Brain Areas Involved in the Retrieval of Updated Memories: The Long-Term Effects

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Abstract

When we learn something new, we have to update our memory. The new information is stored together with the old and by doing this some of the old information might destroyed. The questions I wanted to answer were what brain areas are activated by the retrieval of symbols associated with either a sound or a face and if any residual activation would be found for the old associations (when association was changed during training) even though it had been 18 months since the last study was conducted. 11 participants were included, 5 females, 6 males between the ages of 23-29 (mean 24.67). Data was collected using fMRI. In an earlier study (Stiernstedt, 2009) participants had studied a symbol-sound or symbol-face combination. After two, of a total of five days, half of the symbol associations changed (faces to sounds and vice verse). The same symbols and associations were used here. The results showed activation in fusiform gyrus for faces and primary and secondary auditory cortex for sounds, residual activation was found in secondary visual cortex for faces and secondary auditory cortex for sounds. This implicates that the same areas involved with encoding the information is also involved in retrieving it and that the old information is not deleted but still accessible.
Brain Areas Involved in the Retrieval of Updated Memories: The Long-Term Effects

Maria Ölund

Do you remember trying to memorize a friend’s new phone number, later trying it and seeing that you dialled the old one? You might ask yourself “What happened?” The probable answer is that you learnt the new information together with the old one and now you remember both. But how is it done? How come we remember things we are supposed to have forgotten? This is one of the things I will be looking at here.

For people to be able to learn new things memory is necessary.

Memory
Human memory is usually divided into three different parts depending on how long they can store memory. Short-term memory handles small parts of information for short periods of time while working memory processes and decides what you are going to do next. Long-term memory (LTM) is the part where we store information for long periods of time (Purves et al., 2008). To be able to store memories we first have to encode them into LTM and when we later want to use them we have to be able to retrieve them. These are all parts of LTM. Encoding deals with how information is incorporated into the brain (Nyberg, Cabeza, & Tulving, 1996), storage deals with passively retaining the encoded information in memory over time (Purves et al., 2008), and retrieval handles the recovery of encoded, stored information to make it usable again (Nyberg et al., 1996; Kompus, Larsson, Olsson, & Nyberg, 2008).

LTM is usually divided into two different types depending on what type of information it handles; the two parts are declarative and non-declarative memories. Non-declarative memories are implicit and therefore cannot be shared with others. Therefore people usually do not know they have these kinds of memories. Declarative
memories on the other hand consist of things we can declare, are aware of (Purves et al., 2008). Usually they are divided into two parts, semantic and episodic memories. Semantic memories contain our knowledge about the world and our capacity to recollect facts. Episodic memories deal with our capacity for recollecting things that have happened in the past, remembering episodes such as what we did the day we graduated high school (Squire & Zola, 1998; Nyberg et al., 1996; Kompus et al., 2008).

Encoding
To be able to keep the information we have gather from our surroundings we have to encode it into memory. This is usually referred to as encoding and activates specific areas. Episodic encoding has been shown to be lateralized to the left prefrontal cortex (PFC) in several studies (Nyberg et al., 1996; Nyberg, Persson et al., 2000). But other areas are also involved in encoding memory, activation have been found in the striatum (Dahlin, Stigsdotter-Neely, Larsson, Bäckman, & Nyberg, 2008) as well as the hippocampus (Anderson et al., 2004). But not all agree that encoding is unique in the areas involved. Danker and Anderson (2010) suggests that it is the same areas that are involved in encoding and later retrieval.

Retrieval
The next step after encoding memories is being able to reach them later when they are needed. This is called retrieval and episodic retrieval activates the right PFC (Cabeza & Nyberg, 1996; Habib, Nyberg & Tulving, 2003; Nyberg et al., 1996). What exact areas activated are debated but activations has been found in the right anterior PFC (Buckner, Raichle, Miezin & Petersen, 1996; Cabeza & Nyberg, 1996; Nyberg, Persson et al., 2000) as well as the posterior medial-parietal and bilateral frontal-opercula areas (Buckner, Raichle, Miezin & Petersen, 1996). But activation have also been found in the left parietal (Nyberg, Persson et al., 2000) and frontal areas (Naghavi & Nyberg, 2005) in contrast to the right lateralization mentioned earlier. But these are not the only areas said to be involved in episodic retrieval, activation
have also been found in dorso-lateral PFC and parietal cortex (Naghavi & Nyberg, 2005; Braver et al., 2001) as well as the anterior prefrontal areas (Ranganath, Johnson & D’Esposito 2003). Other areas also involved are the intra-parietal sulcus (IPS), inferior parietal lobule and other focal areas in the superior parietal cortex (Wagner, Shannon, Kahn & Buckner, 2005).

