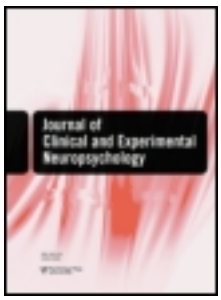

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Mere exposure effect can be elicited in transient global amnesia

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Transient global amnesia (TGA) is one of the most severe forms of anterograde amnesia seen in clinical practice, yet patients may show evidence of spared learning during the amnesic episode. The scope of spared learning in such a severe form of amnesia remains uncertain, and it is also unclear whether findings from single-case studies hold up in group studies of TGA patients. In this group study, we found evidence that extended the domain of spared learning in TGA to include the mere exposure effect, whereby enhanced preference is primed by prior exposure to stimuli. We demonstrate this effect during an acute episode in a group of TGA patients, where they showed enhanced preference for previously exposed faces, despite markedly impaired performance on standard anterograde memory tests.

Keywords: Mere exposure effect; Transient global amnesia; Amnesia; Memory disorders; Memory.

"Transient global amnesia" (TGA) is a transient memory disorder with well-established clinical characteristics, but there is still no clear understanding of its etiology. TGA is a neuropsychological syndrome that is characterized by a sudden and transient loss of the ability to create new memories, as well as a variable degree of retrograde amnesia (Fisher & Adams, 1964). For the diagnosis of TGA the following diagnostic criteria must be fulfilled (Hodges & Warlow, 1990): (a) There must be clear anterograde amnesia during the attack; (b) loss of consciousness and loss of personal identity must be absent, and the cognitive impairment must be limited to the amnesia; (c) the patient's neurological examination is otherwise normal; (d) epileptic features must be absent; (e) there can be no recent history of head trauma or seizures; and (f) the attack must resolve within 24 hours. Studies have highlighted different patterns of memory impairment during the acute and periacute phase (Guillery-Girard et al., 2004) and also the role of emotional factors in recovery (Noel et al., 2008). TGA is generally associated with transient brain changes in the mesiotemporal region, specifically in the hippocampal formation (Bartsch et al., 2006), but the mechanisms underlying these changes remain unclear. Classical hypotheses include migraine-related mechanisms and vascular abnormalities as possible etiologies, although none of these seems to offer a satisfactory

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explanation on its own (Bartsch & Butler, 2013; Bartsch & Deuschl, 2010; Hodges, 1998).

TGA and implicit memory

During the TGA episode, patients are able to carry out complex or routine activities and learn new procedural skills. The complex or routine activities, such as performing an organ recital (Byer & Crowley, 1980), driving a car (Shuping, Rollison, & Toole, 1980), or conducting an orchestra in a concert (Evers, Frese, & Bethke, 2002), are considered to be expressions of procedural memory. These activities can be executed during the amnesic episode since patients preserve procedural learning acquired before the TGA. In addition, it seems that TGA patients are able to learn new procedural skills during the acute episode. Eustache et al. (1997) described how a patient during TGA was able to learn reading mirror words at the same speed as a control group, and Guillery et al. (2001) found evidence of semantic priming in TGA.

The mere exposure effect

The mere exposure (ME) effect consists of enhanced preference to stimuli for which there has been previous exposure (Zajonc, 2001). The effect is more pronounced when it is obtained under subliminal conditions or when recognition of the stimuli occurs at random (Monahan, Murphy, & Zajonc, 2000). The robustness of this effect has been demonstrated in more than 200 studies, using different stimuli types, different contexts, and different procedures, as well as being examined both in human subjects and in animals (Newell & Shanks, 2007).

Among classic theories of the ME effect, the primacy of affect theory (Zajonc, 1980) states that cognition and affection are two dissociated processes. Thus, the ME effect is an affective process which is an expression of a presemantic, emotional system that is independent of recognition memory. By contrast, the perceptual fluency/attribution theory (Bornstein & D'Agostino, 1992, 1994) proposes that the repeated and nonreinforced exposure to stimuli increases the subjective feeling of perceptual fluency or ease of processing. Experiencing this fluency with a stimulus, with a nonconscious process of codification, is interpreted as a preference or as an increase of the positive affect towards it. Consequently, repetition-induced fluency drives preference (Moreland & Topolinski, 2010).

The mere exposure effect in clinical populations

The ME effect has been studied in patients with other cognitive disorders. It has been shown that the mere exposure effect is preserved in people with prosopagnosia (Greve & Bauer, 1990), patients with Alzheimer's disease (Willems, Adams, & Van der Linden, 2002), and patients with schizophrenia (Marie et al., 2001).

