Neuropsychologia 51 (2013) 2526–2533

Contents lists available at ScienceDirect

Neuropsychologia

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

Priming and statistical learning in right brain damaged patients

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ARTICLE INFO

Article history:
Received 29 October 2012
Received in revised form
12 September 2013
Accepted 14 September 2013
Available online 25 September 2013

Keywords:
Priming
Statistical learning
Spatial neglect
Attention

ABSTRACT

We investigated how right hemisphere lesions affected location priming and statistical learning in four groups of participants: young controls, older controls, and right brain damaged patients with or without spatial neglect. Using a version of the Maljkovic and Nakayama's (1994) priming task, but with all the targets presented at the mid-line, we biased the transition probability for targets to repeat their spatial location. The decrease in response time with spatial repetition allowed us to quantify priming, and the modulation of priming strength as a function of repeat probability allowed us to assess for statistical learning. Contrary to the healthy controls, right brain damage decreased (but did not abolish) spatial priming. Right brain damaged patients did not modulate the magnitude of the spatial priming effect with variation in repeat frequency, as did the control groups. We conclude that damage to the right hemisphere impairs spatial priming and that priming impairment co-exists with, and may contribute to an inability to learn environmental statistical regularities. Such deficits could contribute to functional deficits and a poorer response to rehabilitation.

1. Introduction

Spatial neglect is frequently associated with attention, and the failure of patients to orient or respond to contralesional stimuli (Halligan, Fink, Marshall, & Vallar, 2003; Heilman & Valenstein, 1979) is often characterized as a spatial attentional failure. However, neglect is also associated with deficits that are not obviously spatial, for example working memory impairments (Danckert & Ferber, 2006), increased attentional blink duration (Husain, Shapiro, Martin, & Kennard, 1997) and impaired temporal estimation (Danckert et al., 2007; Merrifield, Hurwitz, & Danckert, 2010). We have suggested (Danckert, Stöttinger, & Anderson, 2012; Shaqiri, Anderson, & Danckert, 2013) that performance on such tasks is an indirect reflection of impaired systems for learning environmental probabilities (Shaqiri & Anderson, 2012) and failing to update them when they change (Danckert, Stöttinger, & Anderson, 2012). In this report, we investigate how these functions relate to right lateralized attentional systems by assessing spatial priming for midline targets in patients with right brain damage without (RBD) or right brain damage with neglect (RBD+N) and evaluating how the magnitude of spatial priming is modulated as positional repeats become more likely and then less likely.

Studies have shown that we are faster to respond to targets in search tasks when features, locations or contexts are repeated (Kristjánsson, Vuilleumier, Malhotra, Husain, & Driver, 2005; Maljkovic & Nakayama, 1994, 1996, 2000). Maljkovic and Nakayama (1994) first studied this priming effect by having participants detect an odd-colored diamond from two distractor stimuli. The authors biased the trial to successively repeat its color or location and found that participants demonstrated a faster reaction time (RT) when the target color or position was repeated.

This priming effect has also been found when targets have the same movement profile before a trial as within a trial (Goolsby & Suzuki, 2001) or when targets are presented within a predictable interval (Los & Van Den Heuvel, 2001). Contextual cuing can also be conceived, broadly, as another example of how repetition – in this case the context or distractor sets – may improve detection performance (Chun & Jiang, 1998; Saevarsson, Jóelsdóttir, Hjaltason, & Kristjánsson, 2008).

Studies in clinical populations have found some of the priming effects to be preserved. In Kristjánsson et al. (2005), for example, the same paradigm as used by Maljkovic and Nakayama (1994) was employed to demonstrate preserved color priming in two patients with spatial neglect. For spatial priming, their neglect patients had to have been given sufficient time to consciously detect the target in order to benefit from spatial repetitions, suggesting that priming effects can fractionate because of RBD and that spatial priming is particularly vulnerable, possibly as a result of spatial neglect. We, too,

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http://dx.doi.org/10.1016/j.neuropsychologia.2013.09.024

found preserved color priming in RBD+N patients and a more fragile spatial priming effect in a task where participants discriminated colored circles (black or white) presented one at a time at a biased location (Shaqiri & Anderson, 2012).

While both these studies found an impairment of spatial priming in participants with neglect, the interpretation of a priming deficit per se is complicated by the utilization of tasks where the targets can appear from left to right in participants with a spatial attentional deficit worse on the left. The results of Saevarsson et al. (2008) suggest that spatial attentional deficits are not a sufficient account for priming deficits, but the mixture of horizontally extended priming tasks in people with spatial attentional deficits makes it difficult to reach an unambiguous conclusion.

While priming is a relatively short time scale effect that emphasizes repetition, statistical learning deals with similar notions and emphasizes transition. A classic example of statistical learning concepts is the study of Saffran, Aslin, and Newoport (1996): two minutes of exposure to a language in which sequential syllables within words followed one another with certainty, and syllables at word boundaries followed each other randomly, was sufficient for 8 month-old infants to demonstrate a capacity to segment the words from uninterrupted speech streams. The authors concluded that the underlying statistical structure generating the syllable sequence has been learned, and can be used for guiding behavior.

The learning of transition probabilities has also been shown for visual material and is dependent on attention. Turk-Browne, Jung, and Scholl (2005) constructed visual triplets with a similar statistical structure to the syllabic stimuli of Saffran et al. (1996). Two separate sequence sets were constructed and each colored distinctly. Participants viewed a single sequence of pictures with items from each colored sequence randomly interleaved and intermingled. The task was to monitor for repeated shapes of a particular color. As in the language task, participants were tested for their ability to recognize the "triplets" statistically encoded in each color family. Even though uninformed of the statistical nature of the stimuli, participants learned implicitly to recognize the triplets, but only for the color that they had been instructed to monitor. The authors concluded that attention was necessary for selecting content, but that after this selection, statistical learning mechanisms could operate autonomously. While attention is a prerequisite for statistical learning, it appears that statistical regularity may also be a cue for attentional allocation (Zhao, Al-Aidroos, & Turk-Browne, 2013).

