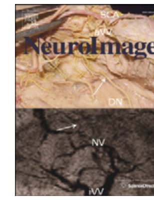
NeuroImage 74 (2013) 179–187

Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg



Picture novelty attenuates semantic interference and modulates concomitant neural activity in the anterior cingulate cortex and the locus coeruleus

Ruth M. Krebs [a,*], Wim Fias [a], Eric Achten [b], Carsten N. Boehler [a]

[a] Dept. of Experimental Psychology, Ghent University, 9000 Ghent, Belgium
[b] Dept. of Radiology and Nuclear Medicine, Ghent University, 9000 Ghent, Belgium

ARTICLE INFO

Article history:
Accepted 13 February 2013
Available online 21 February 2013

Keywords:
Anterior cingulate cortex
Conflict
fMRI
Locus coeruleus
Novelty
Saliency

ABSTRACT

Goal-directed behavior requires the ability to focus on information that is relevant to a given task and to ignore information that might interfere with it. In the Stroop task, for example, the influence of an irrelevant word needs to be overcome, which is believed to be difficult because it arises in a fast and automatic fashion, which effectively renders it very salient. Here we address the question of whether this can be counteracted by increasing the saliency of the task-relevant input, for example by modulating its relative novelty, which increases saliency in a fairly implicit and controlled fashion. To test the influence of novelty on interference processing, we employed a picture–word interference task in the fMRI scanner, in which we manipulated the novelty of the task-relevant picture. We found that picture novelty indeed reduced typical behavioral interference from incongruent words. Moreover, familiar incongruent trials were associated with activity increases in the anterior cingulate cortex (ACC), a prime conflict-processing region, as well as in the noradrenergic locus coeruleus (LC), which entertains connections both to and from the ACC. The lack of analogous activations in novel incongruent trials suggests that the reduction of behavioral interference was not related to enhanced conflict-resolution processes, but rather to the automatic prioritization of novel pictures which appears to avert the influence of irrelevant words at the front end. Interestingly, activity in the ACC and LC was slightly stronger in novel congruent trials compared to incongruent ones, which may reflect increased relevance of novel stimuli when encoded in a congruent context. In summary, the present data demonstrate that stimulus novelty clearly reduces semantic interference, and highlights a complex interaction of interference and novelty processing on the neural level, including an involvement of the noradrenergic system in the processing of cognitively and perceptually salient events.

Introduction

The fast assessment of salient changes in our environment is essential for flexible behavioral control. Even when we pursue a clear goal, our behavior can be influenced by salient information, regardless of whether it is relevant or irrelevant, compatible or incompatible with respect to our goal. In the laboratory context of a color-naming Stroop task, for example, the influence from irrelevant word meanings needs to be overcome to correctly name the font color (MacLeod, 1991). According to cognitive-control models, the behavioral interference in the Stroop task arises from the fairly automatic processing of the word and the activation of associated response tendencies, despite its behavioral irrelevance (Miller and Cohen, 2001). On the neural level, the processing of interfering words has been associated with activity modulations in the anterior cingulate cortex (ACC),[1] which can in turn trigger cognitive-control processes to resolve the conflict and to correctly perform the task at hand (Carter and van Veen, 2007; Egner and Hirsch, 2005; Kerns et al., 2004; MacDonald et al., 2000; Miller and Cohen, 2001; Nee et al., 2007; Ridderinkhof et al., 2004). It has further been postulated that conflict-related modulations in the ACC are associated with activity changes in the locus coeruleus (LC, Aston-Jones and Cohen, 2005), the source region of noradrenergic projections to frontal cortex (Sara, 2009).

Considering that interference in the Stroop task results from the relative saliency of the task-irrelevant input, i.e., automatic word

* Corresponding author at: Dept. for Experimental Psychology, Ghent University, Henri Dunantlaan 2, 9000 Ghent, Belgium. Fax: +32 9 264 6496.
E-mail address: ruthmkrebs@gmail.com (R.M. Krebs).