In the case of the amnesic populations, the mere exposure effect has been investigated in a few studies, with contradictory findings that are not easy to reconcile, since different types of materials and procedures have been used. On the one hand, it has been found that patients with Korsakoff's syndrome preferred, to the same degree as controls, melodies that they had previously heard over new melodies, so the ME effect was preserved in this population (Johnson, Kim, & Risse, 1985). However, in another study (Redington, Volpe, & Gazzaniga, 1984) eight amnesic patients with a variety of etiologies (global hypoxic ischemia, rupture and repair of anterior communicating artery aneurysm, stroke, and trauma) showed impaired preference to previously exposed items. In addition, Samson and Peretz (2005) reported an amnesic patient with bilateral damage on the temporal lobe who did not show the ME effect. The same study found that patients with left temporal lobe lesions showed a ME effect comparable to that of the control group, while patients with pathology in the right temporal lobe showed a limited ME effect.

To our knowledge, the ME effect has not been studied in patients with transient global amnesia. In view of the severity of the memory loss associated with transient global amnesia, the presence of an ME effect would be an important demonstration of its utility and robustness in showing a dissociation between explicit and implicit memory processes. Our study is, therefore, the first to attempt to document an ME effect in TGA.

METHOD

Participants

The *TGA group* included 11 patients (8 women and 3 men) diagnosed with transient global amnesia according to the criteria established by Hodges and Warlow (1990). During the critical phase of TGA, these patients were treated in two hospitals in Madrid, Spain, where their relatives were asked to give informed consent for patients' participation in this study. The assessment started within the

TABLE 1
Background information relating to TGA patients

Patient	*Age (years)*	*Context in which TGA occurred*	*Psychiatric treatment*	*Migraine history*	*Episode number*	*Computed tomography*
J.C.P.	65	Physical exercise	Antidepressants for 2 years, 3 years before TGA	No	1	No abnormalities on CT scan
J.G.	66	Emotional event	Antidepressants for 1 year, 4 years before TGA	No	1	Cortical atrophy, normal for age
C.P.	59	House cleaning	No	No	1	No abnormalities on CT scan
P.P.	67	Looking after her grandson	No	Yes, all her life	2	No abnormalities on CT scan
E.B.	63	Walking	No	No	1	No abnormalities on CT scan
P.R.	52	On the underground	No	Yes, all his life	1	No abnormalities on CT scan
S.N.	56	At home	No	No	1	Chronic lacunar infarction in the left external capsule, unrelated to TGA episode
E.E.	79	Swimming	No	No	1	Cortico-subcortical atrophy, normal for age
D.C.	69	Endoscopy	Antidepressant history	No	1	No abnormalities on CT scan
L.P.	67	Editing paperwork	No	No	2	Diffuse cortico-subcortical atrophy
R.R.	63	House cleaning	Anxiolytic medication history	No	1	No abnormalities on CT scan

Note. TGA = transient global amnesia; CT = computed tomography.

first 6 hours after the onset of the amnesia. In the Oxford series of TGA patients (Hodges & Warlow, 1990), most attacks ranged from 1 to 8 hours. We did not record the precise point in time during the TGA attack when testing was carried out. Time of onset of attack is difficult to ascertain accurately, since it may take some time for a witness to realize that something is amiss with the TGA patient, and this realization may also vary between witnesses. The mean age of this group was 64.2 years; 72.7% of the sample had a primary level of education, and the remaining 27.3% had university-level education. Background information about the group of TGA patients is given in Table 1.

The control group included 11 volunteers, matched to the experimental group in age (X = 63.5), educational level (primary education 72.7% and higher education 27.3%), and sex (8 women and 3 men). Thus, each experimental participant was yoked to a control participant.

None of the TGA patients had a history of alcohol or drug abuse, and none of them suffered from epilepsy or recent trauma.

Materials and procedure

For the tests that are described below, participants were assessed individually. In addition to the ME task, the following tasks were carried out: free recall, cued recall, and picture recognition memory. These three tasks were used to assess for *explicit memory* dysfunction and to make sure that there was no contamination of explicit memory recovery in the mere exposure task.

The *free recall* test was carried out with a single auditory presentation of 15 Spanish words. Immediately after presentation, participants were asked to remember all the words that they could, without a specific order. The test score was the proportion of correct recalled words. Words were selected from a pool of items from normative study by Algarabel, Ruiz, and Sanmartin (1988), and they fulfilled the following criteria: (a) substantives with two syllables or more; (b) medium levels of "imageability," "familiarity," "concreteness," and "significance"; and (c) use frequency 5–53 (total range 5–941).

The *cued recall test* consisted of an auditory presentation of 20 words organized into five groups of four words, and each group was preceded by its semantic category name. Immediately after one presentation of stimuli, participants were asked to write the words after being cued with the five category names. Categories were selected from Soto, Sebastian, Garcia, and del Amo (1994). The test score was the proportion of correct recovered words.