Studies in clinical populations have found many statistical learning effects to be right hemisphere dependent. In a study that was conducted on a split-brain patient, Roser, Fiser, Aslin, and Gazzaniga (2011) presented fixed pairs of shapes to the left or right visual field where the shapes had defined statistical relationships. When stimuli were presented to the left visual field, the patient had no trouble learning the visual features or statistical properties of the stimulus, which was not the case when the target was presented to the right visual field. In Danckert, Stöttinger, Quehl, and Anderson (2012), control and brain damaged participants played the children's game Rock, Paper, Scissors against a computerized opponent that was biased to gradually increase the proportion of plays it chose over the others, such that at the end, one choice (for example, rock), was played 80% of the time. Control participants and left-brain damaged (LBD) learned to exploit this bias, but RBD participants did not.

In contrast to an assertion of right hemisphere dominance for statistical learning, Geng and Behrmann (2002, 2006) showed intact probability cuing in people with spatial neglect. The authors tested healthy controls and spatial neglect patients on a simple search task: participants had to look for the letters L and F (with T and E as distractors). The targets appeared on the left half of the screen 80% of the time. Both controls and neglect patients used probability as a cue to direct their attention, even though the stimuli were on the patients' contralesional side.

Walthew and Gilchrist (2006) challenged those conclusions by questioning if instead of distributional learning, the results of Geng and Behrmann (2002, 2006) might not simply be the expression of spatial priming. Walthew and Gilchrist (2006) highlighted that biasing the target position to be repeated mostly on one side of the computer screen would favor the spatial priming on that side as well. While attempting to reproduce the results of Geng and Behrmann (2006) with control participants, Walthew and Gilchrist (2006) failed to find evidence for probability cueing when they guarded against unequal distributions of spatial repeats. But when successive repeats were unlikely, the authors found uneven transition probabilities of exactly the type purported to be the object of statistical learning (Druker & Anderson, 2010; see Section 4). Also, Jones and Kaschak (2012) have since reported that statistical distributions can be used to improve performances, even without inter-trial repetitions.

Our investigation of the relationships between statistical learning, priming, and attentional systems was motivated by their important role as aids to prioritization. The world around us contains more information than we are able to process, therefore we depend on mechanisms that help us to select the items or locations where important items are most likely to occur. Such considerations are the motivation behind salience maps (Itti & Koch, 2001; Wolfe, 1994) that emphasize particular stimuli or spatial locations for perceptual processing.

Supporting the idea that prioritization takes place, Bichot and Schall (1999) had monkeys perform a simple visual search task using eye movement responses. The monkeys' errors were more likely to be to distractors that shared target features (which maps onto the concept of the priming effect) and to distractors that resembled targets from earlier sessions (mapping on to the concept of statistical learning). These patterns of errors matched firing rate profiles from neurons recorded in frontal eye fields. Fecteau and Munoz (2006) combined these estimates of salience, driven by bottom-up stimulus features, with top-down estimates of relevance in order to generate the concept of *priority* maps.

Studies in clinical populations have also demonstrated that the top-down component of the priority map is present in neglect patients (Danckert, Maruff, Kinsella, Graaff, & Currie, 1999; Ptak & Schnider, 2010; Snow & Mattingley, 2006). When required to respond to stimuli that were accompanied by task-relevant or task-irrelevant distractors on the ipsilesional or contralesional side, neglect patients showed goal-driven implicit processing of relevant information, even on their contralesional side (Danckert et al., 1999; Ptak & Schnider, 2010). Priority maps must also integrate prior experience and stored memories (Hutchinson & Turk-Browne, 2012), therefore two contributors to the notion of priority are persistence and statistical expectancy.

In summary, while we certainly can learn transitional statistics (Saffran et al., 1996), it is not clear how integral priming effects are apparent demonstrations of statistical learning and probability cuing, as well as if the impairment of those functions is explained by RBD.

The objective of the present study was to test controls and RBD participants for repetition priming in the short term, as well as to assess their ability to learn longer time scale distributions. To do this, we had our participants perform a simple visual search task of vertically aligned stimuli presented centered on the computer screen. We could determine the magnitude of repetition priming by comparing RTs for repeated and non-repeated trials (which we call repeats for short). In addition, we assessed these priming effects under three different probability distributions. First, to develop familiarity with the task, was the uniform condition, where the location of the target was chosen uniformly from all three positions and independent of prior trials. Second was a *high repeat* condition where target position was picked dependent on the prior trial, in order to increase repeats of target position. Third was a *low repeat* condition, where spatial repeats were improbable. Based on prior results (Shaqiri & Anderson, 2012),

we expected RBD and RBD+N participants to show impaired spatial priming, even for mid-line stimuli. We expected that control participants, contrary to RBD groups, would show modifications of RTs that demonstrated knowledge of repeat probability.

2. Methods

2.1. Subjects

The experiment was performed on four groups of participants: 20 healthy undergraduate university students (14 males, mean age=21 years and standard deviation (sd = 3 years), 20 healthy older participants (11 males, mean age=73, sd=8), 4 right brain-damaged (RBD) without neglect (2 males, mean age=64, sd=17, Table 1) and 5 right brain damaged patients (RBD+N) with signs of clinical neglect (3 males, mean age=67, sd=5, Table 1).

