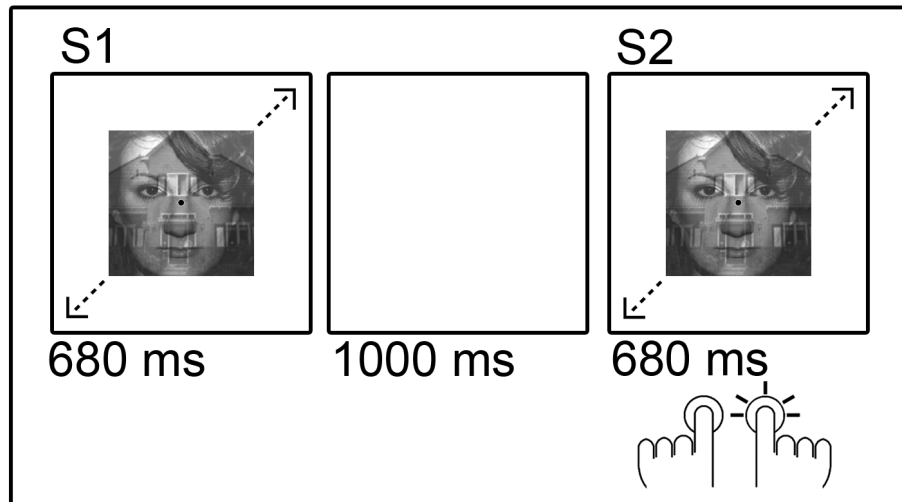


Figure 4. An example trial. On each trial two face-house compound stimuli (S1 and S2) were presented. Either the face or the house moved, in a left-up right-down or right-up left-down oscillatory fashion. Participants were instructed to watch S1 and to give a two-choice response to the direction of motion in S2, irrespective of the object that moved.

Methods

Participants

Fourteen healthy, young undergraduate students volunteered in exchange for course credit or money.

Experimental protocols

Each stimulus was composed by transparently superimposing one of eight grayscale front-view photographs of male (4) and female (4) faces on one of eight

grayscale photographs of houses, following O'Craven et al. (1999). The images were cropped to fit a square size (10° by 10°) and adjusted to assure the same average luminance. Either the face or the house oscillated in a straight path on one of two possible non-cardinal directions (left-up/right-down vs. right-up/left-down), while total size of the combined images remained the same. The maximal displacement caused by the motion was less than 10% of the size of the image. The moving image oscillated 2 cycles with a constant speed of 9° per second.

A trial started with a face-house compound stimulus (S1), randomly selected from all possible combinations of identity of the face and the house, direction of the motion, and the object that moved. Following the presentation of S1 for 680 ms, a black screen was presented for 1000 ms. Then, a second face-house compound stimulus (S2) was presented, in which the identity of the face and the house were repeated from S1. Both the direction of the motion and the object that moved could be the repeated or alternated between S1 and S2. Participants were instructed to watch S1 and make a speeded left-right key press to the direction of the motion of S2, disregarding the identity of the moving object. S2 was followed by a fixation circle (0.5°), which remained on the screen for a randomly chosen duration between 1000-2500 ms, varied in 100-ms steps. After every seven trials, a fixation circle was presented for ten seconds. The experiment consisted of a total of 182 trials and 26 ten-second rest periods. At the start, halfway, and at the end of the experimental run, a fixation circle with a duration of 30 seconds was presented to provide a stable baseline measure.

The experimental run was followed by a localizer run that we used to identify each participant's face-selective and house-selective regions of interest (ROIs). This run consisted of a series of blocks in which either stationary grayscale images of houses, faces or fixation circles were presented, of the same size and luminance as the compound images in the experimental run. The images of houses and faces were presented for 680 ms, followed by a 320-ms black screen. A total of 24 images were presented per block. In the fixation-circle block, a fixation circle was presented for 24 seconds. Each house block and each face block was repeated three times and these blocks were interleaved with the fixation-circle blocks.

Image acquisition

Images were recorded with a Philips Achieva 3-T MR scanner (Philips Medical Systems, Best, The Netherlands). Functional images were acquired using a SENSE parallel imaging gradient echo EPI sequence of 38 axial slices (resolution = 2.75 mm^3 isotropic; repetition time [TR] = 2211 ms; echo time [TE] = 30 ms; flip angle = 80° ; field of view = 220 mm; matrix = 80×80). During the experimental run, lasting 21.5 minutes,

580 volumes were collected. During the localizer run, lasting 7 minutes, 190 volumes were collected. A T1-weighted structural image (MPRAGE; 1.2 mm³ isotropic) and a high-resolution EPI scan (2 mm³ isotropic) were obtained for registration purposes.

Image analyses

MRI data analysis was carried out using FEAT (FMRI Expert Analysis Tool) version 5.4, which is part of FSL (FMRIB's Software Library, fmrib.ox.ac.uk/fsl). Image pre-processing consisted of: slice-time correction using Fourier-space time-series phase-shifting; motion correction (Jenkinson, Bannister, Brady & Smith, 2002); non-brain removal (Smith, 2002); spatial smoothing using a fullwidth at half maximum Gaussian kernel of 8 mm; and mean-based intensity normalisation of all volumes. Furthermore the data were temporally high-pass filtered with a cut-off of 60 seconds to remove low-frequency artefacts using Gaussian-weighted least-squares straight line fitting. Time-series statistical analysis was carried out using FILM (FMRIB's Improved Linear Model) with local autocorrelation correction (Woolrich, Brady & Smith, 2001).

Below, a three-character code is used to summarize the experimental conditions. The first two characters indicate which objects are moving in S1 and in S2: house (H) or face (F). The third character indicates whether the direction of motion in S1 is the same as the direction of motion in S2 (=) or different (≠). For analysis of the experimental run, explanatory variables of stimulus events were created for: HH=, HH≠, HF=, HF≠, FF=, FF≠, FH=, FH≠, segregated at the onset of S2. Errors and instruction displays were modeled separately. S1 was also modeled separately, comprising all four combinations of moving object and motion direction. The hemodynamic response to each event was estimated by convolving each explanatory variable with a canonical hemodynamic response function.

The primary data analysis focused on ROIs that showed significant task-selective activity during the localizer scans. To analyze the localizer data we used a fixed-effects analysis to identify, separately for each participant, regions showing significantly ($P < .001$, uncorrected) greater activity during house blocks than during face blocks (PPA), and regions showing the opposite pattern (FFA). To examine the presence of the hypothesized neural reactivation effects, we computed for each of these two ROIs (PPA and FFA) and for each participant the average percent increase in fMRI signal from baseline. The resulting averaged data set allowed us to test our main hypotheses: whether motion repetition results in automatic reactivation of the previously associated moving object (a face or a house).

Results

Mean reaction times (RTs) and percentages of errors for responses to S2 were analyzed using ANOVAs. The behavioral results replicated earlier findings with the same stimuli [20] and with other variants of the basic task [9]: RTs were slower if only one feature repeated between S1 and S2 (motion direction: 586 ms, moving object: 559 ms) compared to when both features repeated (547 ms) or alternated (556 ms). This was indicated by a significant interaction of moving-object repetition/alternation and motion-direction repetition/alternation ($F[1,13]=25.42$, $p<.001$). The interaction was mainly driven by an increase in RT on motion-repeat/object-alternate trials compared to complete-repetition trials ($t[13]=3.11$, $p<.01$) and complete-alternation trials ($t[13]=5.26$, $p<.0005$). Percentages of errors (4.6% across all task conditions) did not show an interaction of these variables ($p=0.76$).

Reactivation effect in the PPA (S1: house moving, S2: face moving)

To examine the presence of a reactivation effect in the PPA we contrasted the conditions in which the house in S1 and the face in S2 moved in the same direction versus in different directions (HF= minus HF $\neq$). If repeating the direction of the motion reactivated the representation of the house, we would expect increased RTs and increased activation in the PPA compared to the alternating condition. The contrasts confirmed our expectations (Figure 5A): Repeating the direction of motion was associated with a reliable RT cost relative to alternating the direction of motion (562 ms vs 542 ms, $F[1,13]=4.99$, $p<.05$). Furthermore, the right PPA was more active on motion-repeat than on motion-alternate trials ($t[13]=2.31$, $p<.05$), suggesting that on motion-repeat trials the presentation of the moving face in S2 reactivated the representation of the moving house in S1. Importantly, there was a significant positive correlation between the RT cost and the reactivation effect in the PPA (i.e., the difference in activation between motion-repeat and motion-alternate trials, indicating that participants with a larger reactivation effect in the PPA in general had a larger RT cost (Figure 5B).

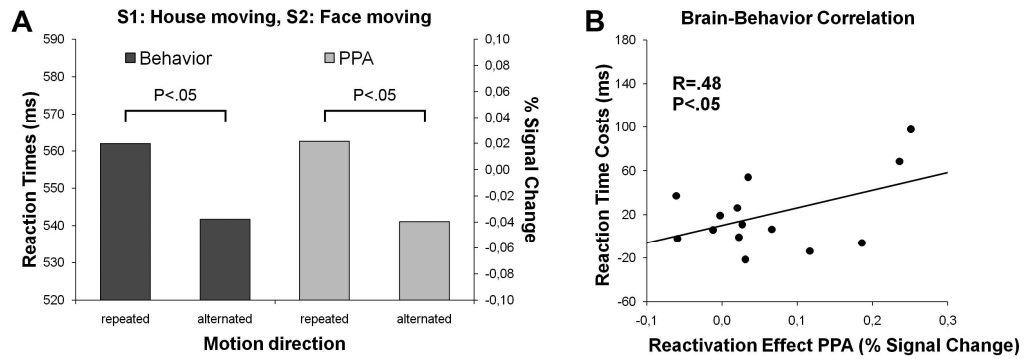


Figure 5. S1: house moving, S2: face moving. (A) Average reaction times and percent fMRI signal change in the PPA as a function of motion direction (repeated vs alternated) for trials in which a house moved in S1 and a face in S2 (i.e., alternation of moving object). Consistent with our predictions, reaction times and activity in the PPA were significantly increased when motion direction was repeated. (B) There was a significant correlation across participants between the reaction time costs and the PPA reactivation effect associated with the repetition of motion direction (in the context of an alternation of moving object).

Reactivation effect in the FFA (S1: face moving, S2: house moving)

To examine the presence of a reactivation effect in the FFA we compared two different experimental conditions: the conditions in which the face in S1 and the house in S2 moved in the same direction versus in different directions ($FH = \text{minus } FH \neq$). If repeating the direction of the motion reactivated the representation of the face, we would expect increased RTs and increased activation in the FFA compared to the alternating condition. These predictions were only partly confirmed (Figure 6A): Repeating the direction of motion was associated with a substantial RT cost relative to alternating the direction of motion (610 ms vs 570 ms, $F[1,13]=8.94$, $p=.01$). However, the FFA did not show a reactivation effect ($t[13]=0.17$, $p=.87$). As for the PPA, there was a significant positive correlation between the reactivation effect in the FFA and the corresponding RT cost (Figure 6B). The two participants with (by far) the largest FFA reactivation effect had large RT costs, whereas the participant with (by far) the smallest FFA reactivation effect had the smallest RT costs (or rather an RT benefit). Although these observations are consistent with our hypothesis, the dominant cluster of participants did not display the predicted positive correlation, either because this correlation is not present in the hypothetical population, or because there was not sufficient range in the individual FFA reactivation effects to reveal an existing correlation.

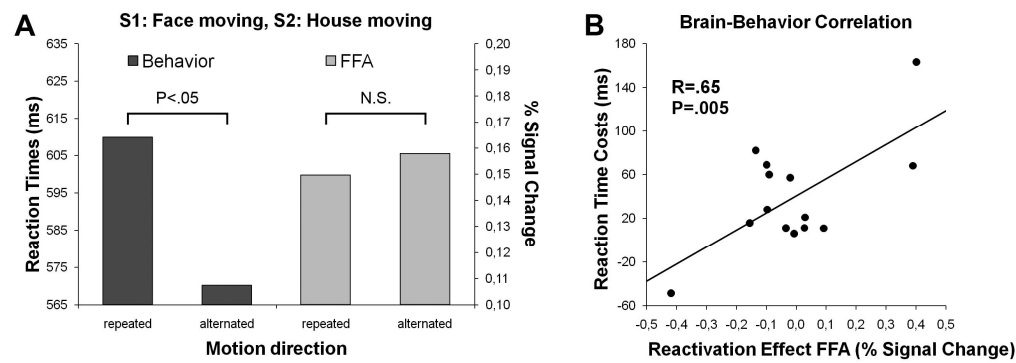


Figure 6. S1: face moving, S2: house moving. (A) Average reaction times and percent fMRI signal change in the FFA as a function of motion direction (repeated vs alternated) for trials in which a face moved in S1 and a house in S2 (i.e., alternation of moving object). Reaction times were significantly increased when motion direction was repeated. This was not the case for activity in the FFA. (B) There was a significant correlation across participants between the reaction time costs and the (nonsignificant) FFA reactivation effect associated with the repetition of motion direction (in the context of an alternation of moving object).

Discussion

The behavioral results replicated previous findings in showing that the partial repetition of stimulus features impairs performance (Hommel, 2004; Hommel et al., 2001; Keizer et al., 2008). This pattern has been attributed to the binding of feature representations upon stimulus (S1) presentation and the automatic retrieval of the whole object file if one or more features are encountered again (in S2). If this retrieval includes a feature that does not match the present stimulus, feature conflict occurs, yielding an increase in RT. In this study we investigated whether there is neural evidence for a corresponding object-file retrieval effect in brain areas representing specific stimulus features. Such evidence would provide critical support for theoretical accounts of feature binding and its consequences on subsequent information processing (Hommel et al., 2001).

The fMRI data provide encouraging support for our hypothesis. The right PPA, a house-selective brain area, showed increased activation to moving faces (in S2) if a couple of seconds earlier the same direction of motion had been paired with a house (in S1), compared to when both the direction of motion and the moving object alternated. This supports the view that the presentation of a stimulus feature (a particular direction of motion) reactivates features it was previously bound with in an

object file (house). The finding of a reliable positive relationship between the observed reactivation of the PPA and the partial repetition cost is consistent with the possibility that the neural reactivation effect *caused* the corresponding performance costs. Thus, neural and behavioral measures of the reactivation of the inappropriate feature (the house, when a face was actually moving) were closely correlated across participants.

The fMRI data for the FFA, a face-selective brain area, did not reveal unequivocal evidence for our hypothesis. On the one hand, the reactivation effect in this area showed the predicted positive relationship with performance costs, suggesting that repeating the motion does modulate activity in the FFA. On the other hand, however, the correlation was not clearly representative of the majority of the participants, and even though the individual RT costs were generally substantial (and larger than those associated with the PPA reactivation effect), most of the participants did not show the predicted FFA reactivation effect. At this point, we can only speculate why the FFA showed a different behavior than the PPA. For example, there is evidence that stimuli of greater biological significance, such as faces, attract more attention and induce more activation (Vuilleumier, 2000; Ro, Friggel & Lavie, 2007). As a result, activation in the FFA may be less sensitive to subtle modulations like the reactivation effect.

Conclusion

These caveats notwithstanding, the current findings are important for the vast body of behavioral research focusing on the after-effects of feature integration [8], and provide evidence concerning the neural underpinnings of the principles summarized in the Theory of Event Coding (TEC; Hommel et al., 2001), which addresses the origin of performance costs observed in the partial repetition of features. Our findings also extend the study of O'Craven et al. (1999) in providing new insights into the way the representation of multi-featured objects in visual brain areas has an impact upon reviewing those objects. In particular, our study provides the first neural evidence that the brain binds together the features of an object on a single presentation, and reactivates all the bound features when at least one of these features is encountered later on.

Chapter 4

The Control of Object-file Retrieval

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Abstract

Perceiving visual objects calls upon mechanisms that integrate the features of these objects. Previous research has suggested that features are bound together even though they are irrelevant to the task at hand. However, in these studies, the apparently bound features always included at least one task-relevant feature. In the present study we show that no binding-related effects are obtained if this is not the case, at least for arbitrary combinations of simple shape and color features. This did not change by introducing a working memory task that attracted attention to all features of the to-be-bound object, suggesting that it is retrieval processes that are affected. We conclude that bindings of simple features are automatically retrieved if, and only if these bindings contain at least one feature that falls on a dimension that is relevant for the current task. Retrieval is less selective for stimuli that are likely to be represented by means of long-term conjunction detectors.

Introduction

The brain consists of a multitude of specialized regions, each representing different types of information. For instance, the visual cortex consists of a region that is specialized in processing color (Zeki et al., 1991) and a different region that is specialized in processing shape (Kourtzi & Kanwisher, 2000). When confronted with multiple colored objects, the different types of information that are represented in these regions need to be integrated in order to correctly match colors and shapes, commonly referred to as the binding problem (Treisman, 1996). Research has shown that when features are bound together, partially repeating the features involved in these bindings automatically reactivates all features that have been integrated in what Treisman (1996) the 'object-file' (Hommel, 1998; Colzato, Raffone & Hommel, 2006; Keizer, Colzato & Hommel, 2008). Furthermore, these effects have not only been demonstrated between arbitrary visual features of an object such as shape and color, but these bindings can also involve representations in different sensory domains (Zmigrod & Hommel, 2009) and representations of actions (Hommel, 1998).

A way to study these object files is to investigate behavioral effects on subsequent encounters of previously bound features—the so-called “preview design” (Kahneman, Treisman & Gibbs, 1992). Participants are commonly presented with at least two objects in a row, which for instance may consist of particular shape-color combinations, and have to respond to the second object (S2) while ignoring the first (S1). In such tasks, the effects of the repetition of stimulus features interact: performance is regularly better (fast RTs and few errors) if both features are repeated or alternated from S1 to S2 than if one of the features is repeated but the other alternates. If we assume that the features of S1 are automatically integrated into an object file, it can be hypothesized that repeating one feature on S2 results in the reactivation of all features that accompanied it on S1, which induces conflict between feature codes and thus impairs performance (Hommel, 2004). Evidence for this hypothesis has recently been provided by an fMRI study, which showed that if two features are presented simultaneously on S1, repeating one of these features on S2 results in increased activation in the brain area that codes for the other feature (Keizer et al., 2008).