The *picture recognition test* was carried out by a single presentation of 15 pictures, one at a time,

with participants being asked to name each picture. After stimuli presentation, participants were asked to identify studied pictures from a sheet with 30 pictures randomly ordered, 15 studied and 15 new. Black-and-white pictures were selected from the Snodgrass and Vanderwart collection (1980). A correction for chance was applied using the following algorithm (Frary, 1988): $S = C - [W/(n - 1)]$, where S = proportion of corrected score, C = proportion of correct answers, W = proportion of wrong answers, n = number of response alternatives. Since they had two response options (recognized/not recognized), in this case, $n = 2$.

In order to evaluate the *ME effect*, 24 photographs of men's faces were selected from Warrington's Recognition Memory Test (Warrington, 1984). All of the faces were in black and white and included no famous personalities; they were all taken from a frontal orientation and under the same illumination conditions. It is assumed that there is no difference in the natural preference for the pictures between groups. The pictures were randomly grouped according to the number of times they were presented: Eight only appeared once, eight appeared three times, and eight appeared five times. The 72 pictures were randomly ordered, creating a unique order of presentation for all participants, and each face was presented for approximately 3 s. In the case of exposure duration, a 3-s exposure rather than subliminal exposure was chosen for practical reasons, since having a computerized set-up for this type of clinical condition would not have been readily feasible. Using 3 seconds exposure duration also meant that the test and any effects could be more easily translated into clinical settings (cf. Guillery et al., 2001).

During the exposure phase, participants were instructed to look at the pictures of faces that were being shown to them. Once the participants had seen all the pictures, for approximately 5 min they had to perform another task from the memory battery, which acted as a distracting task.

Then, in the preference test, where the ME effect was examined, subjects were randomly presented with 24 target–distractor faces pairs. In each pair, the target face had been seen in the exposure phase, and the distractor face was a new picture. The pairs of faces were presented horizontally together, and the photographs that had been previously seen appeared 12 times on the right side and 12 times on the left side in a random order. The photographs of new faces were also extracted from the same Recognition Memory Test and had similar characteristics to those that had been presented in the exposure phase. Participants were asked to perform forced-choice preference judgments between the two pictures for each pair; they were told to choose the one that they liked more, acting on their first impulse.

RESULTS

In order to analyze differences between the TGA and the control group in the explicit memory tests, a one-factor analysis of variance (ANOVA) was carried out with the proportion of each task's scores. The mean proportion correct scores for each task are shown in Figure 1. In the free recall task, the TGA group performed significantly worse than controls, $F(1, 20) = 21.053$, $MSE = .004$, $p < .001$. In the cued recall task, TGA patients were impaired relative to controls, $F(1, 20) = 31.154$, $MSE = .027$, $p < .001$. In the picture recognition memory test, there were significant differences between groups, $F(1, 20) = 23.593$, $MSE = .071$, $p < .001$, with a lower performance by TGA patients. Similar results were obtained with nonparametrical analyses.

For the analysis of the ME effect, a repeated measures ANOVA was carried out with group (control or TGA) as between-subject factor and number of repetitions [0 (new), 1, 3, 5] as within-subject factors; proportion of preference was the dependent variable. This analysis allowed us to examine the preference effect, comparing preference to targets (1, 3, 5 repetitions) with preference to distractors (0 repetitions or new), and to study the influence of the number of previous exposures of stimuli on subsequent preference. Assumptions of normality (Shapiro–Wilks test), of homogeneity of variance (Levene's test), and of sphericity (Mauchly's test) were tested and were found to be satisfactory. Results showed (Figure 2) a principal effect of number of repetitions, $F(3, 60) = 4.583$, $MSE = .028$, $p < .01$, and of group $F(1, 20) = 4.704$,

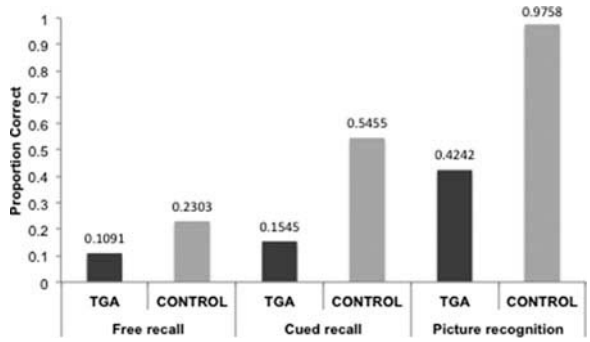

Figure 1. Mean proportion correct scores of transient global amnesia (TGA) and control groups in free recall, cued recall, and picture recognition tasks.