[1] *Abbreviations*: ACC, anterior cingulate cortex; BOLD, blood-oxygen level-dependent; dlPFC, dorsolateral prefrontal cortex; EPI, echo-planar image; fMRI, functional magnetic-resonance imaging; GLM, general linear model IPL, inferior parietal lobe; LC, locus coeruleus; MLF, medial longitudinal fasciculus; MNI, Montreal Neurological Institute; PPI, psycho-physiological interaction; PT, pontine tegmentum; PWI, picture–word interference task; rANOVA, repeated-measure analysis of variance; ROI, region of interest; RT, response time; SPM, Statistical Parametric Mapping; TSE, turbo-spin echo.

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http://dx.doi.org/10.1016/j.neuroimage.2013.02.027

processing, it seems possible to counteract this influence by increasing the saliency of the task-relevant input, for example by modulating its relative novelty. Stimulus novelty is not only processed fairly automatically and is considered behaviorally salient (Nyberg, 2005; Ranganath and Rainer, 2003), but has several methodological advantages over other salient events, e.g., performance errors and low-level perceptual properties. Most importantly, stimulus novelty can be systematically manipulated with regard to event probability, which is not the case for task errors for example, and does not entail systematic differences in visual stimulation, such as changes in luminance or visual contrast. Moreover, previous studies have demonstrated that novel stimuli not only capture attention (Parmentier and Andres, 2010), but can facilitate associated task-relevant processes, e.g., visual discrimination (Schomaker and Meeter, 2012) and reward anticipation (Krebs et al., 2009). Based on the observation of such beneficial effects, we sought to investigate the influence of stimulus novelty on interference processing along with its neural underpinnings.

To this end, we manipulated conflict and stimulus novelty in a trial-by-trial fashion while acquiring functional magnetic-resonance imaging (fMRI) data. Specifically, we used a picture–word interference task (PWI, cf., Egner and Hirsch, 2005; MacLeod and MacDonald, 2000), in which the relevant stimulus (picture) was overlaid by an irrelevant stimulus (word), which could be congruent or incongruent with regard to the picture content. Similar to the traditional color-naming Stroop task, incongruent picture–word stimuli entail conflict on the stimulus level due to the non-matching pictorial and semantic input, as well as on the response level, due to the competing response mappings (Egner, 2007). For simplicity, we will use the generic term *conflict* throughout the manuscript, and label the associated experimental factor *word congruency*. In addition, half of the employed picture set was familiarized prior to scanning yielding novel and familiar pictures (*picture novelty*), which however was entirely unrelated to the task, resulting in a 2×2 factorial design. Importantly, novel and familiar pictures occurred with equal probability in the present paradigm, ensuring that any effect of stimulus novelty is driven by perceptual saliency itself (Krebs et al., 2009; Nyberg, 2005) rather than by the mere surprise value of an event, as commonly investigated using oddball paradigms (Friedman et al., 2001).

With regard to the influence of stimulus novelty on the processing of interfering information, different outcomes are possible. Stimulus novelty might not influence conflict processing at all, given that the novelty/familiarity dimension is implicit and entirely irrelevant for the task. It is more likely, however, that stimulus novelty can counteract the behavioral interference from irrelevant incongruent words. More specifically, the automatic encoding of novel information might selectively increase attention to the task-relevant dimension (picture) and reduce the detrimental influence from the task-irrelevant dimension (word). To explore the neural underpinnings of such influences on interference processing, the fMRI analysis will be focused on the prime region associated with conflict processing, namely the ACC, and in a more exploratory fashion on the subcortical LC.

Materials and methods

Participants and experimental procedure

Eighteen healthy right-handed individuals completed the PWI task in the fMRI scanner (mean age: 22.5 years; range: 19–28 years; 6 male). Two additional participants had to be excluded, one due to a high number of error trials in all conditions (>40%) and one due to substantial head movements (>1.5 mm). All participants were recruited from the student population of Ghent University and gave written informed consent. The experimental protocol was approved by the ethical committee of the Ghent University Hospital.