The aim of the present study was to investigate whether, or in which way the creation and retrieval of feature bindings depends on attentional processes. The available evidence provides a cluttered picture. The fact that the preview design does not require any binding of S1 features suggests that binding is relatively automatic, which does not seem to fit with the argument that attention is a necessary requirement for binding to occur (Treisman, 1996). Moreover, Hommel and Colzato (2004) showed

that binding effects are not affected by whether or not participants are required to report the feature combination present in S1. As we can assume that this requirement increases the amount of attention directed to S1 and devoted to processing its features, the absence of any effect supports the idea that feature binding as such is automatic (even though it is still possible that binding uses attentional resources).

And yet, binding-related effects of attention have been obtained. For instance, bindings that include task-relevant features affect subsequent trials more than bindings including irrelevant features, if they have any impact at all. For instance, participants responding to the shape of S2 exhibit particularly strong binding-related effects involving shape repetition whereas participants responding to the color of S2 show stronger effects involving color repetition (e.g., Hommel, 1998). Even trial-to-trial switches between shape and color as S2-relevant feature induce stronger binding-related effects for the currently task-relevant feature dimension (Hommel, Memelink, Zmigrod, & Colzato, 2009). Interestingly, this effect of attentional set does not depend on whether the set is switched and established before or after S1 presentation, suggesting that the attentional set selectively targets the retrieval but not the encoding of bindings (Hommel et al., 2009). Other demonstrations of the impact of attention, even though presumably of a different kind, stem from Colzato, Raffone, and Hommel (2006), and from Hommel and Colzato (2009). These authors investigated whether trial-to-trial bindings between real objects (bananas and strawberries) and arbitrary colors would be stronger than between arbitrarily combined features, such as shapes and colors. Bindings between real objects and colors had indeed stronger effects but this was even the case for arbitrary object-color combinations, such as with red bananas and purple strawberries. The authors suggest that real objects are likely to match corresponding episodic traces in long-term memory, which elicits top-down attentional priming of all features involved in the object file (cf., Duncan, 1984).

The present study was designed to get one step forward in integrating these observations. Our reasoning goes as follows. The objects of a preview display (S1) are automatically and fully integrated into object files, with all features becoming a part of the binding, as long as the complexity of the display and the number of objects are low enough to not exceed capacity limits (Luck & Vogel, 1997; Lavie, 1995). A subsequently processed stimulus can induce the retrieval of object files that share at least one component (feature value) with it, and this retrieval result in the reactivation of all components of the object file. However, this retrieval occurs only if at least one of two conditions is met.

First, an object file is only retrieved if feature in which it matches the current stimulus falls on a currently relevant feature dimensions. We assume that preparing for a task involves the top-down priming of feature dimensions (i.e., the pre-activation of

neural maps coding for features of that dimension; cf., Fagioli, Hommel & Schubotz, 2007; Hommel, 2009; Kühn, Keizer, Colzato, Rombouts & Hommel, 2009), and that this priming regulates the selection of target stimuli and the retrieval of object files. Consistent with this assumption, the size of sequential effects in preview designs is reduced in people of high fluid intelligence (Colzato, van Wouwe, Lavender & Hommel, 2006) and elevated in children and older adults (Hommel, Kray & Lindenberger, 2009)—populations that are notorious for the particularly efficient or inefficient control of working memory, respectively.

Second, the filter provided by dimensional priming can be overruled if the present object or event resonates with internal feature-conjunction detectors. Following Hommel and Colzato (2009) we assume that arbitrary and frequently changing feature combinations are exclusively represented by ad hoc binding processes (probably operating by means of neural synchronization; see Colzato et al., 2006), whereas feature conjunctions that are *significant* (in the sense of reliably indicating a particular stimulus event) and *diagnostic* (by allowing the reliable discrimination of the stimulus from alternative stimuli), like with yellow bananas and red strawberries, are also represented by object-specific conjunction detectors. If a conjunction detector resonates with a perceived stimulus, top-down processes are initiated that direct attention to all features of that stimulus and that, as a consequence, allow for the activation of object files according to any feature match—hence, irrespective of whether the matching feature falls on a task-relevant dimension. The resonance can be triggered by partial evidence, so that both red and yellow bananas can induce top-down priming.

This scenario accounts for the available evidence, as it fits with the observation that the binding process as such is not very sensitive to attentional manipulations, while the retrieval of bindings is, as it considers the observed difference between arbitrary feature combinations and real objects. However, independent evidence is needed to support our scenario, as it is basically post hoc. The rationale underlying the present study was motivated by the claim that object file retrieval for conjunctions of arbitrary features should take place only if a feature from a currently relevant feature dimension is part of the to-be-retrieved bindings. We carried out an otherwise standard preview-design study but never presented a feature from the task-relevant feature dimension (i.e., the S2 dimension that signaled the required responses) as part of S1. No binding of S1 features would thus include a task-relevant feature, so that the presentation and processing of S2 should not be able to reactivate any object file. Accordingly, the typical sequential effects of interactions between feature repetitions and alternations should be absent. However, things should be different with real objects. Real objects should overrule dimensional priming and thus

enforce object file retrieval. Accordingly, the standard sequential effects should be obtained with real objects even if no task-relevant feature would be presented as part of S1. Experiment 1 set out to test these predictions, and Experiment 2 sought to provide converging evidence.

Experiments 1A and 1B

Two modified versions of the S1-S2 paradigm introduced by Hommel (1998) were used. Stimuli consisted of arbitrary feature conjunctions (letters superimposed on colored squares) in Experiment 1A and of conjunctions of real object photographs (faces superimposed on houses) in Experiment 1B. An example trial of Experiment 1 is shown in Figure 7. As explained in the introduction, we expected an interaction between face- and house-repetition effects in Experiment 1B but no reliable interaction between shape and color in Experiment 1A.

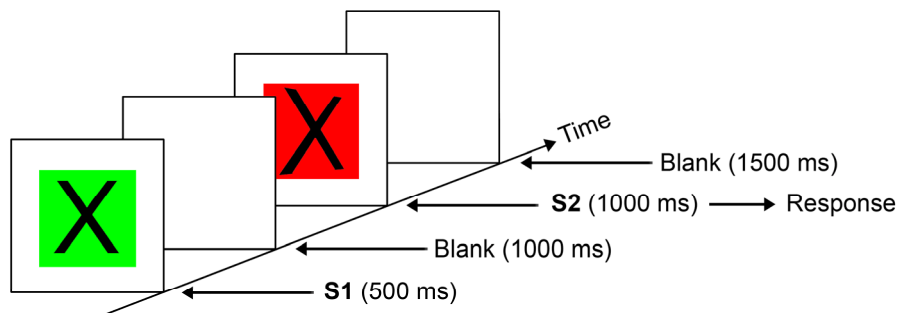


Figure 7. Time sequence of an example trial of Experiment 1A. Subjects had to make a discriminative response to the orientation of either the letter or the colored square on S2 (oriented left versus oriented right). Subjects needed to refrain from responding to S1.

Method

Participants

Sixteen right-handed volunteers (3 male, mean age: 20.1 years) participated in Experiment 1A and 16 right-handed volunteers (3 male, mean age: 21.0 years) participated in Experiment 1B for course credits or a fee.

Stimuli and Task

In Experiment 1A, S1 and S2 were composed of a black letter 'X' or 'O' (4° by 4°) superimposed on a green or red square (5.5° by 5.5°). The letter-color combinations of the 128 trials were constructed by randomly drawing from the two possible letters and colors, except that the stimuli were chosen to result in equal proportions (32 trials) in the four cells of the 2x2 design (letter repetition vs. alternation x color repetition vs. alternation). S1 and S2 of Experiment 1B were composed the same way, except that the stimuli consisted of two transparently superimposed, equally-sized grayscale front-view photographs of either a male or a female face and one of two grayscale photographs of a house (10° by 10°). The face and the house could either be repeated or alternated on S2. On S2, one of the two photographs was vertically tilted to the left or right by 9°, and subjects were to make a discriminative response (with the left or right index finger pressing the 'z' or 'm' key of the qwerty-keyboard) to left vs. right tilts, respectively. In Experiment 1B, the end of the trial was followed by a screen which consisted of the photographs of a face and a house (10° by 10°), located 2.75° on the left and right side of a central '+' sign (1.85° by 1.85°). The position of the face and house varied randomly. Subjects were to make an approximately equal amount of right and left responses (middle finger key press on the 'a' or 'k' button), irrespective of the stimuli presented on the screen. Even though the end of the trials in experiment 1B was unrelated to the task that had to be performed on S2, we wanted to make experiment 1B as similar as possible to experiment 2B, where this part of the trial reflected the test of short-term memory retention. The presentation of the stimuli was terminated after a response was made, which was followed by a final blank interval lasting 1000 ms.

Results

Binding effects were assessed by means of repeated measures ANOVAs of reaction times (RTs) and error rates with repetition versus alternation of letter and color (Experiment 1A) and face and house (Experiment 1B) as two-level factors. In the omnibus ANOVAs across the two experiments (with Experiment as between-subjects variable), we arbitrarily coded letters and faces as "Feature 1" and houses and colors as "Feature 2". This is justifiable because it is only interactions between repetitions and alternations of the two features or stimulus attributes that are of theoretical relevance, whereas main effects are unimportant. Trials in which subjects responded to S1 were excluded from the analyses and RTs < 200 milliseconds and > 1000 milliseconds were considered as outliers and discarded (11% of the data in Experiment 1 and 7% in Experiment 2).

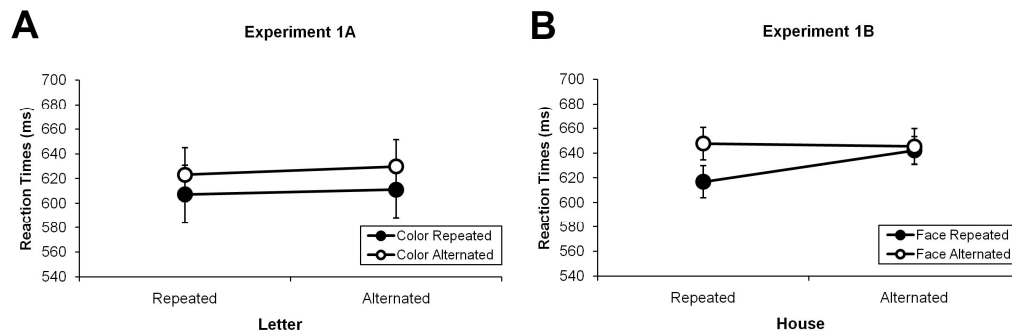


Figure 8. Error bars represent standard errors in all graphs. Mean reaction times for Experiment 1A-1B, as a function of repetition vs. alternation of letter and color in Experiment 1A (A) and of face and house in Experiment 1B (B).

The significance level was fixed at $\alpha = .05$ for all analyses. RTs revealed main effects of the repetition versus alternation of both features, $F(1,30)=4.51$, $p<.05$ (letters/faces), and $F(1,30)=18.77$, $p<.001$ (colors/houses), no interaction between these two effects, $p = .09$, but a three-way interaction, $F(1,30)=4.71$, $p<.05$. Separate ANOVAs revealed that the repetition effects of faces and houses in Experiment 1B interacted significantly, $F(1,15)=9.2$, $p<.01$ (Figure 8B), whereas the repetition effects of letters and colors in Experiment 1A did not, $F(1,15)=0.1$. The separate ANOVAs also showed that the main repetition effects of color in Experiment 1A and of faces in Experiment 1B were reliable, $F(1,15)=13.7$, $p<.01$, and $F(1,15)=7.1$, $p<.05$. The analysis of the error rates did not reveal any reliable effect.

Discussion

In contrast to numerous previous studies that used the same stimulus material and basic task, we found no evidence for binding-induced interactions between arbitrary combinations of shapes and colors (Experiment 1A). The only difference between Experiment 1A and the successful demonstrations of binding-induced effects is that in the former no task-relevant feature appeared as part of S1. Apparently, then, the presence or absence of a task-relevant feature in the binding created to represent S1 decides whether or not the binding is retrieved upon processing S2. However, this is only true for combinations of arbitrary features, whereas significant binding-related effects were obtained with real objects (Experiment 1B). This fits with the idea that real objects cause resonance of internal representations (Colzato et al., 2006; Hommel &

Colzato, 2009), which in one way or another enables object-file retrieval even in the absence of task-relevant features.

Experiments 2A and 2B

Experiment 1 provides evidence for our claim that two factors are important for binding-related effects do occur: the presence versus absence of a task-relevant feature in S1-related bindings and whether or not real objects are involved. However, the characteristics of the task we used does not allow for an unequivocal attribution of these effects. For instance, the absence of task-relevant features in S1 may not, or not only prevent retrieval of object files but it may prevent their creation altogether. For instance, it may be that combinations of arbitrary stimulus features are bound only if the presence of a task-relevant feature attracts attention to S1, the to-be-bound stimulus. With respect to the real-object effect, one may consider that real objects as S1 attract more attention, which may increase the likelihood of binding S1 features. The sequential effects that we consider as evidence for binding require the successful binding of features upon S1 processing as well as successful retrieval of this binding upon S2 processing, so that it is impossible to unequivocally attribute the lack of an effect to the creation or the retrieval of a binding.

On the one hand, we have already discussed independent evidence suggesting that object-file retrieval is very sensitive to attentional manipulations (Hommel et al., 2009) while the creation of object files is not (Hommel, 2007; Hommel & Colzato, 2004). For instance, Hommel and Colzato (2004) asked participants to report the feature combinations present in S1 after each trial (i.e., after R2 was carried out), which should have attracted attention to the otherwise task-irrelevant S1. The absence of any substantial effect of this manipulation suggests that the binding of S1 does not benefit from increasing its task relevance. This implies that our present manipulation of the task relevance of S1 features in Experiment 1 affected the retrieval of bindings. On the other hand, however, the S1 used in the study of Hommel and Colzato (2004) always contained a task-relevant feature. This might have attracted sufficient attention to S1 in any case, so that introducing the memory task did not add much. In other words, having a task-relevant feature as part of S1 may produce an attentional ceiling effect that cannot be further increased.

The implication of this objection is that dropping the task-irrelevant feature of S1 may prevent attention from being attracted to that stimulus, thus preventing the binding of at least arbitrary features altogether. If so, adding a memory task that does attract attention to S1 and renders one of its features task relevant, as in the Hommel and Colzato (2004) study, should ensure that S1 binding takes place. If thus the lack of

sequential effects observed in Experiment 1A would have been due to a failure to bind S1 features, adding the memory task should bring back the sequential effects. In contrast, if the lack of sequential effects in Experiment 1A was due to a lack of retrieval, adding the memory task should not help, so that no sequential effects would be expected from that perspective. We thus replicated Experiment 1 but asked participants to report the features of S1 after each trial.

Method

Participants

Sixteen right-handed volunteers (4 male, mean age: 19.3 years) participated in Experiment 2A and 16 right-handed volunteers (2 male, mean age: 21.1 years) participated in Experiment 2B for course credits or a fee.

Stimuli and Task

The stimuli and task of Experiment 2A were identical to that of Experiment 1A, with the following exception: At the end of the trial a screen was presented which showed the letter 'X' or 'O', superimposed on a grey square (4° by 4°) and a red or green square (5.5° by 5.5°), located 2.75° on the left and right side of a central '+' sign (1.85° by 1.85°). The position of the letter and color varied randomly. The color and the letter could match or mismatch the color and letter presented as S1 (equally proportioned across trials), and participants decided whether the two presented features would match S1 or not by pressing the 'a' or 'k' button with the middle finger (the mapping was counterbalanced across subjects). The presentation of the stimuli was response-terminated and was followed by a final blank interval lasting 1000 ms. The stimuli and task of Experiment 2B were identical to that of Experiment 2A, except that the stimuli consisted of faces and houses instead of letters and colors (sized as in Experiment 1B).

Results

Performance on the short-term memory task was good, as evidenced by the percentage of correct responses (mean accuracy of .80 (SD=.23) in Experiment 2A and .89 (SD=.13) in Experiment 2B. Memory performance did not differ between the two groups, $T(30)=1.3$, $p>.1$. 14% of the trials in Experiment 2A and 10% of the trials in Experiment 2B were discarded according to the same criteria applied in Experiment 1. The omnibus ANOVA of RTs did not reveal a single reliable effect, all $ps > .16$, and the same was true for the analysis of the error rates, all $ps > .05$. As obvious from Figure

9, there was not even a hint to the standard result pattern—if anything it was (numerically) reversed.

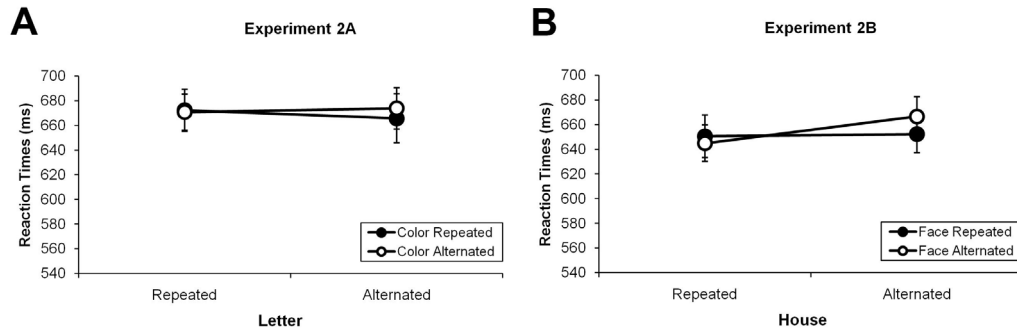


Figure 9. Error bars represent standard errors in all graphs. Mean reaction times for Experiment 2A-2B, as a function of repetition vs. alternation of letter and color in Experiment 2A (A) and of face and house in Experiment 2B (B).