The same lateralization found for episodic memories have also been found for semantic memories but in this case it has a left lateralization (Nyberg et al., 1996; Tulving, Kapur, Craik, Moscovitch & Houle, 1994). But even though most activation has been found in the left PFC some activation was also found in the right middle frontal gyrus and the right inferior temporal gyrus (Burianova & Grady, 2007).

**Face and sound specific areas**

This study was done to try to extend the results found by Stiernstedt (2009). He used visual stimuli consisting of pictures of Japanese signs (Kanji-signs) that had been associated with either a face or a sound. The same symbols and associations will be used in this study. An increased activation in the right posterior visual and temporal regions of the brain has been found during picture processing (Nyberg, Persson et al., 2000). There is also an area in the left fusiform gyrus (referred to as the fusiform face area) that is significantly more activated by faces than other objects. The same study also found greater activation in a more superior and lateral location in the right hemisphere in the middle temporal gyrus/superior temporal sulcus (STS) in half of their subjects (Kanwisher, McDermott & Chun, 1997). Other studies have also found activation in posterior cortices and left frontal regions during retrieval of faces (Kompus et al., 2008) while the left ventro-lateral prefrontal cortex was activated during processing of non-verbal items such as unfamiliar faces (Braver et al., 2001).

For sound activation have been found in the auditory cortex during retrieval of words that were previously studied together with sounds, even when participants were not instructed to retrieve the sound (Nyberg, Habib, McIntosh & Tulving, 2000).
Research Questions

Memory is a field that have been subjected to research for decades. This report will focus on a specific part, the retrieval of memories. It has been shown that retrieval of studied memories strengthens those (Larsen, Butler & Roediger, 2009). But why is that and how is it done? When we learn something new a memory trace is formed, involving the hippocampus (Anderson et al., 2000). But for memories to stabilize, reorganization has to be done in the brain. This can lead to the removal of the hippocampal involvement. For each time the memory is retrieved it can change some (update), new information can be added to the memory and by doing this some old information might be lost (Dudai, 2004). The dorso-lateral PFC has been shown to be involved in updating the LTM (Murty & Ranganath, 2007). An important role have also been suggested for the hippocampus together with the fronto-striatal regions in helping to prevent the elimination of the old information in memories by reactivating it while new memories are being encoded (Khul, Shah, DuBrow & Wagner, 2010).

Several studies have shown that retrieving information reactivates the areas involved in encoding the information. This test was done to see if the same type of results can be seen here, considering that it had been 18 months since the last time the participants used the memories. A study by Nyberg, Tulving et al. (2000) showed that auditory cortex is activated during retrieval of words earlier studied together with sounds although participants was not asked to remember the sounds. The same concept have been found to be true for visual stimuli, it was showed that retrieval of sensory specific information reactivated areas involved in sensory processing (Wheeler et al., 2000). Originating in the research I expect to see similar findings in this study. The study will also look to see if there is any difference in how well the participants remember faces contra sounds and original contra updated stimulus.

To answer the questions put forward in this report regarding which parts of the brain are activated during retrieval of stored memories, functional magnetic resonance imaging (fMRI) will be used. fMRI is a non-invasive technique that makes
it possible to see which parts of the brain is activated during the completion of the test (see section in method for further information) (Purves et al., 2008).

In this study we will try to extend the results found by Stiernstedt (2009). In his study Stiernstedt asked participants to learn to associate a symbol with either a sound or a face. On the third (of five) day, half of the associations were changed, sound associations became face associations and vice verse (see figure 1). The goal of the study was to see if any residual effect was left by the old stimuli association. In this study the participant’s memory of the associations to the earlier learned symbols was tested to see if it was still there, 18 months later. It also tries to answer what brain areas are involved in the retrieval of the old memories. It will more specifically look at which brain areas are activated during the retrieval of the face and sound associated symbols. Excluding areas not specific to these two cases. The main question to be answered is if any residual activation will be found for the old associations in the case where the association was changed during training (either from sound to face or face to sound).