The PWI stimuli consisted of colored photographs (outdoor and indoor scenes) that were overlaid by a congruent or incongruent word. Like in the classic color-naming Stroop task, incongruent displays in the PWI task are usually responded to more slowly than congruent ones (Egner and Hirsch, 2005; MacLeod and MacDonald, 2000; van Maanen et al., 2009). Outdoor and indoor pictures were adjusted in luminance using custom-build image-processing routines based on MATLAB (The MathWorks Inc., Natick, MA, United States). Prior to the fMRI session, participants completed a familiarization task (Fig. 1A), in which half of the picture stimuli (80) were repeatedly presented in random order (four times each) intermixed with 40 non-repeat pictures that were not used in the PWI task. Each picture was presented for 1500 ms with a variable stimulus-onset asynchrony between 2300 and 2700 ms. In order to guarantee that participants paid attention to all pictures, they were asked to indicate for each picture presentation whether they had seen the current picture before or not by responding with the index and middle finger of the left hand, respectively (button assignments were counterbalanced across participants). All pictures were presented in the center of a black screen (visual angle 9×6°). Participants were instructed to keep their eyes on a white fixation dot in the center of the screen (0.3°).

In the PWI task (Fig. 1B), the 80 familiarized and 80 completely novel indoor and outdoor pictures were displayed once in random order for 900 ms each in the center of a black screen (9×6°; sets of familiar and novel pictures were counterbalanced across participants). Each picture was overlaid with a capitalized word in red ink, which could be congruent (50%) or incongruent (50%) with the content of the current picture (i.e., the Dutch words for outside and inside: "BUITEN" and "BINNEN"; capitalized Arial font, 7×2°). This resulted in an event-related 2×2 factorial design systematically manipulating both *picture novelty* (novel vs. familiar) and *word congruency* (congruent vs. incongruent). The onset of the word preceded the picture onset by 100 ms to augment the influence of the irrelevant dimension (e.g., Debener et al., 2005) and remained on the screen until picture offset. Participants were asked to attend to the picture while ignoring the word and to decide as quickly as possible whether the picture displayed an outdoor or indoor scene by responding with the index or middle finger of the right hand, respectively (counterbalanced across participants). Importantly, the familiarity/novelty manipulation of the pictures was orthogonal to the congruency manipulation and was entirely irrelevant to the task. Throughout the entire experiment, a small white dot was visible in the center of the screen and participants were instructed to keep accurate fixation. Trial onsets were pseudo-randomly varied with an stimulus-onset asynchrony between 2000 and 8000 ms to allow for effective event-related blood-oxygen level-dependent (BOLD) response estimation (Hinrichs et al., 2000).

fMRI data acquisition and preprocessing

Data was acquired using a 3 T Siemens Magnetom Trio MRI system (Siemens Medical Systems, Erlangen, Germany) with a standard 8-channel head coil. For all participants, anatomical T1-weighted 3D MPRAGE images (TR = 1550 ms, TE = 2.39 ms, TI = 900 ms, acquisition matrix = 256×256, FOV = 220 mm, flip angle = 9°, voxel size = 0.86×0.86×0.9 mm) were acquired to enable coregistration, normalization, and localization of areas of interest. Additionally, T2-weighted anatomical scans were acquired for 14 out of 18 participants (TR = 11,490 ms, TE = 86 ms, acquisition matrix = 256×256, FOV = 220 mm, flip angle = 120°, voxel size = 0.86×0.86×1.2 mm). T2-weighted scans are susceptible to the iron content of neurons and are most prominently used to visualize the substantia nigra (e.g., Eapen et al., 2011). Although the LC is much smaller in diameter compared to the substantia nigra, and contains slightly less iron (Zucca et al., 2006), it is possible to localize the LC on individual T2-weighted scans with additional reference to other landmarks in the brainstem (see also Supplementary data). During the PWI