Discussion

Results are clear-cut: adding the memory task that arguably increased the attention being directed to S1 did not produce any reliable sequential effect. With regard to Experiment 1A, this implies that it is not the amount of attention involved in the binding of features that counts for sequential effects by whether or not the binding includes a feature that has any bearing on the processes carried out on S2. That is, there are reasons to assume that the disappearance of sequential effects in Experiments 1A and 2A are due to the failure to retrieve object files but not to create them. Another interesting outcome was the disappearance of sequential effects with real objects in Experiment 2B. Given that adding the memory task should have increased rather than decreased the amount of attention involved in S1-feature binding, we doubt that this effect has anything to do with the creation of object files either. Rather, maintaining S1 information in working memory may have impaired the maintenance of the task-relevant feature dimension in Experiment 2B. If our assumption that object-file retrieval is controlled by top-down dimensional priming is correct, the working-memory load may thus have impaired the retrieval of object files by interfering with the priming process.

Conclusion

Even though our conclusions mainly rely on the absence rather than the presence of sequential, binding-related effects, our study points to the importance of two factors that influence the retrieval of object files. First, an arbitrary binding is retrieved if, and only if it includes a feature code that is relevant for the task at hand (i.e., for identifying and discriminating S2 in our design). Second, this type of selectivity or retrieval control is overruled if the stimulus is a real object, or at least refers to a real object. Given that any arbitrary feature may be considered an object in some sense, crucial issue seems to be whether a long-term representation or conjunction detector has been developed for the object at hand (Hommel & Colzato, 2009). These long-term representations may be created only if the particular feature combination is relevant and diagnostic, whereas frequently changing conjunctions, as between geometric shapes and colors or letters and fonts, are not stable and diagnostic enough to be worth of the cognitive effort to create a conjunction detector. However, Experiment 2B provided evidence that the real-object effect is not invulnerable but can be eliminated by introducing a working-memory task. More research on this issue is certainly necessary, but we speculate that loading working memory interferes with the top-down priming effects evoked by resonating “object detectors”.

Chapter 5

Enhancing Gamma Band Power (36-44Hz) with Neurofeedback Improves Feature- binding Flexibility and Intelligence

A modified version of this chapter is published as: Keizer, A. W., Verschoor, M. Verment, R. S., & Hommel, B. (2010). The effect of gamma enhancing neurofeedback on the control of feature bindings and intelligence measures. *International Journal of Psychophysiology*, 75, 25-32.

Abstract

Neural synchronization in the gamma band has been associated with feature binding and intelligence. Using neurofeedback, we aimed at changing the power of the gamma band and investigated whether these changes would influence behavioral measures of feature binding and intelligence. The results show that people are indeed able to alter the power in the gamma band if provided with neurofeedback. Moreover, the increase of gamma band power was related to a decrease of binding costs and an increase in intelligence, suggesting that the control of feature binding and intelligence share a common underlying mechanism.

Introduction

Visual information is analyzed by different specialized brain areas, each coding for different features in the visual field, such as shape (Kourtzi & Kanwisher, 2000) and color (Zeki et al., 1991). Even though visual information processing in the brain is so dispersed, we still perceive visual objects as integrated wholes. The question of how the brain is able to do this has often been referred to as the 'binding problem' (Treisman, 1996). A possible mechanism for the binding of features in the brain is the temporal coupling of neural populations, which is assumed to be achieved by coordinating and synchronizing the firing rates of cells referring to the same event. That is, feature conjunctions may be coded through the temporal coherence of their neural codes, presumably in the gamma frequency band (~30-100 Hz; for an overview, see Engel & Singer, 2001; Jensen, Kaiser & Lachaux, 2007). However, there still remains to be a large amount of controversy regarding the functional relevance of gamma band activity. For instance, some studies suggest that gamma band activity are harmonics of alpha activity (Jürgens, Rösler, Henninghausen & Heil, 1995), while other studies showed that gamma and alpha are independent (Müller, Junhöfer, Elbert & Rochtroh, 1997). It has also been argued that gamma band activity cannot be reliably measured in the human EEG (Juergens, Guettler & Eckhorn, 1999) and that both neural synchrony and asynchrony play important roles in binding processes (Friston, 2000).

Even though direct links between gamma activity and feature integration are yet to be demonstrated, there is converging evidence that processes involved in the creation and maintenance of (visual) feature bindings are accompanied by, and systematically related to neural activity in the gamma band. In particular, gamma band power is correlated with visual awareness (Engel & Singer, 2001) and visual working memory (Tallon-Baudry, Bertrand, Peronnet & Pernier, 1998). Moreover, gamma synchronization and visual feature integration seem to be related to the same neurotransmitter system. Gamma synchrony in the primary visual cortex of the cat is enhanced by muscarinic-cholinergic agonists and disrupted by muscarinic-cholinergic antagonists (Rodriguez-Bermudez, Kallenbach, Singer & Munk, 2004). This fits with observations that, in humans, caffeine—a muscarinic-cholinergic agonist—facilitates visual feature integration (Colzato, Fagioli, Erasmus & Hommel, 2005), whereas alcohol—a muscarinic-cholinergic antagonist—impairs it (Colzato, Erasmus & Hommel, 2004). These findings could be replicated with more selective, pharmacological interventions in the rat, Botly & De Rosa, (2007), and in humans, Botly & De Rosa, (2008). The relationship between muscarinic-cholinergic pathways and visual feature binding seems to be rather specific, as visual feature integration is not affected by

nicotinic-cholinergic or dopaminergic manipulations (e.g., Colzato & Hommel, 2008), and muscarinic-cholinergic manipulations have no impact on visuomotor integration (Colzato et al., 2004, 2005).

Given that most of the empirical evidence on the role of synchronization in feature integration points to a connection between gamma-band activity and visual integration, our study focused on this possible relationship. The second variable we considered in our study was intelligence, mainly because it seems to be related to both feature integration and neural activity in the gamma band, and may thus be an important mediator in the link between integration and synchronization. Several authors have assumed and provided preliminary evidence that fluid intelligence in humans relies on gamma-band synchronization (Jausevec, 2004; Jausevec & Jausevec, 2005, 2007; Lee, Williams, Breakspear & Gordon, 2003; Stankov et al., 2006). With regard to binding, people high in fluid IQ have been found to be more efficient in updating feature bindings in the case of feature changes (Colzato, Raffone & Hommel, 2006). How intelligence and binding may interact is not entirely clear however. On the one hand, it is possible that higher fluid intelligence is associated with more efficient integration processes, and one may even imagine that is this higher efficiency that allows for more intelligent behavior. On the other hand, however, it is also possible that fluid intelligence does not affect binding itself but the handling and cognitive control of bindings. Indeed, fluid intelligence correlates with executive control processes (Duncan, Emslie, Williams, Johnson & Freer, 1996), which are assumed to operate on cognitive structures and processes. Support for this latter possibility comes from the Colzato, van Wouwe, Lavender & Hommel (2006) study where higher intelligence scores were associated with *smaller* rather than larger effects of trial-to-trial feature changes. In other words, intelligence may be related to the control of bindings rather than to their creation.

Even though theoretical considerations and converging empirical evidence support the idea that neural synchronization in the gamma band is associated with feature integration, the functional relevance of synchronization is still under heated debate, on a theoretical level (Ghose & Maunsell, 1999; Reynolds & Desimone, 1999; Shadlen & Movshon, 1999; Treisman, 1999) and due to empirical studies showing an absence of neural synchrony during integration demanding situations (Lamme & Spekreijse, 1998), contour grouping (Roelfsema, Lamme & Spekreijse, 2004) and motion coherence (Thiele & Stoner, 2003). One of the reasons for the ongoing debate is that most of the supporting empirical evidence is correlational, which makes it difficult to rule out that synchronization is epiphenomenal to binding and other cognitive processes. A more powerful way to investigate the functional relevance of the gamma

band would be to manipulate synchronization directly and to see whether and how this affects performance, which is what we attempted to do in the present study.

One way to manipulate particular frequency bands in the EEG signal is neurofeedback (Bird, Newton, Sheer & Ford, 1978; Vernon et al., 2003). With neurofeedback training, brain waves are measured using electrodes that are likely to pick up signals from theoretically relevant brain areas. An online spectrum analysis is performed, which makes it possible to reward participants so to guide them to increase or decrease the power in the targeted frequency band(s). Neurofeedback has been studied mainly as a possible treatment for various kinds of psychological disorders like ADHD (Fuchs, Birbaumer, Lutzenberger, Gruzelier & Kaiser, 2003), migraine (Kropp, Siniatchin & Gerber 2002), and epilepsy (Kotchoubey et al., 1999). These and other studies demonstrate that people are indeed able to alter (enhance or reduce) the power of specific frequency bands in their own EEG-signal.

Even though little fundamental research has been done which uses neurofeedback as a method to study cognitive processes and their relation with specific frequency bands (notable exceptions are: Egner & Gruzelier, 2001, 2003, 2004; Vernon et al., 2003), it may provide a powerful tool to study these relationships in theoretically meaningful ways. Manipulation of gamma band power by neurofeedback training has already been successfully demonstrated in a study by Bird et al. (1978). In this study, significant differences in gamma band power were demonstrated after 8 neurofeedback sessions, each lasting 30 minutes. In order to investigate the role of gamma in binding and intelligence-related performance, we studied whether and how this performance would change as a consequence of neurofeedback training designed to enhance or reduce the power of cortical activity in the gamma band.

One group of our subjects was thus trained to enhance gamma-related cortical activity in 8 neurofeedback sessions as in the Bird et al. (1978) study. In a second group, we intended to reduce gamma activity. One alternative would have been placebo neurofeedback training. However, this has the disadvantage that subjects may notice the absence of consistent neurofeedback and engage in elaborate hypothesis testing, which would result in uncontrollable differences between the experimental and control group. Another possibility would have been the presentation of negative feedback, that is, of feedback that directly encourages a reduction of gamma-related activity. However, little is known about how people actually manage to increase or decrease power in a particular frequency band. If the aim is to increase power in a given band, the goal is very likely the same for all participants—however they may achieve it. If the aim is to decrease the power, however, the individual goals may be very diverse: some people may manage to directly reduce the power but others may

try to achieve that indirectly by targeting other frequency bands. In an attempt to encounter these problems we thus tried to equate the two investigated groups as far as possible, and we did so by rewarding one group for increasing the power in the gamma band at the cost of beta activation and the other group for increasing the power in the beta band at the cost of gamma activation. That is, we put these two frequency bands in opposition in both groups and varied the preference for one band over the other. In the following, we will refer to the group with an induced gamma preference as the *Gamma-Up* group and the group with an induced beta preference as *Control* group.

There are two reasons why we chose to include beta power in the neurofeedback training procedure. First, it has been speculated that the beta band may have different binding properties than the gamma band (Colzato et al., 2005; Schnitzler & Gross, 2000). Whereas feature integration in perception is commonly associated with the gamma band (e.g., Engel & Singer, 2001), sensorimotor binding seems to be more related to neural synchronization in the beta band (e.g., Roelfsema, Engel, Koenig & Singer, 1997). In principle, these considerations would allow for interesting hypotheses with regard to the Control group as well; however, we will see that inducing a preference for beta power was more successful in preventing an increase in gamma power than in increasing beta power, which does not permit testing beta-related hypotheses. In other words, our Control group turned out to be a true control group rather than a Beta-Up group. Second, the findings of Bird et al. (1978) show that power changes in the gamma band impact power in the beta band as well, even though the beta band was not included in their neurofeedback design. By putting the beta band power into opposition to the gamma band we intended to get a clearer distinction between the power changes in these two frequency bands.

The rationale of our design was to test the two groups on measures of visual feature binding and intelligence before the start of the first neurofeedback training (the pretest) and again after the end of the last neurofeedback training (the posttest). Note that our design includes a repetition of all relevant tests. This invites all sorts of practice- and time-related effects and thus renders main effects of time of testing equivocal. More interesting for our purposes were interactions between time of test and group, as these interactions would indicate a differential effect of neurofeedback. To tap into feature integration, we employed a version of the task developed by Hommel (1998). In this task, participants are presented with pairs of trials, in which the features of stimuli and responses vary orthogonally. The important observation is that the repetition and alternation of a given feature depends on whether other features are repeated as well. For instance, if shape and location of a stimulus repeats or alternates, shape repetition results in better performance if the location repeats as well whereas, with shape alternation, performance is better if the location alternates as well

(Colzato et al., 2006; Hommel, 1998). This suggests that shape and location are spontaneously integrated into a kind of event file, which is retrieved if at least one feature is repeated (Hommel, 2004). Along the same lines, repeating the response is beneficial if stimulus features also repeat but impair performance if stimulus features alternate (Hommel, 1998). In the present study, we will focus on the repetition and alternation of stimulus shape and location, and assume that interactions between shape- and location-repetition effects are indicative of visual feature binding. The second measure of interest was intelligence, which we measured by using Raven's Standard Progressive Matrices (Raven, 1938).

If neurofeedback would be successful in increasing power in the gamma band in the Gamma-Up group, and if gamma band activity would be associated with feature binding and intelligence, we would expect that training would have a specific effect on our binding and intelligence measures. With regard to intelligence, one might speculate that gamma training improves performance in an intelligence-related task, suggesting better Raven scores in the Gamma-Up group. The predictions regarding binding depend on exactly how the training affects binding-related processes. One possibility is that it directly improves the binding process itself, suggesting that binding-related effects should increase in the Gamma-Up group. Another possibility is that training improves the handling of event files (Colzato et al., 2006), that is, the efficiency of retrieving and updating feature bindings, suggesting that binding-related effects decrease in the Gamma-Up group.

Method

Participants

Fourteen right-handed volunteers (2 male, mean age: 22 years) participated in the experiment. Informed consent was obtained from all participants after the nature and possible consequences of the study were explained to them. The protocol was approved by the local medical ethical committee (Leiden University Medical Center).

Procedure

Each subject was randomly assigned to one of the two groups. In a double-blind procedure, both the subject and the experimenter were unaware which of the two possible neurofeedback training protocols was given to the subject until the last subject finished the experiment. Subjects filled out a questionnaire before the start of each neurofeedback training session, enquiring for any notable changes in appetite, sleep pattern, ability to concentrate, memory capacity, and mood. The order of the behavioral tests (binding and intelligence) was counterbalanced across subjects.

Neurofeedback training

Each subject completed 8 neurofeedback sessions, 1 training session per day lasting 30 minutes. The neurofeedback sessions were spread over a period of 10 or 11 days. For the EEG measurements, a QDS Focus amplifier and electrodes were used (www.brain-trainer.com). The EEG signal was received from one electrode attached to the scalp of the subject, on the Oz position, according to the international 10-20 system. Reference electrodes were placed on both earlobes and forehead of the subject. The EEG power spectrum analysis was calculated online with negligible delay, using the Bioexplorer software package (www.cyberrevolution.com). Two elliptic filters were applied to the signal, extracting frequencies in the gamma range (36-44 Hz) and in the beta range (12-20 Hz). Two types of thresholds were implemented, an 'upper' and a 'lower' threshold. Both types were adapting to the power of the frequency band it was applied to. More specifically, the power level was based on a moving average of 30 seconds that was updated continuously with the average power that was calculated over epochs of 0.125 seconds and both types of thresholds were set to the power level that would be surpassed 75% of the time during the preceding 30 second window. The width of the gamma band was made identical to that of the beta band, to prevent possible effects of a band-width difference in the gamma and beta band. Even though the gamma band has been defined in the range of 30 and 100 Hz, we chose to operationalize the gamma band around 40Hz, since this seems to be the most widely accepted and most referred to indicator of the gamma band (i.e. Tallon-Baudry & Bertrand, 1999).

The subjects were randomly assigned to one of the two neurofeedback groups. In the Gamma-Up group, a tone was generated whenever the following two criteria were met: (1) gamma power exceeded the upper threshold and (2) beta power exceeded the lower threshold. For the Control group, a tone was generated when both the gamma power exceeded the lower threshold and the beta power exceeded the upper threshold. In other words, positive feedback was given when both thresholds were surpassed simultaneously. Both groups were instructed to attempt to increase the rate of the tone occurrences. The maximum rate of the tones was set to one tone per second. Using these criteria, subjects achieved a high rate of tones when the power of their frequency bands was recurrently exceeding the adapting thresholds.

Binding

Binding processes were tested by using a modified version of the task used by Hommel (1998), which is designed to study the behavioural effects (reaction times and errors) of feature binding. An example trial of this task is shown in Figure 10. Subjects

were instructed to respond with a left or right key press on S1 (z- or m-key), according to the preceding arrow (3.8 cm X 2.7 cm), ignoring the picture (5.0 cm X 4.3 cm) and its location (top or bottom). On S2, subjects were instructed to respond to the picture (apple or bananas) while ignoring its location, again with a left or right key press (z- or m-key, counterbalanced across subjects). The arrows were presented in the middle square of three equally sized squares (6.3 cm), placed in vertical alignment, the images of an apple or bananas were placed in either the top or the bottom square. The task consisted of 320 trials, equally divided across conditions. The rationale of this design is that on S1, the picture, location and response are integrated into an 'event file' (Hommel, 1998, 2004; Hommel & Colzato, 2004). On S2, the picture, location and response can independently be repeated or alternated. It has been shown in previous studies using a version of this paradigm, that the performance on S2 is impaired when the features of S1 (shape, location, and response) are partially repeated on S2 (Hommel, 1998, 2004; Hommel & Colzato, 2004). The partial-repetition or binding costs can be divided into visual binding costs, which refer the binding between the two visual features (shape and location), and visuomotor binding costs, which refer to visual features and the action.