Figure 1. A schematic over Stiernstedt study (2009) (taken from his report, p.13). Shows how the training was done, changing half the associations on the 5th day. The stimulus updated while in the scanner was not used in this study.
Method

Pilot-study
To be able to improve the results in the actual study, a pilot-study with two participants was conducted. The participants were asked to look at the symbols they had learnt in Stiernstedt (2009) study and answer which association they had to each symbol. Two things were learned from the pilot study; One, that the performance was quite low and therefore it was decided that each stimuli would be repeated three times in the study to be sure that enough data (of correct answers) was collected. Two, comments were given about the time-span used, that it was too short and that the participants did not feel like they had enough time to think back and remember the associations. To correct for this a pre-test was added. By having a pre-test the participants would be exposed to the symbols before the main test. Since no feedback was given of whether the participant’s answers where right or wrong the memory would remain intact and not be exposed to any changes. Since no time-limit was used during the pre-test each participant could take the time needed to be able to remember. By doing this they had an idea about the symbol association before the test and would not have to remember it in the scanner for the first time.

Participants
Because of the follow-up nature of this experiment the same participants will be used here as was used by Stiernstedt (2009). At the time they participated in the study done by Stiernstedt, all of them where students at Umeå University. All of the original participants was contacted by email and phone and asked to participate again. The participants were not allowed to have studied Kanji-signs since the last time due to the nature of the study. They were also screened for any possible accident that could affect their performance in the fMRI camera. 12 of the original 20 participants agreed to participate, 5 females and 7 males. The age ranged from 23 – 29 years (mean age of 24.67 years). A sum of 300 SEK was given as compensation to the participants that
completed the study. All participants gave written informed consent. The study had been ethically approved by Umeå University.

Apparatus and Procedure
The stimuli combinations used in the experiment was made up of 86 symbols taken from a prior study; 14 of the symbols had only been associated with a sound, 24 had change association from a face to a sound, 14 had only been associated with a face, 24 had changed association from a sound to a face and 10 of the symbols was new or had no associations to it. All symbols were then repeated three times during the test in the scanner. The symbols used were Kanji-signs taken from Stiernstedt (2009) study. In Stiernstedt study the participants had been divided into two groups and each group had been trained on different symbol associations. Which symbols used in the study conducted here depended on whether the participants had belonged to group one or two in the previous study. All participants were tested on the same symbols in this study as they had learnt in the original study (Stiernstedt).

They used the same symbols as they had trained on earlier and the new symbols used was symbols they had not seen or had not associated with any stimuli in the previous study. The test was conducted on a PC, using a program written in E-prime 2.0 (Psychology Software Tools, Inc. USA).

The test
The study was divided into two parts, both conducted on the same day. The first part was conducted outside the scanner and the second part was the test conducted while the participants lay inside the scanner.

Pre-test
First the participants were asked if they remembered what they had done in the earlier study, if not they were given a brief explanation about what they had done. Afterwards they were informed that they were going to conduct a test on a PC and
where asked to read instructions explaining what they were about to do and asked if they had any questions. Then they were tested on the previously learned symbols on a PC and were asked to decide whether they associated the symbol on the screen with a face, a sound or if they did not know/thought it was a new symbol. During this task there was no time-limit, they were asked to take the time they needed to remember.

**Test in scanner**

After finishing the pre-test the participants were instructed that they where to conduct a second test in the scanner. During this test the same stimulus would be shown and they were informed that they expected to answer what, if any, association they had to the stimuli and that they were allowed to change their answer from what they had answered during the pre-test. For each stimulus there were three different answers that could be given, if they associated the symbol with a face, a sound or they thought the symbol was new/had no association. It was also pointed out that this test would have a time-limit; each stimulus would be shown for two and a half second followed by a cross shown for two seconds before the next stimulus was shown. The time they could answer was during the stimuli and the subsequent cross was shown (see figure 2). They were also informed that every stimulus would be shown several times regardless of whether they had answered right or wrong.
Figure 2. An example of how the stimulus was presented and during what time the participants could answer. First a Kanji-symbol (Japanese) was shown, then a cross, then a new symbol.

Imaging technique

To answer the questions put forward regarding which parts of the brain is used during the retrieval of memories; functional magnetic resonance imaging (fMRI) was used. fMRI uses a magnetic field, a radio frequency transmitter and receiver together with some data processing to explore what parts of the brain are activated during different tasks. The magnet field makes the hydrogen atoms in our body align in the same direction. When the radio frequency transmitter is activated it sends out a pulse that sends the atoms into a higher energy-state. Later when the transmitter is turned off the atoms goes back to their original energy-state releasing the access energy which can be detected by the radio frequency receiver. Depending on the time it takes for this to happen, which is affected by the immediate surrounding environment, contrast between different types of tissues can be detected (Purves et al., 2004).