University students were obviously younger than our stroke participants. We tested if the stroke groups were similar in age to each other and with our normal older controls by pairwise comparisons. There were no significant differences in age ($t(7)=0.38$, $p>0.05$; $t(23)=1.7$, $p>0.05$ and $t(24)=1.6$, $p>0.05$), between RBD and RBD+N and then between those two brain damaged groups and older controls, respectively. The ethics committee of the University of Waterloo approved the protocol and all the participants gave a written informed consent.

2.2. Brain lesions

The RBD group was formed by patients with a right fronto-parietal lesion (2 patients), one patient with a lesion of the right basal ganglia, and finally, one patient with a lesion of the right parietal region (see Table 1). All RBD+N patients had lesions of the right parietal lobe, two of them had also a lesion of the frontal lobe, two had a lesion of the temporal lobe and JI's lesion extended to the basal ganglia.

2.3. Tests to assess spatial neglect

To asses for the presence of neglect, participants performed the line bisection, letter cancellation and copying of the shapes tests from the Behavioral Inattention Test (BIT, Wilson, Cockburn, & Halligan, 1987). Spatial neglect was determined to be present when patients had positive results for two of those tests. Although the convention to diagnose spatial neglect with the BIT tests stipulates that neglect should be present if patients have at least one of the following results for the tests – more than 5% of deviation from the center of the lines on the line bisection test, more than 10% of letters missing on the contralesional side and fail to copy parts of the 3 shapes – Halligan, Marshall, and Wade (1989) suggest that in order to have a more settled result about the presence of spatial neglect, patients should show positive results for at least two tests, and this was also the convention we followed to diagnose our patients.

2.4. Apparatus and stimuli

For this experiment, we adapted the protocol originally created by Malkjovic and Nakayama (1994, 1996) and also used by Kristjánsson et al. (2005) in order to test priming in healthy subjects and patients with brain damage. We adapted and extended this protocol in order to be able to test statistical learning in addition to the priming effect. The protocol was designed using PsychoPy, a psychophysics software library written in Python (Peirce, 2007). Stimulus presentation and response recording were carried out by a Gateway NV53 computer laptop with a 17-in. monitor and 1366 × 768 resolution. The experiment was divided into 3 blocks (conditions) of 150 trials each. Each trial began with a white fixation cross presented on a gray background. After 1 s, two white and one black diamonds (or vice versa) appeared vertically in the middle of the screen. One of the diamonds, the target, was odd-colored and had a notch cut off at its top or bottom (see Fig. 1). The color of the target was determined randomly. The diamonds were squares of 2° visual angle rotated 90°, and they were located at 5° down from the center of the screen (position 1), at the center of the screen (0° visual angle, position 2) and the last one at 5° visual angle up from the center of the screen (position 3). The size of the cutoff on the targeted diamond was a triangle of 0.4° base and 0.2° height of visual angle. The task required searching for the odd-colored diamond and responding as quickly and as accurately as possible as to whether the top or the bottom part was missing. Participants had 3 s to respond and made their report by using a Logitech Dual Action gamepad. If the top or the bottom part of the diamond was missing, participants pushed "up" or "down" on the right analog joystick of the gamepad, respectively.

The location of the targeted diamond was the main manipulation of the experiment. Participants did 3 blocks of 150 trials each, and each block consisted of a different probability of the target repeating its position. The first block served as a baseline and familiarized participants with the task procedures. The position of

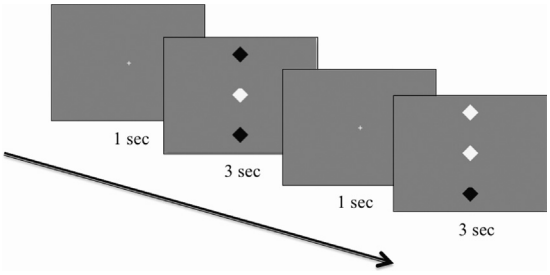

Fig. 1. Presentation of the 3 diamonds on the screen. Participants first saw a white fixation cross on a gray background. After 1 s, the fixation cross disappeared and 3 diamonds were presented vertically on the center of the screen. The targeted diamond was odd-colored and had a notch cutoff at the top or the bottom. Participants had to detect the diamond that was from a different color than the two others and decide if it had its top or bottom missing. They had 3 s to make their decision. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Table 1
Two groups of brain damaged patients. We tested four right brain damaged patients without neglect (RBD) and five right brain damaged with neglect (RBD+N).

Participant	Sex	Group	Age	Handedness	Lesion	Line bisection (−mm for L and mm for R)	Mean deviation in % for line bisection	Letter cancellation (missed for the 4 parts from L to R)	Shape copying
1. CB	F	RBD	71	L	R parietal	5, 2, −5	0.28	0/10, 0/10, 0/10, 0/10	Cube, bottom left missing
2. GP	M	RBD	58	R	R basal ganglia	6, −3, 0	0.42	0/10, 0/10, 0/10, 0/10	Cube shorter on the right
3. MS	F	RBD	83	R	R fronto parietal	−10, −7, 0	2.4	2/10, 1/10, 2/10, 1/10	OK
4. LG	M	RBD	44	R	R fronto parietal	2, −1, 3	0.56	0/10, 0/10, 0/10, 0/10	Start tilted to the right, cube longer on the left
1. RR	M	RBD-Neglect	69	R	R fronto parietal	59, 35, 0	13.27	9/10, 3/10, 1/10, 1/10	Cube left side missing
2. JI	M	RBD-Neglect	70	R	R fronto-parietal, temporal and basal ganglia	−31, 3, 30	0.28	3/10, 2/10, 2/10, 3/10	Cube left side missing
3. GH	F	RBD-Neglect	63	R	R temporo parietal	59, 61, 82	28.53	10/10, 10/10, 10/10, 0/10	Cube and flower left side missing
4. EG	F	RBD-Neglect	74	R	R parietal	−25, −7, 16.5	2.2	3/10, 0/10, 6/10, 1/10	Cube left side missing
5. BM	M	RBD-Neglect	60	R	R parietal	3, −12, −17	3.7	10/10, 9/10, 9/10, 2/10	Star, cube left side missing

the target for this block was distributed randomly: regardless of where the target was located on the current trial, every potential target position had an equal likelihood of 33% to be the location of the target on the next trial.