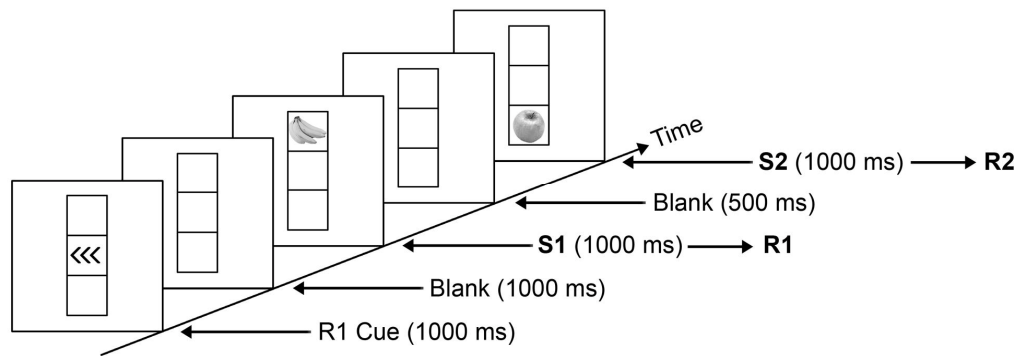


Figure 10. Time sequence of an example trial in the binding task. Subjects had to respond with a precued response on S1 (according to the preceding arrows) and to the picture of S2 (e.g. bananas->press left, apple->press right). Performance costs were measured on the response to S2, in the conditions where features are partially repeated, in comparison with complete repetition or complete alternation of features. It is assumed that the response, picture and location are integrated on S1 and that repeating one, two or all of these features on S2 would automatically reactivate the previously associated features. In the partial repetition conditions, automatic reactivation would lead to inappropriate reactivation of previously associated features, resulting in the performance costs.

Intelligence

Intelligence was tested by using the Raven's Standard Progressive Matrices (SPM, Raven, 1938). The performance on this task correlates with Spearman's *g* factor and has also been associated with visual short-term memory capacity (Carpenter, Just & Shell, 1990) and flexibility in handling event files (Colzato et al., 2006). The test consists of 60 trials of increasing difficulty. Subjects either received the even 30 trials on the pretest and the odd 30 trials on the posttest or vice versa (counterbalanced across subjects).

Results

Neurofeedback training

Figure 11 shows the results of the neurofeedback training on the gamma power for both groups. Using an ANCOVA that considers gamma power of session 1 as a covariate, a significant difference in gamma power was found between the two groups on session 8, $F(1,13)=11.41$, $p<.01$ (Figure 11A). There was a reliable increase in gamma power in the Gamma-Up group but no changes in gamma power in the Control group. No significant differences in beta power between groups were observed, implying that the subjects were unable to modulate their beta band in the current neurofeedback training protocol. No significant group differences were found on any of the items of the questionnaire.

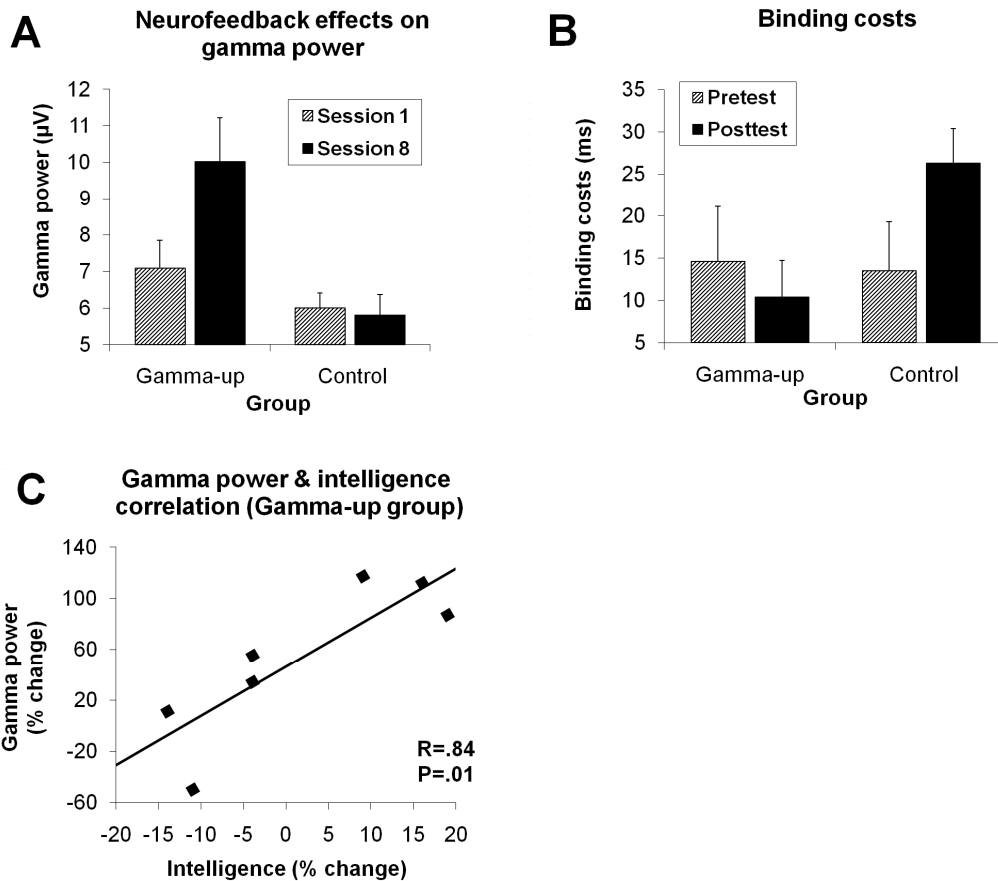


Figure 11. The neurofeedback training resulted in (A) an increase of gamma power in the Gamma-Up group, compared to the Control group, (B) a decrease of binding costs in the Gamma-Up group and an increase of binding costs in the Control group, and (C) a positive correlation between the percent change in gamma power and the percent change of intelligence. Error bars depict standard error of the mean.

Binding

Binding effects were assessed by means of repeated measures ANOVAs of reaction times and error rates with repetition versus alternation of stimulus shape, stimulus location, and response as two-level factors. Reaction times below 200 milliseconds and above 1000 milliseconds were considered as outliers and were discarded (3% of the data). Significant main effects were found for

repetition/alternation of shape, $F(1,13)=8.96$, $p<.05$, location, $F(1,13)=11.75$, $p<.005$, and response, $F(1,13)=6.95$, $p<.05$. More importantly, the pretest replicated earlier findings by showing significant interactions in reaction times between the repetition/alternation of shape and location, $F(1,13)=20.79$, $p<.005$, location and response, $F(1,13)=52.13$, $p<.00005$, and shape and response, $F(1,13)=15.21$, $p<.005$, (Table 1). All three effects were due to better performance if the stimulus feature and/or the response were both repeated or alternated as compared to the repetition of one but not the other. Error rates mirrored the reaction time results for the interaction between shape and response $F(1,13)=30.12$, $p<.0005$, and between location and response $F(1,13)=8.59$, $p<.05$, but not for the interaction between shape and location, $p>.4$. None of the main effects was significant for error rates in the pretest, $p's>.2$.

Table 1. Means of Mean Reaction Times and Standard Deviations (SD) for Responses to Stimulus 2 (RT; in ms) and Percentages of Errors on R2 (PE), as a Function of Group (Control vs Gamma-up), Test Instance (Pretest vs. Posttest), the Match Between Response 1 and Response 2, and the Feature Match Between Stimulus 1 and Stimulus 2.

Pretest					Pretest				
<i>Control</i>					<i>Gamma-up</i>				
	Response Repeated		Response Alternated			Response Repeated		Response Alternated	
Match	RT(SD)	PE(SD)	RT(SD)	PE(SD)	Match	RT(SD)	PE(SD)	RT(SD)	PE(SD)
Neither	493 (43)	9.3 (11.3)	452 (50)	2.9 (4.1)	Neither	533 (57)	6.4 (6.6)	483 (41)	1.5 (2.5)
L(ocation)	509 (67)	4.4 (7.3)	488 (46)	6.6 (5.7)	L(ocation)	575 (56)	5 (5.8)	499 (37)	3.6 (2.5)
S(hape)	466 (43)	1.4 (3.8)	488 (40)	5.8 (4.5)	S(hape)	492 (48)	0.8 (2)	514 (39)	2.3 (2.8)
LS	457 (35)	2.1 (3.9)	490 (52)	3.9 (5.3)	LS	482 (46)	0 (0)	533 (67)	7.8 (9.2)

Posttest					Posttest				
<i>Control</i>					<i>Gamma-up</i>				
	Response Repeated		Response Alternated			Response Repeated		Response Alternated	
Match	RT(SD)	PE(SD)	RT(SD)	PE(SD)	Match	RT(SD)	PE(SD)	RT(SD)	PE(SD)
Neither	458 (64)	7.3 (5.8)	442 (62)	1.4 (3.8)	Neither	527 (68)	5.2 (5.1)	488 (59)	1.4 (2.4)
L(ocation)	503 (85)	6 (7.1)	473 (34)	2.9 (4)	L(ocation)	546 (64)	2.8 (5.4)	502 (54)	1.4 (2.4)
S(hape)	466 (53)	0.7 (1.9)	481 (53)	5 (5.8)	S(hape)	500 (68)	0.7 (1.9)	484 (49)	7.3 (9.9)
LS	435 (51)	1.5 (4)	471 (40)	8.8 (8.2)	LS	468 (63)	0.7 (1.9)	514 (55)	5.2 (2.9)

The posttest showed similar results for the main effects in reaction times of repetition/alternation of shape, $F(1,13)=6.31$, $p<.05$, and location, $F(1,13)=6.09$, $p<.05$, but not for response, $p>.1$. Similar results were also found for the interactions in reaction times between the repetition/alternation of shape and location, $F(1,13)=52.82$, $p<.00001$, and location and response, $F(1,13)=76.14$, $p<.000005$, but not for shape and response, $p>.1$. Error rates mirrored the reaction time results for the interaction

between shape and location, $F(1,13)=13.28$, $p<.005$, but not for the interaction between shape and response, $p>.1$, and location and response, $p>.1$. None of the main effects were significant for error rates in the posttest, $p's>.7$.

To assess the impact of neurofeedback on binding, we considered the data from the first and the second halves of pretest and posttest separately. The reason was that binding effects have been found to be particularly sensitive to practice, especially those related to the integration of visual features (Colzato et al., 2006). The advantage of Hommel's (1998) task version is that it renders the integration process itself task-irrelevant (i.e., the task does not require any binding), which provides a relatively process-pure, strategy-free estimate of the binding process. The flipside of this advantage is that only one of the two stimulus features is actually task relevant (shape in the present case) but the other (location in the present case) can safely be ignored. People seem to learn ignoring the irrelevant feature rather quickly, so that binding effects often disappear in the course of a session (Colzato et al., 2006). To provide a more sensitive measure of binding we thus focused on the first half of the trial¹, that is, on the data from the first 160 trials.

From the first and second halves we calculated individual binding costs for all three feature combinations (shape-location, location-response, and shape-response) by subtracting the mean reaction times and error percentages for the complete repetition condition and the complete alternation condition from the means of both partial repetition conditions², for both the pretest and posttest. In three independent ANCOVAs, the binding costs for the three feature combinations on the posttest were entered as dependent variables, the binding costs for the three feature combinations on the pretest were entered as a covariate and group (Gamma-up, Control) was entered as a fixed factor. For the reaction times, the ANCOVAs revealed a significant impact of training on the interaction between shape repetition and location repetition, that is, on the indicator of visual binding costs, $F(1,11)=10.57$, $p<.05$ (Figure 11B). In other words, there was a significant difference on the visual binding costs of the posttest between the two groups, when controlling for differences between the visual

¹ We nevertheless preferred running a relatively long session just in case the more practice-resistant bindings between relevant features (shape and response) would also be affected by neurofeedback training.

² For instance, the shape-location reaction time binding cost would result from $(RT_{\text{shape rep, location alt}} + RT_{\text{shape alt, location rep}})/2 - (RT_{\text{shape rep, location rep}} + RT_{\text{shape alt, location alt}})/2$. This represents the interaction term, which approaches zero for additive effects of shape and location repetition but grows as the interaction increases in size.

binding costs of the pretest. This effect reflects a decrease of visual binding costs in the Gamma-Up group and an increase of binding costs in the Control group. No significant impact of training was found on both indicators of visuo-motor binding costs, location-response: $p > .3$, shape-response: $p > .6$. The effect on visual binding costs was observed only when the first halves of the pre- and posttest were compared; on the second halves of the pre- and posttest, no significant impact of training was found on any of the binding costs, p 's $> .4$. Error rates were not modulated by training, neither in the first half of the experiment, nor in the second half of the experiment.

Intelligence

There were no significant differences between the percentage correct of the Gamma-up group and the Control group, for the pretest, $p > .7$, and for the posttest, $p > .6$. An ANCOVA with the posttest percentage correct as the dependent variable, the pretest percentage correct as covariate and the two different groups as fixed factor did not reveal an effect of group, $p > .5$, suggesting that neurofeedback does not improve intelligence-related performance in a simple, linear fashion. However, in an analysis pooled over both groups the percent change of the intelligence score from pretest to posttest correlated significantly with the percent change in gamma power, $r = .57$, $p = .01$ (1-tailed; Figure 11C). This correlation suggests that neurofeedback targets a common mechanism that is reflected in both intelligence scores and binding costs, so that training-induced changes covary.

Discussion

Neural synchronization in the gamma band has been proposed as the mechanism or medium that enables binding of different types of information coded in different brain areas. The aim of the present study was to investigate whether training people to increase gamma activity in their brain by means of neurofeedback would lead to any changes in binding-related performance. If this could be demonstrated, this would be relevant for theories concerning the functional role of the gamma band as well as for the development of neurofeedback as a valuable research method.

Indeed, our study provides the first direct evidence in humans that the experimental manipulation of gamma activity affects binding-related performance. In particular, we found that the performance costs associated with the only partial repetition of visual feature conjunctions (as compared to complete repetitions or alternations) are significantly smaller after neurofeedback training targeting gamma activity than after beta-targeted training. This difference reflected a decrease in binding costs in the Gamma-Up group compared to an increase of binding costs in the Control

group. While the decrease in binding costs seems to relate to an increase of gamma power in the gamma up group, increased binding costs in the Control group were not accompanied by any measurable changes in gamma or beta power. However, the Control group received a neurofeedback training protocol which was aimed at decreasing the power of the gamma band and it therefore might be that this training protocol had disturbing effects on the gamma band, which led to the increased binding costs. Notably, these changes were restricted to interactions between visual shape and location features but did not affect interactions involving the response. If we consider interactions between repetition effects to indicate binding processes, this result pattern suggests that gamma training affects visual integration but not sensorimotor integration. This dissociation fits with numerous related observations. For instance, measures of visual integration have been found to be sensitive to manipulations of muscarinic cholinergic but not dopaminergic pathways, whereas measures of visuomotor integration are sensitive to manipulations targeting dopaminergic but not cholinergic pathways (Colzato et al., 2004, 2005; Colzato & Hommel, 2008; Colzato, van Wouwe & Hommel, 2007). It has been speculated that visual integration is mainly driven by local neural interactions in the gamma band, whereas visuomotor integration relies more on beta synchronization (Schnitzler & Gross, 2000), which may suggest a close link between cholinergic pathways and gamma synchronization on the one hand and between dopaminergic pathways and beta synchronization on the other. If so, a more successful neurofeedback training targeting beta activity may well impact measures of visuomotor binding but not visual binding. However, as our own attempt to increase beta power systematically failed, we can only speculate with regard to this issue. Although previous studies have shown differences in the power of the beta band as a result of neurofeedback (Bird et al., 1978; Vernon et al., 2003), the neurofeedback protocols that were used in these studies did not include the gamma band. More specifically, Bird et al. (1978) showed that both gamma band power and beta band power could be modulated by neurofeedback, when trained in isolation. That is, one group of subjects received neurofeedback training to modulate gamma band power, while a different group of subjects received neurofeedback training to modulate beta band power. The neurofeedback training that Vernon et al. (2003) used, was also solely aimed at modulating beta band power. Therefore, the reason for an absence of beta power modulation in our study may be the nature of the neurofeedback protocol that was used: targeting both the gamma band and the beta band.

In any case, our findings support the idea that neural synchronization in the gamma band is related to feature integration, especially to the integration of perceptual features (Engel & Singer, 2001; Jensen et al., 2007). Our findings also support the idea that intelligence is related to gamma-band activation (Jausevec, 2004, Jausevec &

Jausevec, 2005, 2007; Lee et al., 2003; Stankov et al., 2006). Neurofeedback training did not simply increase intelligence-related performance but improvements were correlated with, and thus presumably related to feedback-induced changes in gamma band power. Since performance on the SPM undoubtedly depends on a myriad of cognitive functions, it is not likely that all these processes are affected by gamma enhancing neurofeedback. Rather, the effects of gamma neurofeedback on binding demonstrated in our study and the association between intelligence and binding demonstrated in the study of Colzato et al. (2006) suggests that intelligence is codetermined by binding processes, which in turn is related to the gamma band. The fact that neurofeedback reduced rather than increased binding-related effects might provide a clue for how intelligence and integration are related. As mentioned above already, one may consider two ways of how gamma band changes may modify binding effects. Neural synchronization may play a role in the integration process itself and/or the maintenance of bindings over time (Raffone & Wolters, 2001). If so, increasing gamma power should have facilitated the creation and/or the maintenance of bindings, which should result in more pronounced binding costs. Obviously, this is the opposite of what we observed, which discounts this possibility. Alternatively, neural synchronization may represent the medium of how control mechanisms interact with local coding processes (cf., Gross et al., 2004). If so, increasing gamma power might increase the amount of control over the retrieval of bindings (Colzato et al., 2006), which should result in less interference from previously created and now mismatching bindings. This would indeed fit with our observation. Moreover, control processes are commonly related to the frontal cortex (Duncan, 2001; Miller & Cohen, 2001), as is intelligence (Duncan et al., 2000), and control functions and intelligence arguably overlap conceptually (Kane & Engle, 2002). Gamma-targeted training may thus facilitate the handling of feature bindings by improving the communication between binding-related processes and control functions. Evidence for this hypothesis comes from findings that show a relation between high gamma band activity in the visual cortex and improved discrimination between previously presented visual stimuli and new visual stimuli (old/new effect; Gruber, Müller & Keil, 2002; Gruber, Tsivilis, Giabbiconi & Muller, 2008; Sederberg et al., 2007). Related findings suggest that the source of this gamma band activation may be located in frontal, control related areas (Babiloni et al., 2004; Lutzenberger, Ripper, Busse, Birbaumer & Kaiser, 2002).