During activation in the brain more oxygen is needed by the neurons. They start breaking down glucose, which is faster but less energy effective, instead of using oxygen. This leads to an increase in blood flow for a short time and therefore a change in the amount of oxygenated blood. fMRI measures the difference in magnetic
resonance that blood has depending on whether the hemoglobin is oxygenated or not. This method is called Blood Oxygen Level Dependence (BOLD) and is built on the ratio between oxyhemoglobin and deoxyhemoglobin in the body. Higher levels of oxyhemoglobin give higher BOLD signal intensity. By collecting this data and analysing it the areas of activation can be found (Logothetis & Wandell, 2004).

The disadvantage with fMRI is that it does not have the best temporal resolution. It would have been preferable to see the activation immediately but since fMRI rely on blood flow which takes a few seconds before it sets in (Huettel et al., 2004). Another problem with fMRI is that it is only measures neural activity indirectly and therefore there could be other factors that influence the result (Eysenck & Keane, 2005). But it has been found that the BOLD signal still correlate well with neural activity (Logothetis, Pauls, Augath, Trinath & Oeltermann, 2001).

Imaging Procedure
Data collection was made on a 3T Phillips Achieva scanner (Phillips Medical Systems, Netherlands). Functional T2*-weighted images were obtained with a single-shot gradient echo EPI sequence used for blood oxygen level dependent imaging. The sequence had the following parameters: echo time: 30 ms, repetition time: 1500 ms (31 slices acquired), flip angle: 70°, field of view: 22 x 22 cm, 64 x 64 matrix and 4.65 mm slice thickness (3.44 x 3.44 mm in-plane resolution). The coil was an 8 channel SENSE head coil and a SENSE-factor of 2.6 was used. The stimuli were shown on a MR-compatible LCD-monitor placed at the end of the scanner bore. The participants viewed it through a tilted mirror attached to the head coil. The visual presentation and gathering of reaction time was done by a PC using E-prime 2.0 and Lumitouch fMRI optical response keypads (Photon Control Inc., Canada) were used to collect responses.
Analysis of data

Pre-processing
To make the fMRI images analysable it is necessary to do some pre-processing on them before anything else is done. The pre-processing steps used were: realignment and unwarping, slice-timing correction, normalization and spatial smoothing. Realignment is done to correct for any movement that the participant have done during the scan. The first scan is used as a reference volume, the rest of the scans are aligned to this image so that even if the participant moved during the scan all images will have the same spatial location. Unwarping is a different kind of alignment that corrects for the non-linear distortion that might occur near air filled cavities such as oral or nasal cavities.

When collecting the images of the brain it is done one slice at a time. The brain is divided into several slices that are later put together to get a picture of the whole brain; in this experiment 31 slices were used. Slice-timing is done to correct for the shifts in registration that is found due to the effect that the entire brain cannot be scanned at once; it is done one slice at the time. Therefore there is a time-gap between when the first and last slice is collected. All brains have different sizes and structures. Normalization is done so that we can compare brains to each other. The brains are morphed into a standardized brain-template, to be as close to each other as possible according to size and structure. Spatial smoothing is done to make it easier to compare activation between participants and to improve the signal-to-noise ratio (SNR). Spatial smoothing blurs the activations which make it possible to compare different brains even though they might differ slightly anatomically (Huettel et al., 2004).

fMRI data analysis
After the pre-processing the data was analysed using a multiple regression analysis which is used when there is several variables. The regression analysis focuses on the relationship between dependent and independent variables. In this study nine
regressors (independent variables) were used, the updated and original stimuli each divided into two cases with faces and sounds that in turn is divided into two subcategories, hits and misses and the last one is new stimulus. To see what activation could be found in the different cases regressors were compared to each other, also called contrasting (see table 1 for full list of contrasts). Contrasting takes the activation in one regressor and subtracts it from the activation of the other and the result is the activation that is specific for the contrast you are interested in (Huettel et al., 2004). For example if you compare updated faces and original faces, the resulting activation would be the areas where only updated faces are activated or where the activation for updated faces is bigger. SPM 5 running on Matlab 7.7.0 and DataZ 9 (Developed at UFBI, Umeå, Sweden) were used to create and view the results.

