Repetition-related neural plasticity: common memory mechanisms in birds and humans.

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Introduction: Repetition priming refers to a behavioral change (in speed, accuracy,…) associated with the processing of a stimulus due to prior exposure to that same stimulus. It is a form of implicit memory representing one of the most basic expressions of human memory and it is supposed to be shared by other complex nervous systems (1). At the neural level, repeated processing of a stimulus usually induces a reduction of the neural response, called repetition suppression and in few cases, an increase of the neural response, called repetition enhancement. Recognition memory is a form of explicit memory and refers to the ability to appreciate that a stimulus has been previously encountered (is it familiar or novel?). The relationship between repetition priming and recognition memory remains unclear. Whereas some authors argue that both processes are supported by distinct neural substrates and distinct mechanisms (2), others support the view that memory systems are highly interconnected and that priming may contribute to recognition memory (3). Songbirds are a well-known model for learning, plasticity and memory processes. Contrary to non-human primates, they share with humans the capacity to learn their vocalizations. They also possess remarkable memory abilities. Neural mechanisms supporting learning and memory in songbirds are nevertheless poorly understood. In the present study, we investigated at the neural level the effects of stimulus repetitions using conspecific songs as stimuli and assessed the interaction of these repetition effects with the familiarity of the experimental subjects (male zebra finches) with the song stimuli

Material and Methods: Sixteen adult males zebra finches, anesthetized with isoflurane, were used for this BOLD fMRI experiment. Neural activity was measured on a 7T Pharmascan scanner (Bruker) with a spin-echo T2W sequence (TE = 55 ms; TR = 2000 ms). Stimuli consisted of familiar (song from a cage mate) and novel (song from a bird housed in another room) conspecific songs which were presented 25 times each to the anesthetized subject in a block design. Data were realigned, co-registered to an MRI atlas of the zebra finch brain, and smoothed. Statistical results were then analyzed with the General Linear Model implemented in SPM software. A repeated measure ANOVA was used to test the two main effects namely "repetition" (by comparing the first 12 expositions to the stimuli to the last 12 expositions to the same stimuli) and "familiarity" (familiar vs. novel song), and their interaction. The effect of repetition and its interaction with familiarity was further investigated by a regression analysis relating the brain activation level with the number of stimulus presentations and by testing whether the individual slopes of the best linear fit differed from zero and between the stimuli. This approach is more sensitive than the ANOVA described above but assumes that changes are linear.

Results: Familiar songs induced a higher BOLD response as compared to novel songs in the lateral striatum ($p < 0.0001$) and in the frontal nidopallium ($p = 0.0005$) but a lower response in the caudal mesopallium ($p = 0.0003$) and in the caudal nidopallium ($p < 0.0001$). Repetition suppression was found in a large set of regions, including the frontal nidopallium ($p < 0.0001$) and the caudal mesopallium ($p < 0.0001$). An interaction between both factors ("repetition" and "familiarity") was found in the caudal mesopallium ($p = 0.0005$; fig. 1). Post-hoc tests indicated that this interaction resulted from the presence of a repetition suppression triggered only by familiar but not by novel songs. The linear regression approach revealed two additional regions presenting a significant interaction ($p < 0.00001$). One region located in the cerebellum presented a repetition enhancement elicited by novel songs (mean slope = 0.07) but a repetition suppression elicited by familiar songs (mean slope = -0.08). In the other region, located in the frontal nidopallium, neural activation decreased faster when triggered by novel (mean slope = -0.10) than by familiar songs (mean slope = -0.04).

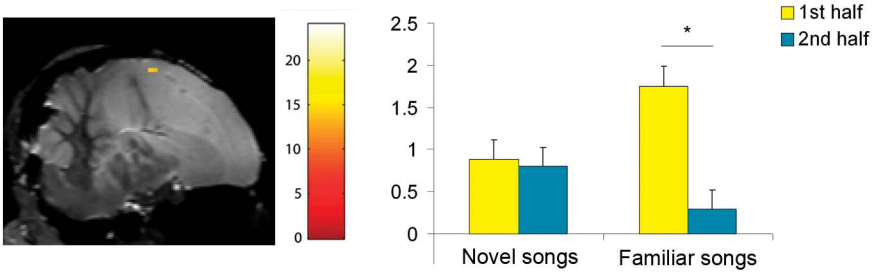

Figure 1: Interaction between "familiarity" and "repetition" factors. Left: statistical parametric F-map of the region where a significant interaction was found at the group level (uncorrected $p < 0.001$). Middle: Color scale of F values. Right: Mean relative amplitude (in %, + SE) of neural activations elicited by novel and familiar songs during the first half (in yellow) and the second half (in blue) of the experiment. Stars indicate statistical significance of post-hoc tests between the first and the second part of the experiment, for each stimulus separately (t tests, corrected $p < 0.05$).

Discussion and Conclusion: As in humans, the neural effects of stimulus repetitions were observed in a large set of cerebral regions of zebra finches. In both species, most effects consisted in repetition suppressions of the neural activity while repetition enhancements were only rarely observed. Additionally some effects were found to depend on the familiarity with the stimulus whereas others did not. A repetition enhancement elicited only by novel songs was found, suggesting the formation of new representations or new memory traces. This study thus reveals the presence of elaborate memory mechanisms in the songbird brain that are similar to those occurring in the human brain. Plasticity phenomena were observed within the time course of an fMRI experiment (40 min.), highlighting how fast these plastic changes can occur. Repetition of stimuli is inherent to fMRI protocols for achieving a good statistical signal-to-noise ratio. Our experiment showed that the effect of repetition at the neural level can differ according to the stimuli. Differential activation triggered by two stimuli can thus potentially be overlapped by differential repetition effects induced by these stimuli. That should encourage researchers to disentangle stimuli effects per se to repetition effects induced by these stimuli.

References

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