To summarize, our study shows that neurofeedback provides a powerful method for studying the functional relevance of frequency bands in the EEG signal. Showing that alterations in the gamma band have consequences for behavioral measures is an important proof of principle, providing more explanatory power than the demonstration of correlations. Even though our results must be considered preliminary,

they do suggest that binding and intelligence are jointly influenced by changes in the gamma band, which points to a common underlying mechanism.

Chapter 6

Enhancing Cognitive Control Through Neurofeedback: A Role of Gamma-band Activity in Managing Episodic Retrieval

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Abstract

Neural synchronization has been proposed to be the underlying mechanism for exchanging and integrating anatomically distributed information and has been associated with a myriad of cognitive domains, including visual feature binding, top-down control, and long-term memory. Moreover, it seems that separate frequency bands have different functions in these cognitive processes. Here we studied whether neurofeedback training designed either to increase gamma band activity (GBA; 36-44 Hz), or beta band activity (BBA; 12-20 Hz), would have an impact on performance of behavioral tasks measuring short-term and long-term episodic binding. Our results show that GBA-enhancing neurofeedback training increased occipital GBA within sessions and frontal GBA across sessions. Both groups showed an increase of GBA coherence between frontal and occipital areas, but the BBA+ group increased BBA coherence between these areas as well. Neurofeedback training had profound effects on behavior. First, we replicated earlier findings that enhancing GBA led to greater flexibility in handling (selectively retrieving) episodic bindings, which points to a role of GBA in top-down control of memory retrieval. Moreover, the long-term memory task revealed a double dissociation: GBA-targeted training improved recollection, whereas BBA-targeted training improved familiarity memory. We conclude that GBA is important for controlling and organizing memory traces of relational information in both short-term binding and long-term memory, while frontal-occipital coherence in the beta band may facilitate familiarity processes.

Introduction

The primate brain, and the human brain in particular, is divided into modules that are (often highly) specialized in processing particular information (e.g., Kourtzi & Kanwisher, 2000; Zeki et al., 1991; Treisman, 1996). This renders communication about, exchange, and integration of distributed information a vital function of human cognition, and poses the question of how neural communication is organized. A possible mechanism underlying this function is the temporal synchronization of neural firing rates (e.g., Singer, 1999; von der Malsburg, 1999). Neural synchronization has been assumed to play a crucial role in the integration of visual features (for an overview, see Engel & Singer, 2001; Jensen, Kaiser & Lachaux, 2007), intermodal integration (von Stein, Rappelsberger, Sarnthein & Petsche, 1999), and visuomotor integration (Roelfsema, Engel, Koenig & Singer, 1997), but also in attentional selection (Fell, Fernández, Klaver, Elger & Fries, 2003), short-term memory retention (Tallon-Baudry & Bertrand, 1999), long-term memory (Klimesch, 1999), and visual awareness (Engel & Singer, 2001). It has been proposed that communication between brain areas may rely on increasingly lower frequency bands as the distance between brain areas increases (Varela, Lachaux, Rodriguez & Martinerie, 2001). More specifically, it has been suggested that neural firings in the gamma range (~30-100Hz) are related to local feature integration and short-term memory (e.g., Tallon-Baudry & Bertrand, 1999), whereas larger anatomical distances are bridged by beta band activity (BBA; ~12-20Hz), such as in intermodal integration (von Stein et al., 1999), visuomotor processing (Roelfsema et al., 1997), or the transfer of frontal control signals to parietal and occipital areas (Gross et al., 2004, 2006).

Even though an increasing amount of studies report correlations between neural synchronization and cognitive processing, the functional relevance of neural synchronization is still under heavy debate (Ghose & Maunsell, 1999; Reynolds & Desimone, 1999; Shadlen & Movshon, 1999; Treisman, 1999). One of the reasons for this debate is that demonstrations of correlations between neural synchrony and cognitive processes cannot rule out that neural synchrony is epiphenomenal to cognitive functions. In order to investigate whether neural synchrony is functionally relevant for cognitive processes, studies in which neural synchrony is treated as an independent variable instead of a dependent variable are needed. In other words, when experimental manipulation of neural synchrony has an impact on behavioral measures of integration, top-down control or memory, inferences can be made about the causal role of neural synchrony in the mechanisms that underlie these different cognitive domains.

A first step in this endeavor would be to show that impairment of neural synchrony leads to decreased performance on tasks that measure cognitive processes for which neural synchrony is presumably important. Indeed, studies have shown patients suffering from schizophrenia show decreased neural synchronization (for an overview, see Uhlhaas, Haenschel, Nikolić & Singer, 2008), including GBA (for an overview, see Lee, Williams, Breakspear & Gordon, 2003). In a recent study by Spencer et al. (2004) it was shown that the abnormalities of GBA in schizophrenia are related to poor performance on tasks that required integration of visual information. Interestingly, 'disintegration' of personality and thoughts is generally regarded as the core symptom of schizophrenia (Spencer et al., 2004). Indeed, the study of Spencer et al. (2004) showed that the severity of the schizophrenia-related symptoms correlates with the poor performance on a visual binding task.

However, studying the effects of neurological impairments on cognition has a number of well-known drawbacks. First, neurological diseases seldom affect neural synchrony selectively and second, patients may have adopted compensatory strategies to cope with their impairments. Moreover, (a history of) medication use may also affect the cognitive processes under investigation. In addition to studies on neurological disorders, studies are needed that manipulate neural synchrony in a more direct way in order to infer causal roles to neural synchrony. In previous research, several methods have been used to manipulate neural synchrony in more direct ways, such as psycho-active drugs (Rodriguez-Bermudez, Kallenbach, Singer & Munk, 2004), visual flicker stimuli (Bauer, Cheadle, Parton, Müller & Usher, 2009), and repetitive transcranial magnetic stimulation (rTMS; Thut & Miniussi, 2009). For instance, it has been demonstrated that muscarinic-cholinergic agonists enhance both GBA (Rodriguez-Bermudez, Kallenbach, Singer & Munk, 2004) and the binding of visual features (Colzato, Fagioli, Erasmus & Hommel, 2005), whereas muscarinic-cholinergic antagonists impair GBA (Rodriguez-Bermudez et al., 2004) and visual integration (Colzato, Erasmus & Hommel, 2004). Other studies have shown that flickering visual stimuli entrain neural activity in the visual cortex and can facilitate cognitive processes, especially with flicker rates in the gamma-range (50-Hz; e.g., Bauer, Cheadle, Parton, Müller & Usher, 2009). Finally, rTMS has been shown to influence neural synchrony in the alpha band (8-14 Hz) and the beta band (14-30 Hz; e.g. Strens et al., 2002; Tamura et al., 2005; Thut et al., 2003).

In the present study, we used neurofeedback to see whether the experimental manipulation of neural synchrony can be demonstrated to lead to systematic changes in cognitive processes. Even though it is true that the widespread advertisement and application of neurofeedback methods in clinical domains is not always based on firm scientific grounds, there is reliable evidence that neural synchronization can be

systematically enhanced or reduced by neurofeedback methods (Bird, Newton, Sheer, & Ford, 1978; Vernon et al., 2003). With neurofeedback training, an online spectrum analysis is performed on the EEG signal that is measured from electrodes attached to the subject's scalp. Providing subjects with real-time feedback regarding the power of a particular frequency band makes it possible for the subject to systematically alter the targeted frequency band(s), at least in some cases.

A few studies have studied the relationship between neural synchrony and cognitive functions as a function of neurofeedback in healthy subjects. Vernon et al. (2003) showed that providing feedback about BBA recorded from the sensorimotor cortex allowed participants to increase performance on a semantic visual short-term memory task. Recent findings from our lab suggest that enhancing GBA with neurofeedback training affects the way people deal with episodic feature bindings (Keizer, Verschoor, Verment & Hommel, 2009). Our results show that subjects who enhanced their GBA were more flexible in handling bindings between two features of visual objects, their shape and location. Changes in GBA also correlated positively with changes in fluid intelligence from pretest to posttest, as measured with Raven's standard progressive matrices (Raven, 1938). This correlation is in accordance with the finding that subjects with a high fluid intelligence show more flexibility in handling visually integrated information (Colzato, van Wouwe, Lavender & Hommel, 2006) and that GBA and fluid intelligence may be related (Jausevec, 2004, Jausevec & Jausevec, 2005, 2007; Stankov, 2006). Since fluid intelligence is arguably related to cognitive control (Kane & Engel, 2002), it can be argued that GBA-targeted neurofeedback may not so much enhance the mechanism underlying the actual integration of information but more the efficiency with which integrated information (episodic memory traces) is organized and controlled. If so, enhancing GBA by means of neurofeedback would be a way to enhance cognitive control, and the control of episodic memory retrieval in particular.

To provide more specific evidence to support this idea, we extended our previous neurofeedback study on feature binding (Keizer et al., 2009) in several ways. First, we increased the number of electrodes used in the neurofeedback sessions. In our previous study we employed one occipital electrode (Oz) to measure the effect of GBA-enhancing neurofeedback on visual processing. Our original idea was that GBA-targeted neurofeedback might enhance local processes subserving visual binding, so that the visual cortex was an obvious choice. However, as already pointed out, the findings of Keizer et al. (2009) suggest that enhancing GBA improves cognitive-control processes, which might affect the visual cortex but are unlikely to have their origin there. Accordingly, we used two electrodes in the current study, one occipital electrode (Oz) and one frontal electrode (Fz). The latter would allow us to monitor frontal activity

and to test whether GBA-enhancing neurofeedback targeting occipital activity would operate directly and selectively on occipital areas only, or whether it would be mediated by frontal activity. In the latter case, one would expect that Oz-directed GBA neurofeedback would also, or perhaps even mainly, increase GBA measured from Fz. In other words, we speculated that subjects might enhance GBA on the occipital electrode indirectly by enhancing GBA on the frontal electrode, which then propagates to the occipital cortex.

A second change with respect to our previous method relates to the criterion for providing neurofeedback. In our previous study, subjects received feedback that was aimed to increase either GBA or BBA at the occipital electrode. The 'GBA+' group successfully enhanced GBA on the occipital electrode from the first to the last neurofeedback session, whereas no significant changes were obtained for the 'BBA+' group. One reason for the absence of any effect on occipital BBA may be that subjects received neurofeedback according to a criterion that coupled the two frequency bands, that is, neurofeedback was provided so to increase BBA *and* reduce GBA at the same time. This dual criterion may have been too difficult to achieve, so that we in the present study provided feedback with respect to the targeted frequency band only. For GBA, the occipital electrode again served as feedback criteria, that is, the feedback was aimed to enhance GBA at the Oz electrode. In contrast to GBA, BBA has been assumed to subserve communication between anatomically remote areas (e.g., Schnitzler, Gross & Timmermann, 2000) and/or the integration of visual and motor features (Colzato et al., 2007), so that we based BBA-related neurofeedback on both the occipital and the frontal electrode. That is, the feedback was aimed to enhance BBA at Oz and Fz.

Finally, we extended our behavioral tests to an episodic long-term memory (LTM) task. As pointed out already, our previous study suggested that GBA neurofeedback may improve the control of retrieval of episodic memory bindings. However, the task we used was tailored to assess the retrieval of implicitly created, task-irrelevant, and only briefly maintained feature conjunctions, so that we were interested to see whether our observations would extend to a more standard episodic memory task with longer retention intervals. A larger body of research indeed suggests that neural synchrony may play a role in LTM (Klimesch, 1999; Sederberg, Kahana, Howard, Donner & Madsen, 2003). For instance, Sederberg et al. (2003) showed that the probability of subsequent recall is predicted by the amount of GBA that occurs during encoding. It has also been suggested that the role of GBA is to match sensory information with representations stored in LTM (Herrmann, Lenz, Junge, Busch & Maess, 2004; Herrmann, Munk & Engel, 2004), which would point to the importance of GBA for retrieval. This is in accordance with findings of Burgess and Ali (2002), who

studied GBA during recognition of visual information stored in LTM. They used a version of the remember/know paradigm, which distinguishes between two subjective states of correct recognition: 'recollection' and 'familiarity'. Recollection refers to the conscious recognition of an event, including contextual information, whereas familiarity refers to weaker recognition—a sense of familiarity without access to contextual information. The results of Burgess and Ali (2002) showed that the subjective experience of recollection was associated with more GBA than the subjective experience of familiarity. Interestingly, recollection was also related with greater functional connectivity in the gamma range than familiarity.

In addition to GBA, many studies also show that theta band activity (TBA; 4-8 Hz) is related with LTM processes (for an overview, see Klimesch, 1999). It has been suggested that GBA and TBA play complementary roles in LTM (Lisman & Buzsáki, 2008), which is supported by the finding that show 'entrainment' of GBA by TBA (Sirota, 2008). Even though both GBA and TBA predict successful retrieval of information stored in LTM, the results of a recent study by Gruber, Tsivilis, Giabbiconi and Müller (2008) suggests that GBA and TBA have dissociable functions in LTM. Gruber et al. (2008) used a source memory task, where familiarity corresponded with the ability to judge whether an item presented in the retrieval phase was also presented in the encoding phase and recollection corresponded with the ability to retrieve information in the retrieval phase that was combined with an item during the encoding phase but not during the retrieval phase. Results showed that occipital/parietal GBA was related to familiarity and frontal TBA was related to recollection. Even though altering TBA with neurofeedback has been demonstrated in previous research using healthy subjects (Egner & Gruzelić, 2003), we have currently not been able to replicate these effects in our lab. Therefore, we chose to focus on GBA and BBA in the present study. To summarize, research on LTM suggests a functional role of GBA but is ambiguous regarding the processes GBA may support. On the one hand, research suggests that GBA is important for recollection but not for familiarity (Burgess & Ali, 2002). On the other hand, the findings of Gruber et al. (2008) suggest that GBA is important for familiarity, but not for recollection. To look into this issue we included a LTM-memory task that could distinguish between recognition and familiarity.

Method

Participants

17 right-handed volunteers (2 male, mean age: 22.6 years) participated in the experiment. Informed consent was obtained from all participants after the nature and

possible consequences of the study were explained to them. The protocol was approved by the local medical ethical committee (Leiden University Medical Center).

Procedure

Each subject was randomly assigned to one of the two groups (eight in the GBA+ group and nine in the BBA+). In a double-blind procedure, both the subject and the experimenter were unaware which of the two possible neurofeedback training protocols was given to the subject until the last subject completed the experiment. Subjects filled out a questionnaire before the start of each neurofeedback training session, enquiring for any notable changes in appetite, sleep pattern, ability to concentrate, memory capacity, and mood. The order of the behavioral tests (binding and long-term memory) was counterbalanced across subjects.

Neurofeedback training

Fifteen subjects completed 8, and two subjects completed 7 neurofeedback sessions. There was one 30-min training session per day. The neurofeedback sessions were spread over a period of 10 or 11 days. For the EEG measurements, a QDS Focus amplifier and electrodes were used (www.brain-trainer.com). The EEG signal was received from two electrodes attached to the scalp of the subject, one on the Oz position and one on the Fz position, according to the international 10-20 system. Reference electrodes were placed on both earlobes and forehead of the subject. Electrode impedances were kept below 10 k Ω . The EEG power spectrum analysis was calculated online with negligible delay, using the Bioexplorer software package (www.cyberrevolution.com). An elliptic filter was applied to the signal, extracting frequencies from the Oz electrode in the gamma range (36-44Hz) for the GBA+ group and from the Oz and Fz electrodes in the Beta range (12-20Hz). An 'upper' threshold was implemented for both groups that was adapting to the power of the frequency band it was applied to. More specifically, the power level was based on a moving average of 30 seconds that was updated continuously with the average power that was calculated over epochs of 0.125 seconds and the thresholds were set to the power level that would be surpassed 75% of the time during the preceding 30 seconds window. Even though the gamma band has been defined in the range of 30 and 100 Hz, we chose to operationalize the gamma band around 40Hz, since this seems to be the most widely accepted and most referred to indicator of the gamma band in humans (i.e. Tallon-Baudry & Bertrand, 1999).

In the GBA+ group, a tone was generated whenever the gamma power of Oz exceeded the upper threshold and in the BBA+ group and a tone was generated whenever the Beta power of both Oz and Fz exceeded the upper threshold. Both

groups were instructed to attempt to increase the rate of the tone occurrences. The maximum rate of the tones was set to one tone per second. Using these criteria, subjects achieved a high rate of tones when the power of their frequency bands was recurrently exceeding the adapting thresholds.

Binding

Binding processes were tested by using the exact same task as was used in Keizer et al. (2009), which is a modified version of the task developed by Hommel (1998; see Figure 12 for an example trial). This task is designed to study the behavioural effects (reaction times and errors) of implicit feature binding. Subjects were instructed to respond with a left or right key press on S1, according to the preceding arrow ($3.6^\circ \times 2.6^\circ$), ignoring the picture ($4.8^\circ \times 4.1^\circ$) and its location (top or bottom). On S2, subjects were instructed to respond to the picture (apple or bananas) while ignoring its location, again with a left or right key press (counterbalanced across subjects). The arrows were presented in the middle square of three equally sized squares (6.0°), placed in vertical alignment, the images of an apple or bananas were placed in either the top or the bottom square. The task consisted of 160 trials, equally divided across conditions.

The rationale of this design is that on S1, the picture, location and response are integrated into an 'event file' (Hommel, 1998, 2004; Hommel & Colzato, 2004). On S2, the picture, location and response can independently be repeated or alternated. It has been shown in previous studies using a version of this paradigm, that the performance on S2 is impaired when the features of S1 (shape, location, and response) are partially repeated on S2 (Hommel, 1998, 2004; Hommel & Colzato, 2004). The partial-repetition or binding costs can be divided into visual binding costs, which refer to binding between the two visual features (shape and location), and visuomotor binding costs, which refer to binding between visual features and the action (shape and response, and location and response). Note that binding is not necessary in this task, as the features of S1 are not systematically related to R1, so that integrating S1 and R1 is neither necessary nor helpful. Also of importance, only one of the three possible binary bindings are related to task-relevant feature dimensions. Response location matters for both R1 and R2, and shape matters for selecting S2, whereas stimulus location is nominally irrelevant. Accordingly, only the binding of shape and response relates to task-relevant dimensions, a fact that has been shown to produce stronger and more reliable binding (Hommel, 1998).