Certain areas were more interesting to look at than others and therefore functional areas of interest (ROI) were defined and used. Two ROI: s were used, one for faces and one for sounds. Stiernstedt study (2009) trained the participants on a symbol-face or symbol-sound association while inside the scanner. They saw a symbol either together with a face or while hearing a sound. By looking at the brain areas activated by either the faces or sounds (during training) ROI: s could be created. The face ROI was made by taking all the activation that pictures of faces generate and calculating where activation in the brain was found. These areas were then used as a mask on the other conditions and it is only activation inside the mask that is looked at, everything else was excluded. It allows for a drastic reduction of the areas needed to be looked at to find the activation of interest. The same method was also used for the sound ROI (Huettel et al., 2004). An uncorrected p-value of 0, 05 was used for the contrasts and a threshold of 10 voxels. The voxel threshold is used to filter out any activation that is smaller than the threshold value since it might be caused by white noise. For the rest of the report only activation inside the mask will be shown. For the masks an uncorrected p-value of 0,001 and threshold of 10 voxels were used.

The output data from the analysis in DataZ 9 was given as Talairach-coordinates (xyz-coordinates). To find the brain areas corresponding to the coordinates the Talairach Client (www.talairach.org/client) was downloaded and used. It uses the
Talairach space atlas (Talairach & Tournoux, 1988) to locate which brain areas corresponds to which coordinates. It gave the exact brain area for each location as well as the Brodmann area. When no brain or Brodmann area was found the parameter was extended with ± 1mm at a time up to ± 5mm until a result was given.

**Behavioural data analysis**

Repeated measure ANOVA was used to see if any significant main effects (for the factors used) or interaction between the factors were found. A main effect shows if there is any significant difference between the conditions but it gives no directionality of the difference or says anything about between which conditions the difference was found. Interaction shows if the results found for the factors are depending on each other. If main any main effects were found a one-tailed independent sample T-test was conducted to get the directionality of the difference. Two different ANOVA were done, one using two factors each with two levels and the other using three factors each with two levels. The factors used were stimuli (face-sound), updated (original-updated) and pre-test (pre-test- main test) in that order (first ANOVA with only the two first factors). The reason behind using a repeated measure ANOVA was because the same participants were tested on all factors. A p-value of 0.05 was used throughout the ANOVA and T-tests.

Table 1. *The different contrast looked at for the fMRI data. The contrasts should be looked at from the top, contrasting original face with updated face for example*

<table>
<thead>
<tr>
<th></th>
<th>Original face</th>
<th>Updated face</th>
<th>Original sound</th>
<th>Updated sound</th>
<th>Hits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original face</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Updated face</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Original sound</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Updated sound</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Misses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>x</td>
</tr>
</tbody>
</table>
Results

Behavioural data

A box plot was done on the results of the participant’s performance for the test in the scanner. The result showed an outlier for participant number two in the updated faces case. An outlier result means that the result deviate significantly from the rest of the results. Warranting for the removal of participant from the analysis. The mean score of the percentage of right answers for each condition was 0, 38 for original faces, 0, and 34 for original sounds, 0, 34 for updated faces and 0, 23 for updated sounds (figure 3). A repeated measure (2x2) ANOVA was conducted on the mean percentage of the results from the main test (in scanner) to see if there were any significant differences between the results. A significant effect was found for both Stimuli (F=7.156, p= 0.023) and Updated (F=5.446, p=0.042) but no effect was found for the interaction (F=2.915, p=0.119) (see figure 4). Using a one-tailed T-test a significant effect for face over sound stimulus were found (t=2, 14, p=0.019) and a significant effect was also found for original over updated stimulus (t=2, 17, p=0.018).

A 2x2x2 repeated measure ANOVA was conducted on the mean percentage of the results from both the pre and the main test to see if there was any significant difference in the performance between the two. The three factors used were Stimuli, Updated and Pre-test (y/n), a p-value of 0, 05 was used. It showed no significance for pre-test (F=3.749, p=0.082).

A comparison was made between the z-values for activation found in this study and those found by Stiernstedt (2009). It showed higher values for Stiernstedt in all but two cases (one case there was no difference) (table 2).
Figure 3. Interval plot over the four cases. The dot shows the mean value and the bars the standard deviation for each case.

Figure 4. Shows the profile plot for the repeated measure ANOVA. Stimuli (1=face, 2=sound). Updated (1=original, 2=updated).
Table 2. Difference in activation (z-value) for the same area between Stiernstedt (2009) and this study expressed in %. A positive result means better value for Stiernstedt.