For the second block, called the "high repeat condition", the distribution was biased so the repeat probability of the same position was high (0.8). Therefore, whichever of the three positions the target was located at for the current trial, 8 out of 10 times it would be located in the same location on the next trial.

The last session was the "low repeat condition". Repeat probability was 0.2. This means that whichever of the three positions the target was located at for the current trial, 2 out of 10 times it would be located in the same location on the next trial. Whenever a target did not repeat its location, it switched to one of the other two locations with an equal likelihood.

The order of the different conditions was fixed for all participants and all groups. The heterogeneity of patient groups, the challenges of recruiting brain damaged participants, and the large number of potential orders for the tasks (6), made counterbalancing impractical. As task order was the same for all groups, it cannot, as a single factor, explain group differences, but it is possible that different results might be observed with different orderings of block probabilities.

2.5. Data analysis

Our RT analyses are restricted to correct responses. The data was analyzed using conventional ANOVAs to evaluate and visualize significant differences within groups and individuals. All analyses were conducted with R (version 2.15.2; R Development Core Team, 2011).

3. Results

3.1. Priming effects

Do participants have a faster RT when the target location is repeated? For all groups, we compared the RT for trials that were in a repeated position to the trials that switched their position. Since the RT distributions were skewed, we first log-transformed them and used the median as a report of the average performance. In addition to the difference for RT across groups (Fig. 2), there was also a significant effect of spatial priming. The detailed results for each group are reported in the subsequent sections.

University students were faster for all trials that successively repeated their position (Fig. 2; $F(1, 19)=116.51$, $p<0.0001$). Increasing numbers of repeats led to significant decreases in RT; trials with exactly one repeat were faster than trials with no repeats ($F(1, 19)=102.63$, $p<0.0001$), and two consecutive repeats were faster than trials with a single repeat ($F(1, 19)=14.63$, $p=0.001$). Finally, when the target was presented three times at the same location, students were faster to respond compared to two repeats (Fig. 3; $F(1, 19)=4.86$, $p=0.03$).

Healthy older controls showed a similar pattern (Fig. 2; $F(1, 20)=258.27$, $p<0.0001$). Controls responded faster to exactly one repeat compared to no repeats ($F(1, 20)=116.61$, $p<0.0001$), and also to two repeats compared to one repeat ($F(1, 19)=33.57$, $p<0.001$; Fig. 3). Although there was a trend towards a faster RT when the number of repeats increased, the results were not statistically significant.

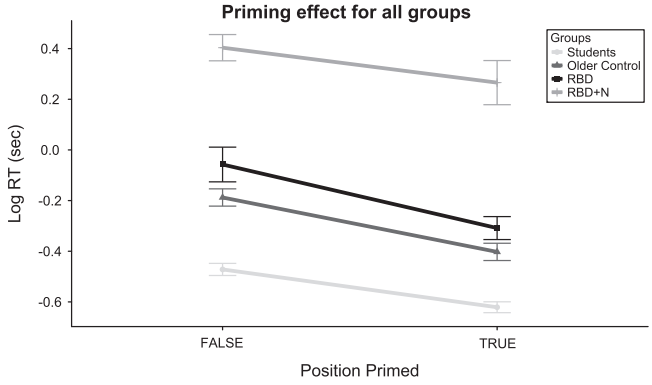

Fig. 2. Priming effect for the four groups of participants. The figure reports the log-transformed RT, as the RT distributions were skewed. All participants had a faster RT when the target was repeated at the same location compared to when it was not-primed and the target was presented in another location. Error bars correspond to standard errors. While there is a large overall effect of participant group on RT, the relative benefit of a spatial repeat seems consistent across groups.

RBD participants who had no clinical signs of spatial neglect had a priming effect when aggregating across all trials with a repeat of position ($F(1, 3)=103.51$, $p=0.002$). Comparing trials with increasing numbers of repeats (Fig. 3) showed the same trend. Trials with exactly one repeat were faster than trials with no repeats ($F(1, 3)=96.71$, $p=0.002$). RBD patients also showed a trend towards a faster RT when the number of repeats increased, but without reaching statistical significance.

RBD+N patients demonstrated an aggregate spatial priming effect: comparing trials where target position switched to all trials with one or greater repeats of target position showed a priming effect ($F(1, 4)=9.65$, $p=0.003$). Comparisons between individual trials with no repeats and 1, 1 and 2 repeats, or more repeats, failed to show significant stepwise declines, and the qualitative pattern is also of a less consistent decline (Fig. 3).

For comparing the magnitude of the priming effect between groups, we performed an interaction analysis with a two-way ANOVA with group as a factor and with the number of sequential repeats as a covariate. There was a main effect of group ($F(3, 45)=65.41$, $p<0.0001$), and a significant effect for the number of sequential repeats ($F(1, 45)=382.32$, $p<0.0001$). The interaction was also significant ($F(3, 45)=5.61$, $p=0.002$), and as can be seen in Fig. 3, this interaction can be accounted for the failure of the RBD+N group to have progressively faster RTs with increasing numbers of spatial repeats.

In summary, all participant groups were faster to respond when trials were spatial repeats, that is, when there was spatial priming. However the RBD+N was the slowest of all the groups; patients' decrease in RT with increasing number of repeats was the least consistent and robust, and the magnitude of the priming effect was less than the healthy older control group.