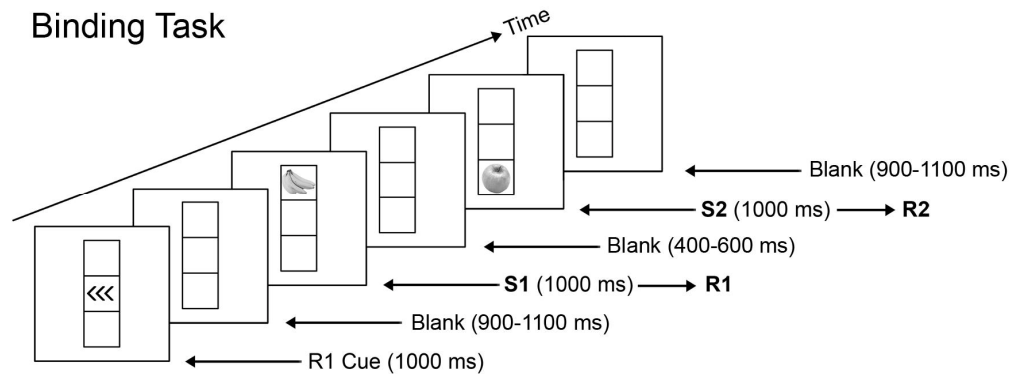


Figure 12. Time sequence of an example trial in the binding task. Subjects had to respond with a precued response on S1 (according to the preceding arrows) and to the picture of S2 (e.g. bananas->press left, apple->press right). Performance costs were measured on the response to S2, in the conditions where features are partially repeated, in comparison with complete repetition or complete alternation of features. It is assumed that the response, picture and location are integrated on S1 and that repeating one, two or all of these features on S2 would automatically reactivate the previously associated features. In the partial repetition conditions, automatic reactivation would lead to inappropriate reactivation of previously associated features, resulting in the performance costs.

Long-term memory

The long-term memory task closely resembled the remember-know paradigm used in the study of Cycowicz et al. (2001). An example trial of the encoding block and of the retrieval block is shown in Figure 13. The stimuli consisted of 260 line drawings that were divided into five lists of 52 items each. The lists were constructed in a way that would result in equal judgements of category membership, concept agreement, name agreement, familiarity and visual complexity, according to the normative data bases published in Snodgrass and Vanderwart (1980), Berman, Friedman, and Hamberger (1989) and Cycowicz, Friedman, and Rothstein (1997). There were no significant differences between lists, for all judgements (p 's > .15). An additional set of 52 drawings were used for the practice block and fillers. Each subject performed the LTM task four times, two times before the start of the first neurofeedback training and two times after the end of the last neurofeedback training. Four sets of pictures were randomly drawn of the five lists for each subject. The task consisted of 2 phases. Each phase consisted of an encoding block and a retrieval block. For each phase, a different list of drawings was used, the order of which was counterbalanced across subjects. 36 of the drawings in a list (half outlined in green and half in red) were shown in the

encoding block, preceded and followed by 2 fillers to avoid primacy and recency effects (subjects were not tested on these fillers). Subjects were instructed to make a discriminative response to the color of the drawing (a left- or right hand response, counterbalanced across subjects) and asked to memorize both the item and the color for the retrieval block.

In the retrieval block 26 black-and-white drawings were presented, 14 new and 12 old (6 that were previously presented in red and 6 in green). Subjects were instructed judge whether the drawing was 'old-remembered', 'old-know' and 'new', by pressing one of three buttons (left and right index finger and middle finger, counterbalanced across subjects, response options presented below the drawing). This part of the task is believed to tap into recognition memory and has also been used as the 'objective' test of familiarity in the study of Gruber et al. (2008). The distinction between 'remember' and 'know' responses is believed to tap into two distinct conscious states with regard to recognition memory, namely recollection and familiarity (Burgess & Ali, 2002).

If the subjects judged the drawing to be new, the next drawing was presented, after a blank interval of 1000 ms. If a subject judged the drawing to be either old-remembered or old-know, the drawing stayed on the screen and subjects were required to judge whether the drawing was presented in red or green in the encoding phase with a left or right button-press (index fingers, counterbalanced across subjects, response options presented below the drawing). This part of the task has been used as the objective test of recollection in the study of Gruber et al. (2008). After a response was made, the next drawing was presented after a blank interval of 1000 ms.

Long-Term Memory Task

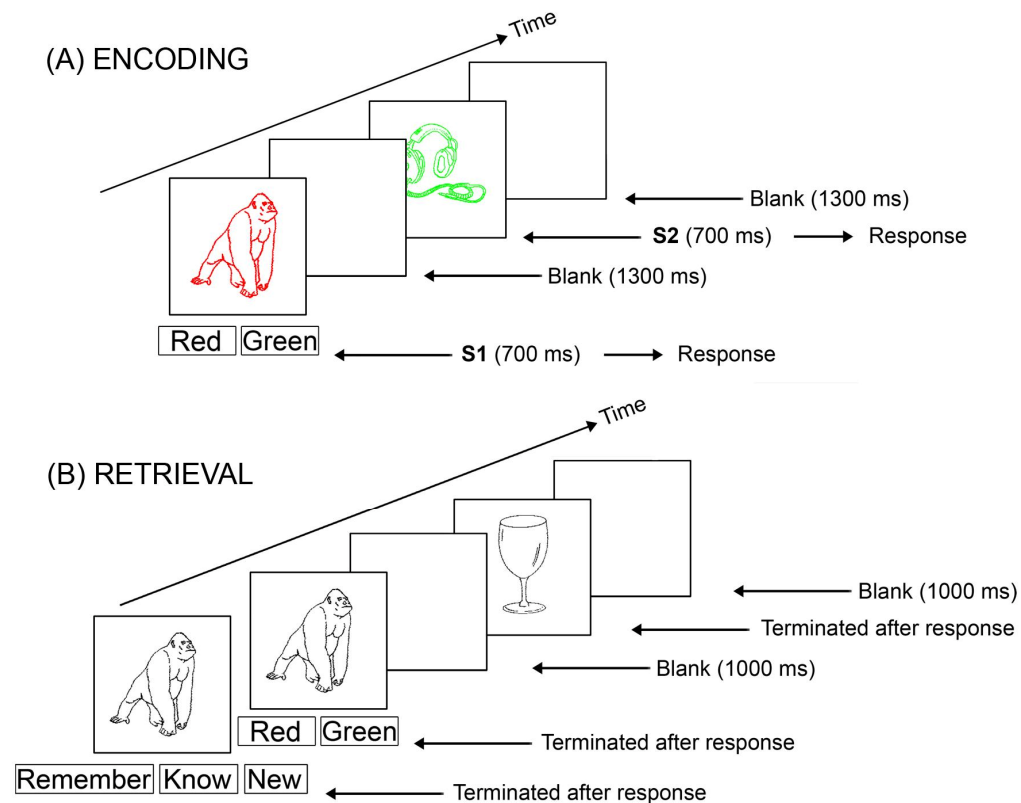


Figure 13. Time sequence of an example trial of the LTM task in the encoding phase (A) and in the retrieval phase (B). Subjects were instructed to make a color discrimination during the encoding phase. Subjects were told that they should try to remember the occurrence of the drawings and their color, since their memory of the drawings and their color would be tested during the retrieval phase. After the encoding phase was completed, subjects were instructed to make a 'remember-old', 'know-old' or 'new' response on the black-and-white drawings that were presented on the screen. When a subject made either a remember-old or know-old response, the drawing remained on the screen and subjects had to judge whether the drawing was either presented in a red or green color during the encoding phase.

Results

Questionnaire

No significant group differences were found on any of the items of the questionnaire. Moreover, independent repeated measures ANOVAs showed no significant interactions between group (GBA+ versus BBA+) and test instance (pretest versus posttest) for any of the items of the questionnaire. However, we did find a significant main effect of test instance on the item inquiring subjects to assess their own ability to concentrate, $F(2,15)=4.9$, $p<.05$, which reflects an increase of the self-assessed ability to concentrate in both groups.

Neurofeedback training

To control for general learning effects, we calculated the GBA to BBA ratio (GBA/BBA) by dividing the absolute power of the gamma band (36-44 Hz) by the absolute power in the beta band (12-20 Hz). Figure 14 shows the results of the neurofeedback training on GBA/BBA for both groups. Two separate repeated measures ANCOVAs for both electrode positions were performed with GBA/BBA as dependent measure, session (first versus last) as a 2-level within-subjects factors and group (GBA+ or BBA+) as between-subjects factor. There was a significant two-way interaction between group and neurofeedback session on the Fz electrode, $F(2, 15)=5.3$, $p<.05$ (Figure 14A). Planned post-hoc comparisons showed that this interaction was mainly driven by a significant increase of GBA/BBA in the GBA+ group, $p<.05$. Group and session did not interact at the Oz electrode, $F(2, 15)=.01$, $p>.5$, but the percent change of GBA/BBA on Oz was positively correlated with percent change in GBA/BBA on Fz. This suggests that subjects enhanced GBA on Oz by means of cortical systems measured by Fz, $r=.7$, $p=.03$ (1-tailed; Figure 14B).

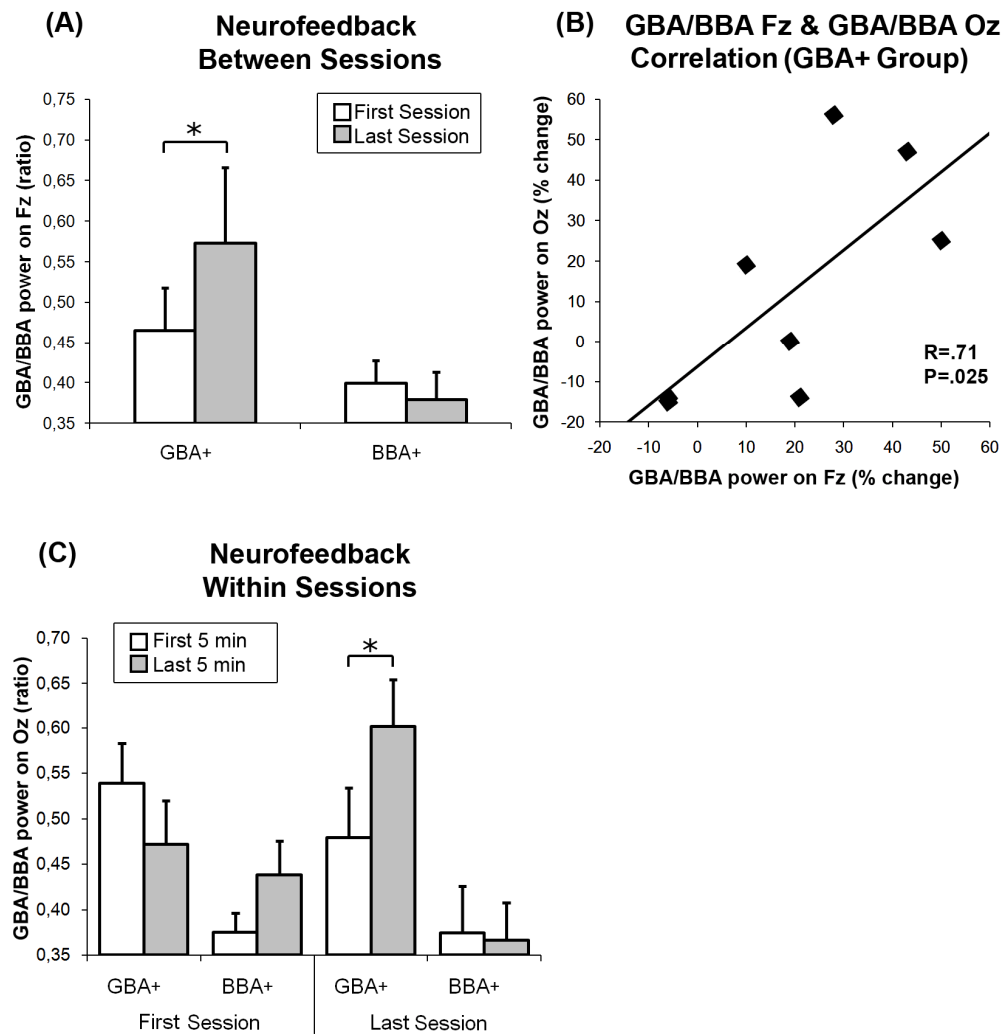


Figure 14. The neurofeedback training resulted in an increase of frontal GBA/BBA ratio in the GBA+ group compared to the BBA+ group across sessions (first session versus last session, (A)). The percent change in frontal GBA/BBA ratio across sessions correlated with the percent change of occipital GBA/BBA ratio (B). The neurofeedback training also led to an increase of occipital GBA/BBA ratio in the GBA+ group compared to the BBA+ group within sessions (first 5 minutes versus last 5 minutes, (C)). Error bars represent standard errors, asterisks indicate significance level of $p < .05$.

This possibility is further supported by the results of the coherence analyses depicted in Figure 15. We calculated the coherence between Fz and Oz for GBA and BBA separately. Two separate repeated measures ANCOVAs were carried out with either GBA-coherence or BBA-coherence as dependent measure, session (first versus last) as a 2-level within-subjects factors and group (GBA+ or BBA+) as between-subjects factor. A significant main effect of session in GBA-coherence, $F(2,15)=4.7$, $p<.05$, indicated that GBA-coherence increased in both groups from the first session to the last session (Figure 15A). However, only the GBA-coherence in the GBA+ group was informative regarding the effects of GBA-enhancing neurofeedback in showing a significant positive correlation between the percent change of GBA-coherence in the GBA+ group and the percent change in frontal GBA, $r=.76$, $p=.014$ (1-tailed; Figure 15B). In contrast, the BBA+ group showed a non-significant positive correlation of $r=.43$, $p=.24$. Again, this suggests that occipital GBA is driven by frontal GBA.

Finer-grained analyses looked into training effects within sessions by comparing the GBA/BBA ratio of the first 5 minutes and the last five minutes of both the first and the last neurofeedback session. A significant three-way interaction between group and the two training factors (within session and between session) for the Oz electrode, $F(2,15)=11.0$, $p<.005$ (Figure 14C), and the following post-hoc comparisons revealed that the GBA+ group did manage to increase GBA power within the final session. The same three-way interaction was significant for the Fz electrode, $F(2,15)=5.4$, $p<.05$, even though the post-hoc comparisons did not show any significant differences.

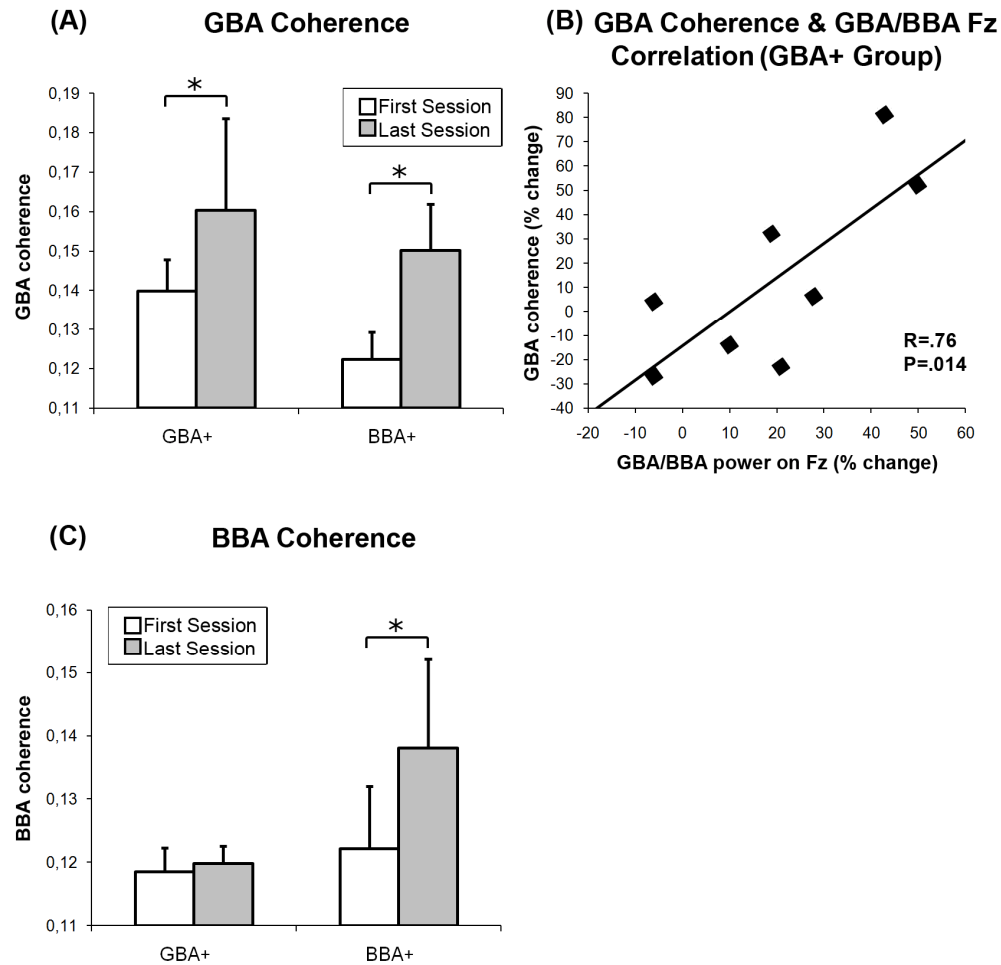


Figure 15. The neurofeedback training resulted in (A) an increase in GBA coherence in both groups (A), a significant correlation between GBA coherence and GBA/BBA ratio on Fz in the GBA+ group and (B) and in a significant increase of BBA-coherence in the BBA+ group (C). Error bars represent standard errors, asterisks indicate significance level of $p<.05$.