<table>
<thead>
<tr>
<th>BA</th>
<th>Z-value</th>
<th>Difference in %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Results</td>
<td>Stiernstedt</td>
</tr>
<tr>
<td><strong>Face</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Original faces</td>
<td></td>
<td></td>
</tr>
<tr>
<td>37</td>
<td>2,51</td>
<td>3,79</td>
</tr>
<tr>
<td>19</td>
<td>3,34</td>
<td>4,12</td>
</tr>
<tr>
<td>Updated faces</td>
<td></td>
<td></td>
</tr>
<tr>
<td>37</td>
<td>2,39</td>
<td>2,73</td>
</tr>
<tr>
<td>18</td>
<td>2,92</td>
<td>2,76</td>
</tr>
<tr>
<td>Residual faces</td>
<td>*</td>
<td></td>
</tr>
</tbody>
</table>

| **Sound** | | |
| Original Sound | | |
| 22 | 3,86    | 2,6            | -0,33               |
| Updated sound | | |
| 22 | 2,63    | 2,63           | 0,00                |
| Residual sound | | |
| 21 | 1,81    | 2,6            | 0,44                |

Regression analysis

One of the contrasts looked at was successful retrieval, the different areas activated by hits compared to misses. It turned out that the only area activated by hits compared to misses was the upper thalamus. In this analysis no ROI was used so a p-value of 0,001 was used.

During the analysis three contrast for faces and three contrast for sound was looked at to see which specific areas where involved in the different cases. A ROI was used for all contrasts looked at, the face ROI for face contrasts and the sound ROI for the sound contrast.
Face specific areas

Activation for the original face contrast (where the difference in activation between original faces and original sounds was used) was found in the fusiform gyrus in the left temporal lobe (BA 37), the right posterior lobe and BA 18 (see figure 5, table 3 gives a complete report). For the updated face contrast (the difference between stimulus that was updated to face during training and original sounds) activation was also found in the fusiform gyrus in the left temporal lobe (BA 37), the right posterior lobe and BA 18 as well as in the cerebellar tonsil in the right posterior lobe of the cerebellum (figure 5). In the residual face contrast (looking at stimulus that was changed from a face to a sound during training and comparing it to original sounds), brain activity related to the previously established face-symbol association that was no longer relevant for the present memory task, activation was only found in one place, the cuneus in the right occipital lobe (BA 18) (figure 5). Strongest activation was found for original faces where no updating was done. The weakest contrast was found for the residual activation in the updated face versus original sound contrast.

An overlap could be seen in the right occipital lobe, the cuneus (BA 18) for all three contrasts. For the first two contrasts overlap could also be found in the fusiform gyrus in the left temporal lobe (figure 6).

Sound specific areas

Activation for the original sound contrast (comparing activation for original sounds against original faces) could be found in the middle temporal gyrus (BA 22) in the left and in the transverse temporal gyrus (BA 42) in the right temporal lobe (figure 7; table 3 gives the complete results). For the updated sound contrast (the difference between stimulus that was updated to a sound during training and original faces) activation was found in the middle temporal gyrus (BA 21) in the left and the superior and sub-gyrus in the right temporal lobe (BA 41, 13/22) (figure 7). In the third contrast, residual sound (looking at a stimulus that was changed from a sound to a face during training and comparing it to original faces) activation was also found in the temporal lobe. More precisely activation was found in the left superior temporal
and sub-gyrus (BA 22, 20) and right superior, middle temporal gyrus (BA 13, 21, 21/22) (figure 7). Of all contrast the strongest was found for the original sound versus original face contrast. The other two did not differ too much from each other.

An overlap could be seen for all three contrasts in BA 21/22, the middle gyrus in the temporal lobe (figure 8).
## Table 3. Activation found using regions of interest.

<table>
<thead>
<tr>
<th>Area of activation</th>
<th>Talairach Coordinates</th>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>ROI face</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Original Face (Original face vs. Original sound)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R PL</td>
<td>#</td>
<td>24</td>
<td>-68</td>
<td>-20</td>
<td>5.89</td>
</tr>
<tr>
<td>R OL cuneus**</td>
<td>18**</td>
<td>12</td>
<td>-104</td>
<td>4</td>
<td>4.91</td>
</tr>
<tr>
<td>L OL lingual gyrus</td>
<td>18</td>
<td>-10</td>
<td>-100</td>
<td>-6</td>
<td>4.80</td>
</tr>
<tr>
<td>L TL fusiform gyrus</td>
<td>37</td>
<td>-38</td>
<td>-54</td>
<td>-16</td>
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The different contrast showing the areas activated as well as the coordinates of the activation. * within ±1mm; ** within ±2mm; *** within ±3mm; **** within ±4mm; # no BA within ±5mm. BA = Brodmann Area; R = right cerebrum; L = left cerebrum; FL = Frontal lobe; OL = occipital lobe; PL = posterior lobe; TL = temporal lobe
Figure 5. Activation for the three face contrasts. Green activation for original faces, red activation for stimuli updated to faces, blue activation for stimuli that was changed from faces to sounds.