3.2. Statistical learning effects

The second goal of the present experiment was to investigate statistical learning and its relation to spatial priming. While all groups had a faster average RT in the high repeat condition, concluding that this is due to statistical learning is challenging, as the high repeat condition also has the greatest number of primed trials. A more informative comparison is to look at the magnitude of the priming effect and its variation as a function of repeat probability (Fig. 4).

For simplicity, we report the statistical analysis of each group individually first and then as a second step, we will report an overall comparison between groups. We started by comparing response speed as a function of whether the trial repeated its position (spatial priming), and whether the trial was in the block with a high repeat probability or in the block with a low repeat probability. As for the priming effect analysis above, we log-transformed the RT distributions and used the median as a report of the average performance.

Undergraduate students showed a main effect of spatial priming ($F(1, 19)=221.8$, $p<0.0001$), probability condition ($F(2, 38)=4.6$, $p=0.02$), and a significant interaction ($F(2, 38)=30.8$, $p<0.0001$). The interaction can be visualized in Fig. 4 (panel A), which shows a crossover. Repeated trials in the high repeat condition are faster than repeated trials in the low repeat condition. And switch trials are faster in the low repeat condition than switch trials in the high repeat condition. In both probability conditions, repeated trials were still faster than non-repeated trials. This resilience of the priming effect is a consistent observation since the study of Maljkovic and Nakayama (1994), who demonstrated that even when participants were informed that switches of the target location or color were highly probable, they were still slower to respond to those trials compared to the primed ones.

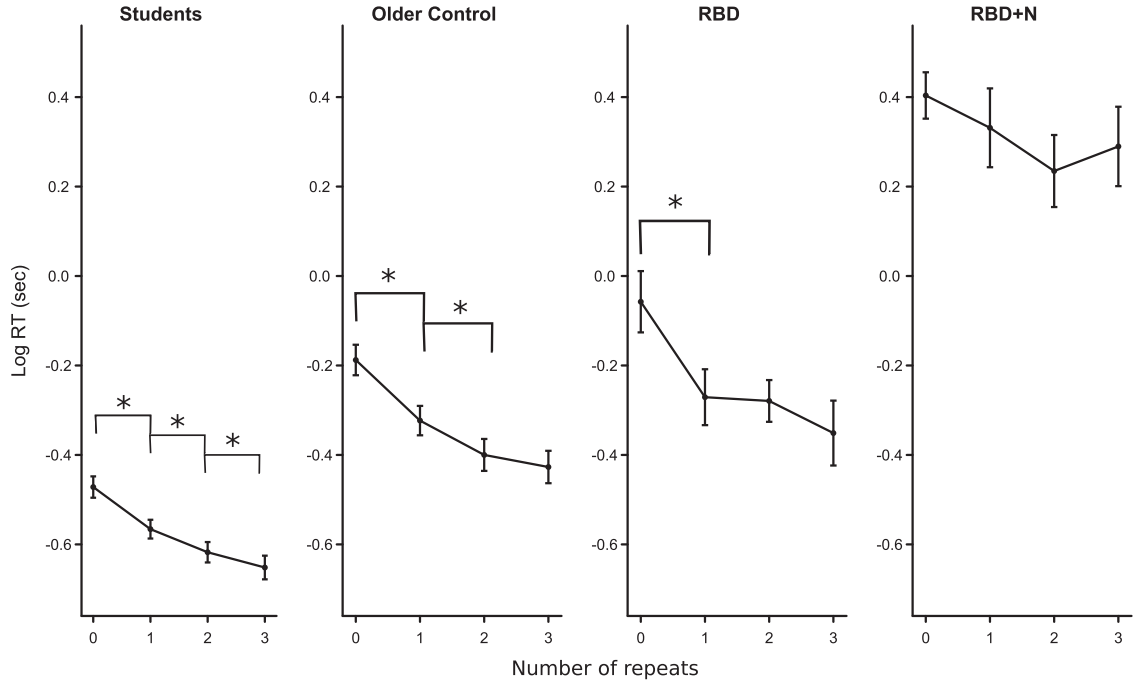

Fig. 3. Log-transformed RT of the four groups when the target repeated spatial locations on subsequent trials (up to 3 repeats). RBD patients show reduced priming relative to the two control groups, who show increased priming over successive repeats, as the asterisks (indicating statistically significant results; *p* values in text) highlight. In contrast, RBD+N patients show no incremental priming benefit, and this group has the slowest average RT. Error bars correspond to standard errors.