For BBA-coherence, we found a marginally significant main effect of session, $F(2,15)=4.5$, $p=.051$, and a marginally significant interaction between session and group, $F(2,15)=4.5$, $p=.051$. Planned post-hoc comparisons revealed that these effects were driven by a significant increase of BBA-coherence in the BBA+ group, $p<.01$ (Figure 15C).

Binding

Binding effects were assessed by means of repeated measures ANOVAs of reaction times and error rates with repetition versus alternation of stimulus shape, stimulus location, and response as two-level factors and group (GBA+ and BBA+) as a between subjects factor. Reaction times below 200 milliseconds and above 1000 milliseconds were considered as outliers and were discarded (<1% of the data). The pretest showed significant main effects for repetition/alternation of the shape, $F(2,15)=10.4$, $p<.01$, and of the location, $F(2,15)=5.8$, $p<.05$. More importantly, the pretest replicated earlier findings by showing a significant interaction in reaction times between the repetition/alternation of shape and location, $F(2,15)=13.6$, $p<.005$, between the repetition/alternation of location and response, $F(2,15)=57.6$, $p<.000005$ and a marginal significant interaction between the repetition/alternation of shape and response, $F(1,15)=4.5$, $p=.051$. These effects were due to better performance if the features were both repeated or alternated as compared to the repetition of one but not the other.

Error rates of the pretest partially mirrored the reaction times results. There was a significant main effect of repetition/alternation of shape, $F(1,15)=7.1$, $p<.05$. Moreover, there was a significant interaction between the repetition/alternation of location and response, $F(2,15)=8.1$, $p<.05$ and between the repetition/alternation of shape and response, $F(1,15)=5.0$, $p<.05$. There were no significant interactions between any of the within subjects factors and the between subjects factor for both reaction times and error rates ($p's>.09$), indicating that the performance of both groups was similar on the pretest.

Individual binding costs were calculated by subtracting the mean reaction times and error percentages for the complete repetition condition and the complete alternation condition from the means of both partial repetition conditions³ for both the pretest and posttest. This generated three measures that reflected binding between shape and location (Shape-Location), between location and response (Location-Response) and between shape and response (Shape-Response). In order to test the impact of neurofeedback training on binding, we used three independent repeated measures ANCOVAs with test instance (pretest versus posttest) as a 2-level within-subjects factor and group (GBA+ versus BBA+) as a between subjects factor we found a significant interaction between Shape-Location and group, $F(2,15)=4.9$, $p<.05$ (Figure 16A). Planned post-hoc comparisons showed that this interaction is most likely

³ The shape-location reaction time binding cost can be calculated using the following equation:

$(RT_{\text{shape rep, location alt}} + RT_{\text{shape alt, location rep}})/2 - (RT_{\text{shape rep, location rep}} + RT_{\text{shape alt, location alt}})/2$. This represents the interaction term, which is not influenced by additive effects of shape and location repetition but as the interaction grows, the result of this equation increases as well.

to originate from a decrease in shape-location binding costs in the GBA+ group, $p=.065$. Second, we found a marginal significant interaction between Location-Response and group, $F(2,15)=4.1$, $p=.06$ (Figure 16B). Planned post-hoc comparisons showed that this interaction is driven by a significant decrease of location-response binding costs in the GBA+ group, $p<.001$. Finally, there was no significant interaction between Shape-Response and group, $F(2,15)=.05$, $p>.8$ (Figure 16C).

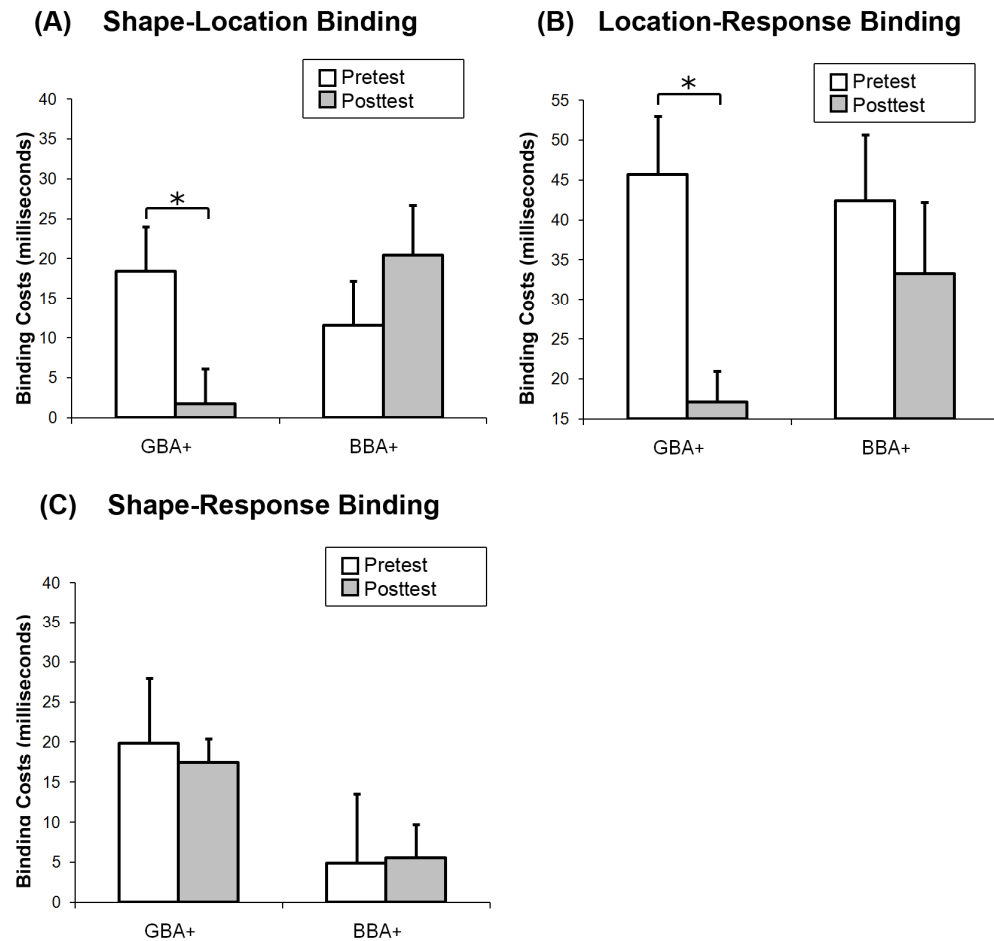


Figure 16. Reaction time data of the binding task. The neurofeedback training resulted in a decrease of binding costs between shape and location (A) and between location and response (B), but not between shape and response (C). Error bars represent standard errors, asterisk indicates significance level of $p<.05$.

The error rates revealed only one reliable finding, an interaction between Shape-Response and group, $F(2,15)=5.3$, $p<.05$. Numerically, binding costs decreased from pre- to post-test in the GBA+ group (4.1% to 1.0%) and increased from pre- to post-test in the BBA+ group (0.5% to 3.7%). However, given that planned post-hoc comparisons did not render any of these changes significant, $p>.1$, the interaction is difficult to interpret.

Long-term memory

Performance on the study block was very good (mean error rate: 85%), indicating that subjects were able to discriminate between the colors of the drawings. Using a repeated measures ANCOVA with test instance (pretest versus posttest), percentage correct of remember versus know responses as within subjects factors and group (GBA+ versus BBA+) as a between subjects factor, we found no significant interaction between test instance, remember/know and group, $F(2,14)=3.4$, $p>.05$. To study the effects of neurofeedback on the more objective measure of familiarity and recollection, we used a repeated measures ANOVA with test instances (pretest versus posttest) and percentage correct of old-new responses (combined over remember/know responses) versus color retrieval responses as within subjects factors and group (GBA+ versus BBA+) as a between subjects factor. We found a significant main effect of test instance, $F(2,14)=8.3$, $p<.05$ which reflects a general increase of performance on the second test instance. A second main effect was found for the error rates of old-new responses versus color retrieval responses, $F(2,14)=24.2$, $p<.0005$, reflecting larger error rates for color retrieval responses. More importantly, we obtained a significant three-way interaction between test instance, old-new distinction versus color retrieval and group, $F(2,14)=8.8$, $p=.01$ (Figure 17A). Post-hoc planned comparisons revealed that this interaction was mainly driven by a significant increase of performance on color retrieval (recollection) in the GBA+ group, $p<.005$, and a significant increase of performance on the old-new distinction (familiarity) in the BBA+ group, $p<.005$. In support of the results of the repeated measures ANOVA we found a significant positive correlation between the percent change of GBA/BBA ratio in the GBA+ group and the percent change in performance on recollection memory, $r=.6$, $p=.04$ (1-tailed; Figure 17B).

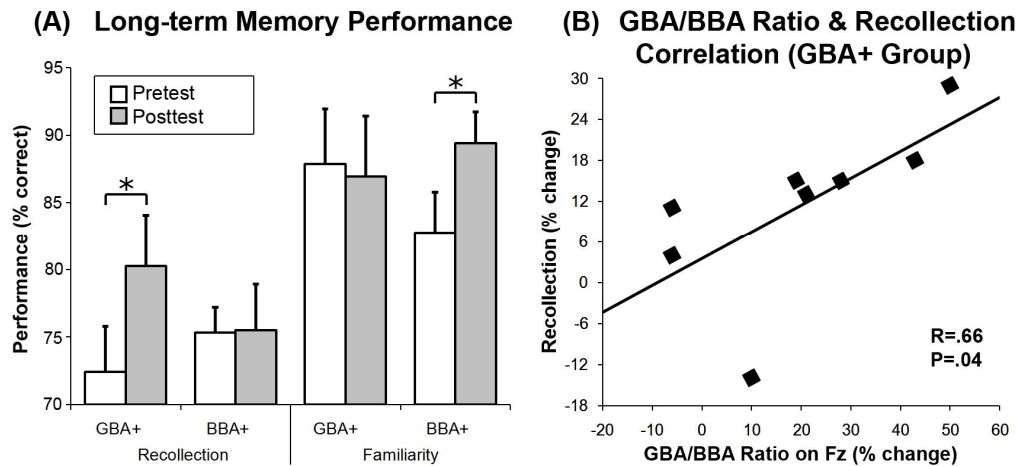


Figure 17. The effect of enhanced GBA on LTM. Subjects in the GBA+ group showed a significant increase of performance on retrieval of the color (recollection), while the BBA+ group showed a significant increase of performance on the old-new discrimination (familiarity). Error bars represent standard errors, asterisks indicate significance level of $p < .05$.

Discussion

Previous research suggests that GBA may play a role in feature integration and/or the management of integrated feature bindings. In the current study we tried to manipulate GBA and BBA by means of neurofeedback, to further investigate and characterize the functional role of neural synchronization in short-term and longer-term feature binding, i.e., episodic LTM. Our results show that subjects were able to learn to increase frontal and occipital GBA through GBA-targeted neurofeedback and to increase BBA-based coherence between frontal and occipital areas through BBA-targeted neurofeedback. The increase of frontal GBA was particularly pronounced and reliable, and it transferred to the final test section. Subjects were also able to increase occipital GBA, within sessions, but in contrast to frontal GBA, this did not transfer across sessions. Given that our neurofeedback training was not explicitly designed to encourage transfer across sessions, it seems premature to exclude the possibility of longer-term occipital GBA learning. Moreover, in our previous study (Keizer et al., 2009) we did obtain evidence for transferable GBA learning at Oz with feedback that informed about the relationship between GBA and BBA, as compared to the pure GBA feedback provided in the present study. Hence, more robust GBA learning in occipital areas seems possible. Nevertheless, the present findings suggest that frontal areas

are more sensitive to GBA feedback and that they did acquire a transferable cognitive skill.

There were even several indications that occipital GBA learning was mediated, presumably even controlled by frontal areas: even though the feedback manipulation targeted and informed about GBA over occipital areas, frontal areas showed more reliable, and more durable evidence of GBA learning, and the amount of occipital GBA learning seemed to be a function of frontal GBA learning. This suggests that subjects enhanced occipital GBA *through* enhancing frontal GBA, which again suggests that frontal areas took over the control of occipital neural rhythms. Even though almost nothing is known about how individuals selectively modulate the power of certain frequency bands via neurofeedback, the possibility that frontal areas may play an important role in such processes is not surprising. Frontal areas are known to be important for top-down control processes (Miller & Cohen, 2001) and to be able to modulate the activity in upstream areas such as the visual cortex (Moran & Desimone, 1985; Spitzer, Desimone & Moran, 1988). Moreover, it has been shown that GBA is enhanced on both frontal and occipital sites during increased cognitive control over visual representations, for instance during attentional selection (Fell et al., 2003) or short-term memory retention (Tallon-Baudry & Bertrand, 1999).

The hypothesis that occipital GBA learning is controlled by frontal areas fits well with our observation that the percent change of GBA-coherence between frontal and occipital GBA correlates positively with the percent change in frontal GBA. GBA-coherence increased significantly in both learning groups and this change was already established in the first neurofeedback session. This does not only suggest that GBA-coherence is very sensitive to neurofeedback manipulations, but also that neural coherence is a means to transfer control signals. Indeed, a recent MEG study provided evidence that frontal areas use neural coherence to prepare upstream areas involved in stimulus processing for anticipated perceptual events (Gross et al., 2006). The idea that inter-area communication and control is mediated by neural coherence fits also with our findings from the BBA+ group. Even though this group showed no evidence of local BBA learning, it did show an increase in BBA-based coherence between frontal and occipital areas—which was not present in the GBA+ group. The feedback that these subjects received was dependent on BBA measured from both electrodes, suggesting that this type of feedback is functional in facilitating long-range neural communication.

Even more important than these considerations is the fact that we found systematic effects of neurofeedback training on the behavioural tasks. First, we found a significant decrease of binding costs between shape and location and between location and response in the GBA+ group. This pattern has a number of interesting

implications. For one, it does not suggest that our neurofeedback manipulation affected feature-integration processes proper. If feedback would have enhanced neural activities that are involved in integration, one would have expected more evidence of integration but not less, that is, an increase of binding costs and not a reduction. This does not necessarily rule out that gamma-band synchronization plays a role in the feature integration (Engel & Singer, 2001), but the method we used does not seem to tap into such processes. Our findings rather suggest that GBA feedback enhanced processes that handle already integrated bindings. Note that significant feedback effects were obtained for bindings that involved task-irrelevant features (location) but not for the binding that relates the two task-relevant aspects, shape and response (see Figure 16). Apparently, GBA feedback reduced the impact of task-irrelevant feature bindings on performance (as in Keizer et al., 2009), suggesting that this feedback enhanced the control and management of bindings in the suppression of irrelevant bindings in particular. Among other things, this fits with our interpretation of frontally mediated GBA learning.

Second, we used an LTM paradigm that allowed us to distinguish between recollection and familiarity, the two dissociable processes that underlie recognition memory. The results of previous research are ambiguous regarding the role of GBA in these processes. On the one hand, the study of Burgess and Ali (2002) suggests that GBA is important for recollection but not for familiarity. On the other hand, a study of Gruber et al. (2008) suggests that GBA is important for familiarity, but not for recollection. Our experiment provides strong support for the first hypothesis: the results of the LTM task show a clear double dissociation between the two neurofeedback groups and the two types of recognition memory. Subjects in the GBA+ group significantly increased their ability to retrieve the color of the drawings in the retrieval phase that was presented during the encoding phase; an ability that is known to reflect recollection processes. Moreover, there was a significant positive correlation between the percent change in frontal GBA and the percent change of recollection. In contrast, the BBA+ group showed a significant increase in the ability to discriminate between 'old' and 'new' items, that is, between items that were previously presented during the encoding phase and items that were presented for the first time during the retrieval phase, which known to reflect familiarity processes. Since the BBA+ group showed an increase of BBA-coherence, but not of BBA power, the increase of familiarity must be attributed to the increase of BBA-coherence between frontal and occipital BBA in the BBA+ group. This conclusion fits with the findings of Sehatpour et al. (2008), which showed that object recognition was related to long-range beta coherence between the lateral occipital cortex (LOC), the hippocampus and prefrontal regions. In summary,

our results clearly show that GBA is important for recollection, and that BBA-coherence between frontal and occipital brain areas is important for familiarity.

It has been shown that recollection and familiarity depend on different brain areas. While recollection has been associated with the hippocampus and frontal-medial brain areas, familiarity seems to depend on the perirhinal cortex and lateral frontal areas (Yonelinas, Otten, Shaw & Rugg, 2005). Whereas the hippocampus is thought to be important for storing information, frontal brain areas have suggested to be related to higher-level retrieval-related mnemonic operations, such as organization, strategic search, monitoring and verification (Simons & Spiers, 2003). In short, frontal brain areas seem to be important for the top-down control of memory traces which are stored in the hippocampus. Since the neurofeedback training primarily increased frontal GBA over sessions, it can be hypothesized that the top-down control processes were facilitated in the GBA+ group. In contrast, the increased BBA-coherence between frontal and occipital brain areas in the BBA+ may reflect a rather control-free mechanism based on long-range communication in the beta range that underlies familiarity. Moreover, it can be hypothesized that the increase of BBA-coherence between frontal and occipital BBA in the BBA+ group reflects enhanced communication between visual brain areas in the occipital lobe and control related brain areas in the frontal lobe. This could result in facilitation of matching incoming visual representations with stored representations, which would enhance familiarity performance.

Conclusion

Taken together, our study demonstrates that neurofeedback can be a powerful tool in research on the functional relevance of neural synchrony in cognitive processes. The findings suggest that enhanced GBA allows for a greater flexibility in handling integrated information in short-term and long-term memory. In contrast, enhanced long-range communication in the beta range seemed to result in facilitation of familiarity-based processes. In both tasks, enhanced frontal GBA seems to have resulted in facilitated top-down control processes that affected the way memory traces of integrated information are organized and controlled. Apart from the important theoretical implications of these findings, the possibility that GBA-targeted neurofeedback can enhance memory control raises interesting questions regarding applicability. For instance, aging is known to hamper the control of memory retrieval (Reuter-Lorenz, 2002) and it would be interesting to see whether such deficits could be encountered by means of neurofeedback.