Figure 6. Face activation overlap. Green = original face vs. original sound activation, red = updated face vs. original sound activation, blue = updated sound vs. original sound activation. Yellow = green + blue activation, pink = red + blue activation, brown = green + red + blue activation (marked with black arrows).
Figure 7. Activation for the three sound contrasts. Green activation for original sounds, blue activation for stimuli updated to sounds, red activation for stimuli that was changed from sounds to faces.

Figure 8. Sound activation overlap. Green = original sound vs. original face activation, red = updated face vs. original face activation, blue = updated sound vs. original face activation. Yellow = green + blue activation, pink = red + blue activation, brown = green + red + blue activation (marked with black arrows).
Discussion

The main purpose of this study was to examine if any residual activation could be found for the associations that had been changed during training in Stiernstedt study (2009). If any residual activation could still be found even though 18 months had passed with no reactivation of the association. The results showed that activation was found for both residual faces and sounds. I was also interested in seeing if the activation found corresponded to the activation found by Stiernstedt (2009). This turned out to be the case.

It has been found that by retrieving memories we reactivate them (Wheeler et al., 2000; Nyberg, Habib et al., 2000) and by doing that we activate the same areas concerned with encoding the information. Therefore the activation expected to be found in this study was to be in the same areas involved in the encoding of the information. This also turned out to be true.

Face-specific representations

For the face region of interest activation was found in the left temporal fusiform gyrus (BA 37) and right occipital cuneus for both original and updated faces. For original faces activation was also found left occipital lingual gyrus (BA 18) and activation for updated faces was also found in the left inferior occipital gyrus (BA 18).

The temporal cuneus (BA 18) was activated by both the original and updated faces. It has been associated with the encoding of pictures (Vaidya, Zhao, Desmond & Gabrieli, 2002), the classification of natural objects (such as people) and retrieval of visual memories (Kalénine et al., 2009).

Activation in the left fusiform area (BA 37) has been associated with face perception in earlier studies (Kanwhiser et al., 1997; Stiernstedt, 2009) and was expected to be found. The left lateralization of the activation has been associated with lexical/semantic processing as well as face recognition (Simons, Koutstaal, Prince, Wagner & Schacter, 2002). The left fusiform gyrus has also been found to be
activated by picture recognition by itself (Vaidya et al., 2002). The lateralization for this study is directed left while Stiernstedt results show a right lateralization. According to Simons et al. (2002) the right fusiform gyrus plays a greater role in processing specific visual form information about objects, where as the left fusiform is involved in lexical/semantic processing. This might indicate that the participants used semantic information when trying to remember the association and that it was not the specific face they remembered, rather if the association was for a face or not. This is also in line with information gathered from the participants. Most of them said that they had made up stories about the symbols to remember the associations and that it was the stories more than the actual faces they remembered.

The activation was significantly stronger for the original than updated stimulus. The reason behind this might be the longer and uninterrupted training the participants had of these stimuli compared to the updated ones where they changed association on the third (of five) day. This could also be seen in how well the participants remembered the associations. Faces was significantly easier to remember than sounds, therefore it seems like original faces are the easiest to remember. They also had the highest percentage (mean) of right answer.

Activation in the fusiform gyrus (BA 37) was expected to be found for all face contrast in line with Stiernstedt (2009). This was not the case, activation was only found for original and updated faces, no residual activation was found. The reason for this might be the long time period between the last and this test. Memory fades away over time, especially if it is not used, reactivated, which was the case here.

Residual activation for faces was found in the secondary visual cortex in the right occipital cuneus (BA 18). This area has been associated with the encoding of pictures (Vaidya et al., 2002) and the classification of natural objects (such as people) (Kalénine et al., 2009). The fact that the secondary and not primary visual cortex was activated might indicate that it is not the faces specifically that the participants remembered but rather the object (a person) compared to a sound. This would explain why no residual activation was found in the fusiform gyrus since no specific face was remembered. Why it was only in the residual case that the fusiform gyrus was not
activated might be explained by the fact that reactivation, in this case by changing association, weakened the strength of the association and that it disappeared over time when no reactivation was done.