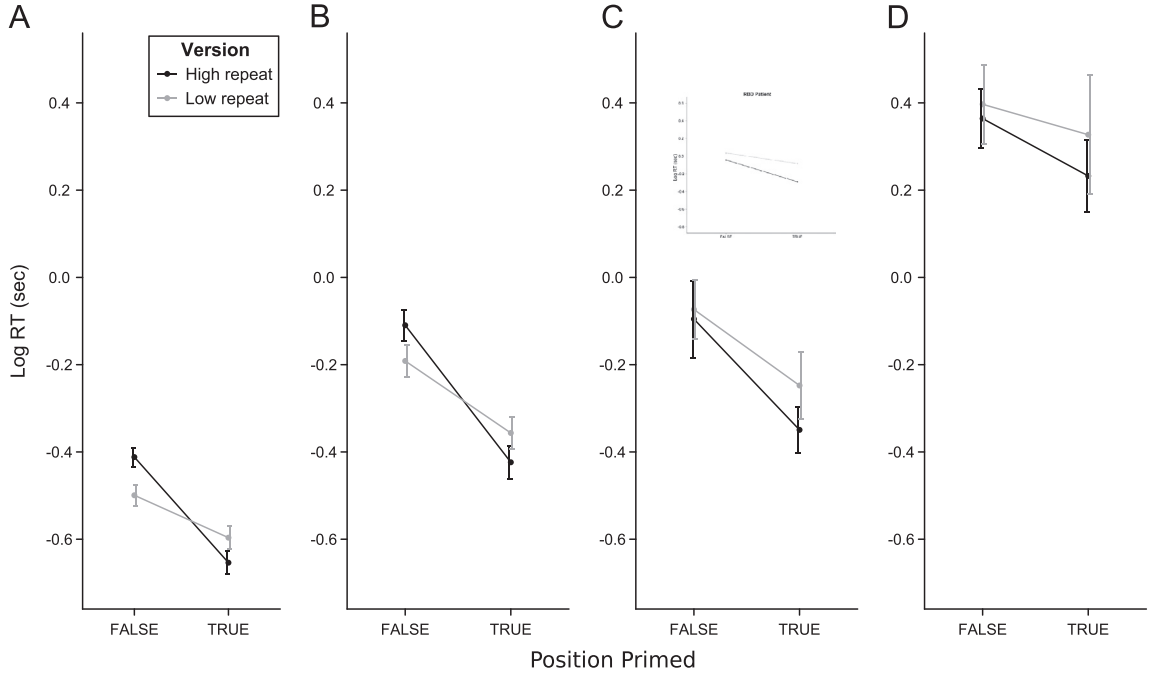

Fig. 4. The magnitude of the priming effect as a function of high repeat or low repeat conditions based on the log-transformed RT. Students (panel A) and older healthy controls (panel B) show an interaction of repeats and condition, as they are faster for repeats of position during the high repeat condition and faster for switches of position during the low repeat condition. RBD patients (panel C) do not show an interaction effect between priming and condition. This group only enhances the magnitude of the priming effect when repeats are frequent. We also plot the results of the one RBD patient whose individual ANOVA yielded a statistically significant interaction (inset panel C); this patient's pattern of performance was qualitatively similar to the RBD group as a whole. There is an improvement for primed trials when repeats are frequent but no increase for unprimed trials when repeats are rare. RBD+N patients (panel D) have a pattern similar to the RBD group, except that no individual neglect patient shows any statistically significant effect for priming, condition or an interaction.

Older healthy controls demonstrated a similar pattern of performance for spatial priming ($F(1, 19)=272.7$, $p<0.0001$). They also showed an interaction between trials that repeated their position with the probability condition ($F(2, 38)=30.2$, $p<0.0001$). We did not find a main effect of probability condition ($F(2, 38)=0.86$, $p=0.4$). The interaction is shown in Fig. 4 panel B which is qualitatively similar to that of student participants. It also shows that trials with a switch of target position were faster during the low repeat condition, and that trials with a repeat of target position were faster during the high repeat condition.

The group of RBD patients demonstrated an effect of repeated position ($F(1, 3)=70.16$, $p=0.004$), and a trend for an interaction

($F(2, 6)=4.11$, $p=0.07$), but RBD patients did not have a main effect of probability condition ($p>0.16$). However, as it can be seen in Fig. 4 panel C there is no crossover for this group, but only the tendency to enhance the magnitude of the priming effect when repeats are frequent.

Because the RBD group has only four participants, and patients' brain injury might make this group heterogeneous, we tested for the consistency of this result by performing ANOVAs for the data of each participant. All four patients showed a main effect when the target position was repeated (all patients have a significant p value up to 0.0001), and two patients showed a main effect for probability condition (both patients have a significant p value that was up to 0.0003), but only one patient showed an interaction effect ($F(2, 424)=4.28$, $p=0.01$). This participant is shown as the inset in Fig. 4 panel C and demonstrated the same pattern as the group. The group shows that a preserved repetition priming effect is not a sufficient condition for demonstrating statistical learning effects on the RT independent of spatial priming, since there is no apparent effect on non-primed, switched trials, when these trials become frequent.

For RBD+N, the results are different. Whether analyzed at the group level or for each individual participant, neglect patients did *not* show a main effect of repeated position ($F(1, 4)=3.84$, $p=0.12$; all p values for individual patients were higher than 0.17). This confirms the results we conducted for the spatial priming. In addition, neither at the group level nor at the individual level was there a main effect of probability condition (all p values were higher than 0.07) or an interaction (all $ps>0.49$). Fig. 4 panel D shows the interaction plot for this group, and is visibly similar to the pattern of the RBD participants.

Individual analyses of the groups revealed that both control groups showed an interaction between the priming effect and condition, but this was not the case for the RBD and RBD+N patients, who only had a main effect for the spatial priming. In order to demonstrate that the two latter groups are impaired in statistical learning and have different results compared to the control groups, we investigated the magnitude of statistical learning across all groups by conducting a three-way ANOVA with group as a factor, whether the trials was primed as a factor, and whether the trial was in the high repeat or low repeat block as a factor. As expected, we found a main effects for group ($F(3, 45)=65.01$, $p<0.0001$), priming ($F(1, 45)=402.38$, $p<0.0001$) and probability condition ($F(2, 90)=5.07$, $p=0.008$). Importantly, the three-way interaction ($F(6, 90)=2.17$, $p=0.05$) demonstrates that the magnitude of the change in priming effect as a function of probability condition is different across the participant groups. As can be seen in Fig. 4, this is due to the fact that both control groups show a cross-over pattern – where unprimed trials are faster during the low repeat condition and primed trials are faster during the high repeat condition – but neither the RBD nor RBD+N groups show this effect.