Chapter 7

Summary and Conclusions

Summary and Conclusions

The binding problem refers to the necessity of the brain to integrate information that is represented in distinct brain areas. A fast, online mechanism is needed in order to perceive integrated sensory information which may be coupled with the actions that accompany it. An increasingly large body of behavioral research has shown that binding processes can be studied by investigating the sequential effects of integrated features on subsequent performance (Hommel, 2004). A very consistent finding across these studies has been that partially repeating previously co-occurring features on a target stimulus impairs performance. The rationale behind this pattern is that co-occurring features are bound together on a single presentation and this association causes automatic reactivation of all features when a single feature is repeated. In addition to the visual features of an object, it has been shown that bindings can also include auditory features (Zmigrod & Hommel, 2009) as well as action features (Hommel, 2004).

This thesis attempted to investigate the underlying (neural) mechanisms of feature integration using behavioral experiments, fMRI and neurofeedback.

The data of chapter 2 showed that binding can occur between features that are known to be processed in the dorsal stream (motion) and features that are known to be processed in the ventral stream (faces and houses). This finding has important consequences for theories that claim that the ventral and dorsal stream are largely independent streams of processing and that the dorsal stream operates exclusively online and has no access to memory (Milner & Goodale, 1995). Since our findings clearly show evidence for memory traces of previous interactions between these two streams, it can be concluded that these theories need to be revised on these points.

The findings that were reported in chapter 3 confirm an important theoretical construct regarding the origin of sequential effects that have been demonstrated in numerous behavioral studies using a version of the paradigm originally designed by Hommel (1998). Using an event-related fMRI design, we showed that repeating the motion that previously accompanied an image of a house automatically reactivates the representation of the house in the parahippocampal place area. In concordance with previous behavioral studies, this partial repetition of features led to impaired performance.

The findings that were reported in chapter 4 showed that retrieval of visual feature bindings depends on the presence of a task-relevant feature, either resulting from a task-relevant feature, or from a conceptual match in long-term memory. Our results showed that the absence of a task-relevant on S1 resulted in an absence of binding costs when the stimuli consisted of arbitrary feature conjunctions. However,

significant binding costs were found when the stimuli consisted of real objects, suggesting that top-down priming is necessary to elicit binding costs. Moreover, explicitly storing the arbitrary visual feature conjunctions in short-term memory did not affect the binding costs, which points to the absence of retrieval of visual bindings, since explicit storage arguably resulted in increased attention to S1. Finally, explicit storage of real objects resulted in the disappearance of binding costs. We hypothesize that retrieval processes that are facilitated by top-down priming are disrupted by short-term memory processes.

Chapter 5 and 6 explored the relation between feature binding and neural synchronization. Many studies using EEG and single-cell recordings have demonstrated correlations between feature binding and neural synchronization in the gamma and beta band (Engel & Singer, 2001). Neural synchronization in the gamma band has also been associated with top-down control during short-term memory (Tallon-Baudry & Bertrand, 1999), long-term memory (Sederberg, Kahana, Howard, Donner & Madsen, 2003) and selective attention (Fell, Fernández, Klaver, Elger & Fries, 2003). However, a lack of research that use methods that directly manipulate neural synchronization in order to demonstrate the functional relevance of neural synchronization has fuelled an ongoing debate on whether or not neural synchronization is epiphenomenal to feature binding and top-down control (Shadlen & Movshon, 1999; Reynolds & Desimone, 1999; Ghose & Maunsell, 1999; Treisman, 1999).

In chapter 5 and 6, we used neurofeedback to manipulate neural synchronization directly. Neurofeedback is a relatively unconventional technique that has seldom been used in fundamental research. However, it has been demonstrated in numerous studies that subjects are able to enhance or decrease neural synchronization in specific frequency bands (Bird, Newton, Sheer, & Ford, 1978; Vernon et al., 2003). In chapter 5 we demonstrated that subjects are able to increase neural synchronization of occipital gamma band activity (GBA; 36-44 Hz) over the course of 8 sessions, lasting 30 minutes each. Enhanced GBA had an interesting effect on the behavioral measure of feature binding, the group that enhanced GBA showed significantly smaller binding costs than the control group, but only for bindings between visual relations and not for bindings between visual and action features. Moreover, the change in GBA correlated positively with fluid intelligence, which points to an increase of top-down control in the group that increased GBA. Our findings are in accordance with previous research that showed that subjects with high fluid intelligence have small binding costs (Colzato, van Wouwe, Lavender & Hommel, 2006). Our findings support the conclusion that high fluid intelligence corresponds with greater flexibility of handling integrated information.

In chapter 6, a slightly adjusted GBA-enhancing neurofeedback protocol resulted in increased frontal GBA over the course of 8 sessions. Moreover, subjects enhanced their ability to increase occipital GBA within neurofeedback sessions. In contrast, subjects that received BBA-enhancing neurofeedback, showed an increase of frontal-occipital coherence in the beta band. Since GBA can be seen as a signature of top-down control processes in frontal brain areas, we hypothesized that subjects attempted to enhance occipital GBA using frontal top-down processes. Increased GBA again resulted in a decrease of visual binding costs, which shows that the effects of GBA-enhancing neurofeedback on visual feature binding are reliable and robust. However, increased GBA also resulted in decreased binding costs between location and response, suggesting that the role of GBA may extend to long-distance bindings. Moreover, enhanced GBA resulted in a selective performance increase of source memory; the ability to retrieve contextual information from long-term memory (Gruber, Tsivilis, Giabbiconi & Müller; 2008). Source memory has been associated with control processes in frontal brain areas and the effect of increased GBA on source memory is therefore in concordance with the hypothesis that GBA is a reflection of top-down control processes. In contrast, enhanced frontal-occipital coherence in the beta band resulted in an increase of recognition memory; the ability to judge whether an item presented in the retrieval phase was also presented in the encoding phase. This is supported by the findings of Sehatpour et al. (2008), who showed that object recognition is related to long-range beta coherence between the lateral occipital cortex (LOC), the hippocampus and prefrontal regions.

The findings presented in this thesis are in accordance with the theory of event coding (TEC) formulated by Hommel, Müsseler, Ascherleben & Prinz (2001). TEC was designed to provide a theoretical framework that takes an empirical stance towards the binding problem. It assumes that binding processes can be studied by analyzing the behavioral consequences of integrated features. These integrated feature-compounds may be comprised of both sensory and action features, leading Hommel et al. (2001) to term these compounds 'event-files'. TEC assumes that features are automatically integrated into an event file upon its presentation/occurrence and retrieved during a subsequent presentation/occurrence of either of the participating features in a kind of pattern completion process. It has been shown that many behavioral effects in the literature can be at least partially explained by this proposed mechanism, such as the flanker-compatibility effect (Mayr, Awh & Laurey, 2003), the Simon effect (Hommel, Proctor & Vu, 2004), inhibition of return (Lupianez, Milliken, Solano, Weaver & Tipper, 2001), and negative priming (Huang, Holcombe & Pashler, 2004). In a paradigm designed by Hommel (1998), these assumptions have been tested explicitly and many papers have reported the behavioral effects of feature binding, showing that they are

reliable and robust (e.g. Colzato, Raffone & Hommel, 2006; Hommel, 1998; Zmigrod & Hommel, 2009). However, it has been largely unknown how these behavioral effects relate to underlying brain mechanisms and phenomena. The current thesis aimed to fill this gap and provide new insights on this topic from a neuroscientific perspective.

Our research has shown that feature binding occurs across clearly dissociable processing streams of visual information processing, suggesting that that feature binding is omnipresent in the brain, occurring between physically separated areas that have often been regarded as operating independently from each other. Moreover, we have shown that the behavioral effects of feature binding is indeed the result of reactivation of previously associated features, which supports one of the basic assumptions of TEC, described above.

A neurocognitive theory of feature binding that is currently receiving a lot of attention proposes that neural synchrony is the underlying brain mechanism of feature binding (Engel & Singer, 2001; Fries, 2005). Many new and interesting studies have been published in recent years that are in line of this view (Sauseng & Klimesch, 2008; Varela, Lachaux, Rodriguez & Martinerie, 2001; Ward, 2003). This development resembles the early days of fMRI research, which could be described as an era of brain mapping research, investigating the information processing characteristics of different brain modules. The current work that is being done could also be viewed as a kind of brain mapping, aiming at the explorations of the functional properties of neural synchrony in different frequency bands. A general picture is beginning to emerge in which neural synchrony is involved in the integration of information that is represented in spatially separated brain modules, with higher frequencies bridging smaller distances and lower frequencies bridging larger distances (Varela et al., 2001).

The research presented in the current thesis supports this idea in that manipulation of neural synchrony in the gamma band resulted in changes of the behavioral measures of feature binding. More specifically, it seems that enhancing neural synchrony in the gamma band via neurofeedback results in enhanced top-down control of event files. This points to a more versatile role of neural synchronization: it may not only be the neural code that represents integrated information, but it may also be the ‘communication channel’ in which specialized brain areas can influence these representations. Indeed, it has been suggested that neural synchrony in the gamma band can represent a top-down bias-signal (Fell, Fernández, Klaver, Elger & Fries, 2003).

Clearly, many issues regarding the neurocognitive basis of feature binding remain to be solved by future research. First, even though the neurofeedback research presented in this paper show that neural synchrony is not only epiphenomenal to feature binding, it is still unknown how spatially distinct brain modules can engage in

the synchronous firings of their neural populations without pre-existing knowledge in the system of the correspondence between different features of an event or object. In other words, we know that neural synchrony *represents* integrated information, but we do not know how neural synchrony is *established* between the to-be-integrated information. Second, the research in the current thesis mainly focused on the brain mechanisms underlying within-modality binding, that is, integration between different visual features. Future research needs to explore the brain mechanisms underlying integration across modalities; between different sensory domains and across perception and action. Finally, the research presented in chapter 4, 5 and 6 showed that top-down processes play an important role in the retrieval of integrated information. However, the investigation of the exact interactions between these top-down (control) processes and binding processes may still provide an interesting avenue for future research, which may be just as informative for the underlying brain mechanisms of feature binding as well as for the way top-down processes operate.

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Summary in Dutch (Samenvatting)

Samenvatting

Onze hersenen worden voortdurend blootgesteld aan een onvoorstelbare hoeveelheid zintuiglijke informatie. Het brein heeft een karakteristieke manier om al deze informatie te verwerken; je zou kunnen zeggen dat het gebruik maakt van het verdeel-en-heers principe. Veel hersengebieden zijn uitsluitend gespecialiseerd in het verwerken van bepaalde informatie. Zo zijn er hersengebieden die basale visuele kenmerken als kleur, vorm of beweging verwerken, maar ook hersengebieden die zogenaamde 'hogere orde' kenmerken, als gezichten of huizen verwerken. Door deze modulaire organisatie van het brein is effectieve communicatie nodig tussen verschillende gespecialiseerde hersengebieden. Wanneer je bijvoorbeeld wordt geconfronteerd met twee objecten, elk met een unieke kleur en vorm, is het noodzakelijk dat er efficiënte communicatie plaatsvindt tussen het gebied dat kleur verwerkt en het gebied dat vorm verwerkt om de juiste kleur met de juiste vorm te associëren. Met andere woorden, de modulaire architectuur van het brein maakt integratie noodzakelijk om een coherent beeld te vormen van zintuiglijke informatie. Het is belangrijk om in te zien dat integratieprocessen razendsnel dienen plaats te vinden om van moment tot moment te begrijpen wat er gebeurt. In dit proefschrift heb ik onderzoek gedaan naar de neurale basis van deze communicatie. Het theoretische kader waarin dit onderzoek is gedaan heet de Theory of Event Coding (TEC; Hommel, 1998). Hierin wordt gesteld dat alle kenmerken van een gebeurtenis automatisch worden geïntegreerd in zogenaamde 'event-files', dus zowel de zintuiglijke kenmerken (bijvoorbeeld kleuren, vormen, geluiden en geuren) als de kenmerken van de handelingen die je op datzelfde moment verricht. Wanneer je bijvoorbeeld president Obama op de treden van het Witte Huis ziet staan, zal er een associatie tussen Obama en Witte Huis in je brein worden gemaakt. Besluit je te reageren op deze input door bijvoorbeeld van achter het hek heel hard *"Keep up the good work!"* te schreeuwen, zal er tevens een associatie gemaakt worden tussen jouw handelen (schreeuwen) op dat moment, Obama en het Witte Huis. Integratieprocessen zijn nodig om te kunnen begrijpen dat Obama op de treden van het Witte Huis staat, maar veel vaker ook om chocola te maken van combinaties die vooraf niet te voorspellen zijn, zoals willekeurige combinaties van kleuren, vormen en locaties.

De manier die ik heb gebruikt om integratieprocessen te bestuderen, is door te kijken naar de effecten van geïntegreerde informatie. In eerder onderzoek is aangetoond dat wanneer je bijvoorbeeld een object twee keer achter elkaar laat zien, de kenmerken die de eerste keer bij dat object hoorden automatisch gereactiveerd worden wanneer je één van die kenmerken herhaalt bij het tweede object. Op deze manier kan je dus kijken of er daadwerkelijk integratie heeft plaatsgevonden tussen de

verschillende kenmerken van een object. Met deze methode heb ik kunnen aantonen dat er automatische integratie plaatsvindt tussen Obama en het Witte huis: Wanneer je opnieuw wordt geconfronteerd met Obama, zonder dat hij op dat moment op de treden van het Witte Huis staat, wordt de representatie van het Witte Huis automatisch gereactiveerd (hoofdstuk 2 en 3). Dit is opmerkelijk, omdat we weten dat gezichten en huizen in hersengebieden worden gerepresenteerd die zich bevinden in twee zogenaamd onafhankelijke informatiestromen. Dit onderzoek laat dus zien dat deze informatiestromen minder onafhankelijk zijn dan voorheen werd aangenomen.

Voorheen werd gedacht dat de herhaling van één kenmerk van een event-file volledig automatisch alle kenmerken activeert waarmee het geassocieerd is. Het zou dus niet uitmaken of je zo'n kenmerk op dat moment belangrijk vindt voor jouw handelen. Het onderzoek dat in hoofdstuk 4 beschreven wordt, laat zien dat automatische reactivatie afhangt van het soort kenmerken dat herhaald wordt. Bij abstracte kenmerken vind alleen automatische reactivatie plaats wanneer dat kenmerk op dat moment belangrijk voor jou is. Wanneer er plaatjes van huizen en gezichten in het spel zijn, blijkt reactivatie altijd op te treden, ook zonder dat deze informatie voor jou op dat moment relevant is. Dit valt te verklaren doordat dit soort informatie oude, bestaande geheugensporen activeren, die op hun beurt weer reactivatieprocessen kunnen triggeren. Wanneer je dus na je bezoek aan het Witte Huis weer geconfronteerd wordt met Obama, zal het Witte Huis sowieso gereactiveerd worden, ongeacht jouw bezigheden op dat moment.

Het doel van het onderzoek dat in hoofdstuk 5 en 6 wordt beschreven, was om meer inzicht te krijgen in de rol die neurale synchronisatie speelt in integratieprocessen. Tot nu toe waren er wel verbanden gevonden tussen maten van integratie en neurale synchronisatie, maar om te onderzoeken of neurale synchronisatie werkelijk belangrijk is voor deze processen, is het nodig om neurale synchronisatie te beïnvloeden en vervolgens de effecten hiervan te meten op integratieprocessen. In mijn onderzoek heb ik gebruik gemaakt van neurofeedback om neurale synchronisatie te beïnvloeden. Neurofeedback is een methode waarbij neurale synchronisatie gemeten wordt met EEG en waarbij proefpersonen directe feedback krijgen over hun neurale synchronisatie op een bepaald moment. Op deze manier kunnen proefpersonen getraind worden om hun neurale synchronisatie te verhogen of te verlagen. In mijn onderzoek heb ik proefpersonen getraind om locale neurale synchronisatie in de gamma band te verhogen, omdat vanuit de literatuur aanwijzingen bestonden dat deze specifieke neurale synchronisatie samenhangt met integratieprocessen. Uit de resultaten van deze studies bleek dat een verhoging van occipitale gamma band synchronisatie ervoor zorgde dat proefpersonen in staat waren om meer flexibel en georganiseerd om te gaan met geïntegreerde informatie

(hoofdstuk 5 en 6). Met andere woorden, na een omhoog getrainde gamma activiteit vind je het makkelijker om de associatie tussen Obama en Witte Huis los te laten en bijvoorbeeld Clinton en het Witte Huis met elkaar te associëren, mocht dat over een tijdje nodig zijn. Tevens blijkt verhoogde gamma activiteit te leiden tot een verbetering in het ophalen van associaties uit het lange termijn geheugen (hoofdstuk 6) en in hoofdstuk 5 werd ook nog een verband gevonden tussen de verandering in gamma band synchronisatie en de verandering in de prestatie op een intelligentietest.

Hoewel het duidelijk is dat er nog veel onderzoek gedaan moet worden om te begrijpen wat de onderliggende mechanismen van integratieprocessen zijn, kan mijn proefschrift wel een tipje van de sluier oplichten. De resultaten van mijn experimenten schetsen een beeld van het brein waarin integratieprocessen alom vertegenwoordigd zijn, waarin integratieprocessen beïnvloedt kunnen worden door het belang van de te integreren informatie en waarin neurale synchronisatie zowel te maken heeft met integratie als met de organisatie van geïntegreerde informatie.

Curriculum Vitae

André Willem Keizer was born in Leeuwarden on June 18th, 1980. In 1999 he completed secondary education at the Comenius College in Leeuwarden. In 2005 he graduated in Cognitive Psychology at the Rijksuniversiteit Groningen and started as a PhD-student at the Leiden University. Here he studied the neurocognitive basis of feature integration and gave lectures on fMRI, workgroups on cognitive neuroscience and supervised internships. Since August 2009, he works as a post-doc at the University of Amsterdam on the neural correlates of consciousness.