One interesting thing that could be seen was that activation was greater for residual than for updated faces in BA 18. The same pattern could also be seen for residual compared to updated sounds at BA 21 but not for BA 22 where the activation was lower for updated than residual sounds.

Sound specific representations
Activation found inside the sound region of interest was located in the left middle temporal gyrus (MTG) for original (BA 22) and updated sounds (BA 21) as well as in the left and right MTG for residual sounds (BA 22). Residual sound activation was also found in the right middle and superior temporal gyrus (BA 21 and 13).

Activation was found for both original and updated sounds in the right primary auditory cortex (BA 41, 42) (Purves et al., 2008). Activation in primary auditory cortex for stimulus associated with sounds have also been found in other studies (Nyberg, Habib et al., 2000) but there the activation was bilateralized. Activation was found in different Brodmann areas for the two contrasts, BA 42 for original sounds and BA 41 f for updated sounds.

It have been found that the MTG plays an important role in sound recognition (Maeder et al., 2001) and that BA 22 in secondary auditory cortex is vital for sound recognition (Purves et al., 2004). The results found by Maeder et al. were bilaterally localized while in this study they were left lateralized. The reason for this might be that the left hemisphere is more involved in sound recognition. It has also been found that the MTG are involved in integrating information both within and across modalities (Beauchamp, Lee, Argall & Martin, 2004). According to research (Tervaniemi et al., 2000) activation for sound during listening should be located mostly in the left hemisphere while the right is activated by music. But not all
research support this, Maeder et al (2001) found bilateral activation in their study which is in line with the results found here.

Residual sound activation was found in MTG (BA 21, 22) as well as in the right superior temporal gyrus (BA 13). As mentioned earlier, the MTG plays an important role in sound recognition (Maeder et al., 2001), BA 22 is vital for sound recognition (Purves et al., 2004) and BA 13 is activated by passive listening (Maeder, et al., 2001). This activation pattern is not totally consistent with Stiernstedt (2009) results, in his case the activation was only found in BA 22 for the original and updated sounds. Residual activation for sounds was instead found in BA 21, the same activation was also found in our study.

There was a large difference between the activation (T-score) for the original and updated sounds, where the original scored almost two times as high. The same tendencies were also found in the results of how well the associations were remembered (mean percentage) were original sounds scored higher than the updated ones. A significant difference was found for original compared to updated stimulus.

Overall results
The original study by Stiernstedt (2009) looked at 20 people but in this study only twelve people was tested and of them only eleven was used for the calculations. This can have affected the result in a negative way. Because of the relative small population the ability to generalize will deteriorate. The study only included university students which might have affected the generalization negatively.

Looking at the difference in activation (z-score) between Stiernstedt and our results it could be seen that the participants performed better during Stiernstedt study for original faces and residual sounds while performing better in our study for original sounds (using a 20% difference as a cutting point).

Considering the time span between the execution of this study and the previous, 18 months, the results must be considered positive. All participants had some memory of the studied symbols and their associations, both the original and updated
ones. But because of the time span the results found was all quite low. Comparing the results in this test to the ones found by Stiernstedt (2009) shows a drastic decrease of the mean performance for all conditions. In accordance with the previous results original faces had the highest percentage of remembrance and updated sounds the lowest. A difference between Stiernstedt and this study was found for the updated faces where the score was lower than for the original sounds in Stiernstedt study but had the same percentage in this one. The reason for this might be that pictures are easier to learn and remember than words (Nyberg, 1999) and therefore can withstand the forgetting that time causes better.

Significant difference was found for what type of stimuli was used and whether it was updated or not. This is in line with results found only looking at the results from the scanner. Because of the poor mean results for all conditions, but especially the updated ones, it would have been interesting to see if the participants, when giving the wrong answer, actually gave the first association (before the change). This was not looked at in this study but is something to have in mind in future studies.

Since there was such a big time-gap between the two tests it would have been interesting to see what the results had been if this study had been conducted closer in time to the first one, seeing if the same results had been found then as well. This is something that future research can try to answer.

**General discussion**

The results found implicates that the same areas involved with encoding information is also involved in retrieving it. The results also supported the theory that old information is not eliminated when new information is learned, rather they seem to be integrated together. During this process some of the information might be lost but most of it will remain intact. Taking these two together will give further support for the complexity of how memory works. The fact that repetition seems to strengthen memories was also supported by this study and is something that should be implemented in schools and learning as a whole.
Overall I would say that conducting this study taught me the importance of planning and also the importance of having a good idea about what you are doing before actually trying to do it. It also showed me work needed to get a working experiment.
References