3.3. Accuracy

In order to verify if accuracy can explain the group differences that we found for priming and statistical learning, we conducted an analysis to test the overall accuracy for priming and statistical learning: there was a significant effect of group on the proportion of correct answers ($F(3, 45)=20.64$, $p<0.0001$). This was principally due to the performance of the RBD+N group that averaged 85% correct answers, while the three other groups were always more than 95% accurate in their responses. In the RBD+N group, two participants had accuracy measures greater than 94%. These two participants showed no appreciable difference from the other three neglect patients on their RT measures for spatial priming, probability condition or their interaction. A three-way ANOVA with group, priming and condition as factors confirmed this group effect ($F(3, 45)=19.39$ $p<0.0001$), and a very small ($\sim$1/2%), but statistically significant benefit for primed trials ($F(1, 45)=8.58$, $p=0.005$), but no higher order interactions (p values >0.15), and so accuracy effects were not further pursued. As a summary, these results reveal that the fact that repeats were more or less probable did not change participants' accuracy. Thus, while the RBD+N group made more mistakes on the task overall, accuracy cannot provide a simple account of the priming and statistical learning effects.

3.4. Timing differences

Our four groups each showed an overall priming effect and each individual participant improved their RT when the same location was repeated, at least numerically, if not always, to a statistically significant degree. This priming effect was robust in the RBD group and less in the RBD+N, while neither group showed the crossover interaction seen in young and older controls (Fig. 4). The difference in priming effects with similar statistical learning deficits suggests that a deficit in spatial priming is not sufficient to explain the poor results of the RBD+N group.

It has been observed since the original work of Maljkovic and Nakayama (1994) that priming effects are short lived (lasting for about 30 seconds or 5 to 8 repeats of the same location, in a task like ours). Could it be that since our brain damaged participants were slower to respond, the longer interval between two trials made it harder for them to benefit from what they observed in the trial before?

In order to evaluate this hypothesis, we plotted participants' RTs for trials as a function of the RT on the preceding trial (see Fig. 5). Except for the general speed advantage of university students, who typically responded in less than 1 s (see gray areas in Fig. 5 that show the density of the trials based on participant's log-transformed RT), all participant groups, except for the RBD+N group, showed a similar relationship for primed and unprimed targets: fast trials were followed by fast trials and slow trials by slow trials. Confirming that this relationship differed across groups, the three-way interaction of an ANOVA with previous RT as a covariate and group and priming as factors was significant ($F(3, 33)=3.77$, $p=0.02$, all lower order interactions were also significant with all p values less 0.0001). The RBD+N patients showed a different pattern from the other three groups, as can be seen in Fig. 5: RBD+N were most different when stimuli switched their position from one trial to the next, as fast trials were followed by slow trials. In addition, the relation between RT and prior RT was flatter for primed trials.

4. Discussion

We tested location priming and statistical learning in four groups: university students, older healthy controls, RBD and RBD+N participants. The four groups performed three different conditions; random, high repeat and low repeat, that allowed us to investigate if each group showed a priming effect, and whether this effect was modulated by repeat probability. The design of our experiment, where we presented all the stimuli on the middle of the screen, made it possible to examine for these effects without having to consider lateralization effects due to the side of patients' lesions. This experiment was motivated by our prior work, that showed an anomaly of statistical learning (Shaqiri & Anderson, 2012) and by other studies that demonstrated a variety of non-spatial impairments in subjects with neglect (Danckert & Ferber, 2006; Husain & Rorden, 2003; Husain et al., 2001; Samuelsson, Hjelmquist, Jensen, Ekholm, & Blomstrand, 1998).

We started by testing students and healthy older participants in order to replicate, with our modified version of the task, the main findings of prior studies on the spatial priming effect. In accordance with previous research (Hillstrom, 2000; Kristjánsson, Vuilleumier, Schwartz, Macaluso, & Driver, 2007; Kristjánsson et al., 2005; Maljkovic & Nakayama, 1994, 1996), both our control

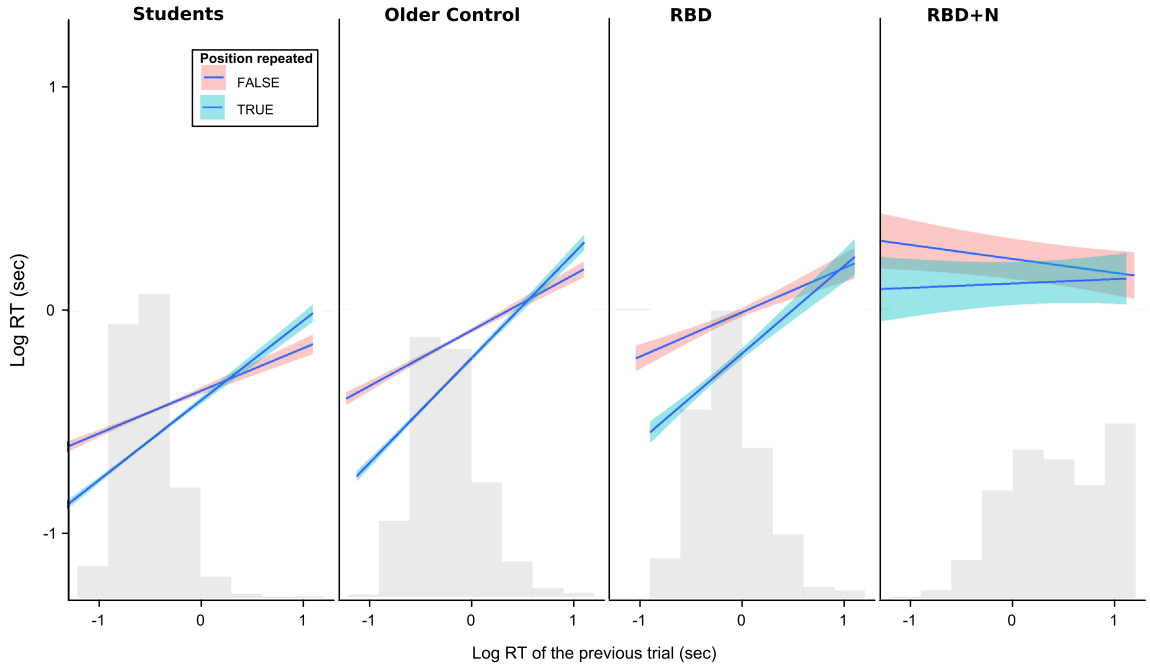

Fig. 5. Log-transformed RT compared to the log-transformed RT on the previous trial. The gray bars are the histograms for the proportion of trials at each time interval, and are included to give a general overview of RT distributions. University students responded to most of the trials in under 1 s and therefore had a shorter interval between trials. Healthy older participants had almost an identical pattern where the regression line of repeated targets is almost parallel to the non-primed trials. But the RBD and RBD+N showed the largest difference between the primed and non-primed trials. When they responded fast to a prior trial, those two groups benefited more from the priming effect than when they were slow to respond. Finally, the RBD+N group showed a different pattern from the other group: participants were greatly affected by the switch of the position, as well as by their RT on the previous trial. When the prior trial was fast, and the location switched, there was a large cost for RT. As RBD+N patients had the slowest RT of all the groups, we hypothesize that their poor statistical learning may be in part an artifact of their overall slower response time profile.

groups demonstrated a priming effect that lasted up to two repetitions of the same location, which is slightly inferior from the 5 to 8 trials reported by Maljkovic and Nakayama (1994). This difference could have several causes, such as the total number of trials that were presented or the interval between them. We also varied the sequences of trials, which could have affected the overall benefit from spatial priming.

The RBD group also demonstrated an overall priming effect, and each individual patient in this group had a significant statistical benefit for spatial priming as well, showing a sensitivity for the repeat of the position, despite their lesion. This was not the case for neglect patients – although the RBD+N group demonstrated an overall priming effect – an individual analysis on each patient revealed that none of the neglect patients achieved a statistically significant spatial priming effect. This highlights an important difference between the two groups: although RBD and RBD+N both have lesions of the right hemisphere, clinical neglect is an important predictor of a greater impairment in benefitting from short term environmental regularities.

One possible explanation for the difficulty that RBD+N patients have in benefiting from spatial priming may be timing. Maljkovic and Nakayama (2000) tested the importance of timing in the priming effect and found that short-term implicit memory is involved in this process. The authors discovered that priming is cumulative, but can decay if the interval between the trials is too long (between 30 and 90 s). Although the authors did not find a difference on priming if the interval between the trials was from 1 to 3 s, they reported that if participants directed their attention somewhere else or made eye movements during that interval, or if they performed a distracting task, the priming effect was affected and decayed faster.

Although our participants were not submitted to any distractors in-between trials, the fact that they benefited less from the priming effect during slow trials might reveal that they had more time to make eye fixations somewhere else on the screen, and this could have contributed to a decreased priming effect. Even though the spatial dimensions of our task are small, a slight adjustment of eye position, as a consequence of learning when targets were likely to repeat or switch, could translate into faster responses. Measuring eye movements in brain damaged participants is challenging though, and the apparatus for eye position recording can influence gaze patterns as well. Therefore, we did not measure eye position for these studies. Now, that we have confirmed an effect, additional experiments incorporating eye movement recording would provide useful information for understanding the absence of statistical learning observed in our brain damaged participants.

Another possible explanation for our group effects are "resetting" differences – as theorized by Serences and Yantis (2006) – who suggested that the attentional network is recruited every time there is a new state, as for example a switch of the position after a few repeats. This reset might explain the additional time needed by some participants when responding to trials that changed position. These effects are most visible for RBD+N patients, who exaggerate this pattern until it is observed after a single switch of position. RBD+N patients showed some benefit when a relatively fast trial was followed by a spatial repeat, but not when the stimuli changed location: the RBD+N group became very slow when the position was switched, even though the previous trial was fast. This was not the case of any of the three other groups. The underlying deficit of the attentional network for these patients might explain why the resetting action (Serences and Yantis, 2006) is more prominent for patients suffering from spatial neglect.

Task demand could also contribute to the results of RBD+N patients. Dukewich et al. (2012) tested visuospatial neglect patients on a RT cued task and on a temporal order judgment (TOJ) task, by asking them to respond to a red or blue pinwheel. After finding a disengagement deficit for the RT task but not for the TOJ task, the authors hypothesized that since the action system needed to be recruited for the RT task, but not for the TOJ, there were different task demands. Our paradigm required our participants to disengage

from the previous position (if the target location switched) and they also needed to recruit the action system in order to respond to the trial as quickly as possible. A disengagement deficit, a major symptom of neglect (Dukewich et al., 2012; Posner, Cohen, & Rafal, 1982), might be most apparent on short trials, where target positions switch.

In addition, neglect patients have difficulty selectively attending to task relevant information, even in their "good" visual field. This has been shown previously for flanker type tasks (Danckert et al., 1999; Ptak & Schnider, 2010; Snow and Mattingley, 2006). In our task, the relevant target is defined by its color relative to the other two distractors. A failure to selectively attend to the target position could obscure the pertinent statistical relationship. The difficulty of keeping in mind sequential relationships between trials could have consequences in the capacity to learn longer time frame statistical distributions.

In summary, the present study showed that RBD+N in particular have a deficient of spatial priming effect, even when targets are presented at the mid-line in a small number of predictable positions. Further, both RBD+N and RBD have an impairment of statistical learning of spatial information. Patients with an impairment in these functions will be less sensitive to environmental regularities and as a result, could be reasonably expected to have increased difficulties in functional activities and rehabilitation. Thus, impaired implicit learning of environmental regularities and sequential effects is a potential target for rehabilitation

Acknowledgment

We would like to thank Grand River Hospital for their collaboration as well as our patients for participating in this study.

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