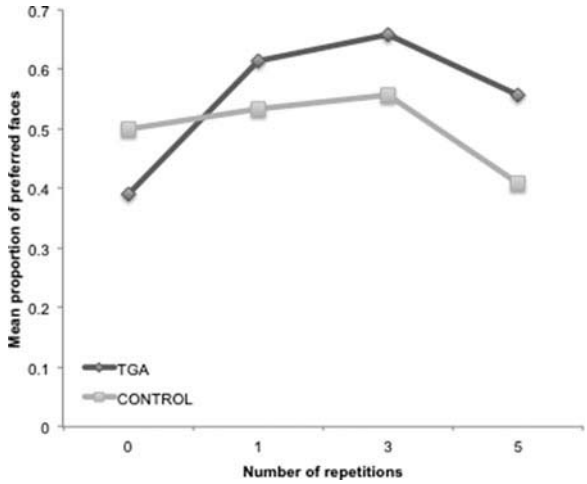

Figure 2. Mean proportion of preferred faces based on the number of repetitions [0 (new), 1, 3, 5] in both groups (TGA/control, where TGA = transient global amnesia).

$MSE = .014$, $p < .05$, and a marginal interaction between two variables, $F(3, 60) = 2.543$, $MSE = .028$, $p = .065$.

In the case of the analysis of this interaction, to examine the differences between number of repetitions in each group, paired t tests was used and yielded the following findings: TGA patients preferred fewer new faces (0 repetitions) than old faces, if old faces were repeated once, $t(10) = -2.251$, $p < .05$, were repeated 3 times, $t(10) = -3.390$, $p < .01$, or were repeated 5 times, $t(10) = -2.092$, $p = .06$. This illustrated the preference effect in the TGA group. There were no significant differences between number of repetitions (1, 3, 5), which means that increasing the repetitions did not change the liking among old faces. In the control group, there were no significant differences between any pairs of repetitions ($p < .05$) except between 3 and 5 times, where participants preferred faces repeated 3 times over faces repeated 5 times, $t(10) = 2.55$, $p < .05$. There was no significant difference in preference ratings between new faces (0 repetitions) and old faces (1, 3, 5 repetitions) in the control group. In order to examine the differences between groups in each repetition [0 (new), 1, 3, 5], a one-way ANOVA was used, and it yield the following results: The difference between two groups was significant only for new faces or 0 repetitions, $F(1, 20) = 4.70$, $MSE = .014$, $p < .05$. Thus, the TGA group preferred significantly fewer new faces than the control group.

Pearson product moment correlations (two-tailed) were computed between the ME effect and explicit memory performance in the TGA group, and no significant correlations were found.

DISCUSSION

We were able to demonstrate that the mere exposure effect can be elicited in a group study of patients with transient global amnesia, in spite of the severe anterograde memory loss that is associated with this condition.

Free recall, cued recall, and picture recognition memory testing confirmed the fact that explicit memory was severely affected during TGA, which reflected the severity of their anterograde amnesia. This loss of the ability to create new memories, which characterizes this syndrome, has been addressed in previous studies (Eustache et al., 1999; Marin-Garcia & Ruiz-Vargas, 2011; Quinette et al., 2003) and is a basic characteristic of chronic amnesias (Kopelman & Stanhope, 2002).

In the case of the ME effect, there was a dissociation between groups. Patients during a TGA episode showed a preference effect; they were more inclined to like faces that they had already seen in the study phase than to like new faces. This ME effect was in fact not present in the control group, as they preferred target and distractor items to a similar degree.

In the case of number of exposures, the level of preference did not significantly vary between one, three, and five exposures in either the TGA group or the control group. This result is consistent with what has been found in healthy control subjects (Bornstein, 1989; Wang & Chang, 2004). This may be due to the fact that the number of exposures (1, 3, and 5) does not differ sufficiently to generate differences between them. We cannot really explain the reduced preference for items exposed 5 times compared to 3 times in the control group.

In line with the findings reported by Liao, Yeh, and Shimojo (2011), it is important to note that faces stimuli may be associated with specific mere exposure effects compared to other stimuli, and also that familiarity and novelty may interact to produce contrasting findings in mere exposure paradigms.

The dissociation of an ME effect between groups may be due to the fact that participants of the control group were affected by conscious recollection of faces, which may have interfered with their preference decision. By contrast, since TGA patients could not remember having seen those faces due to their anterograde amnesia, which is evident in their explicit memory performance, they were likely to have made preference judgments by implicit mechanisms. This observation is consistent with conclusions from other studies where it has been found that the effect is more pronounced when it appears under conditions where people are not aware that

they have seen the material before (Zajonc, 2001). As other studies have explained (Bornstein, 1989; Moreland & Topolinski, 2010), awareness of the repetition of stimuli leads to an "attributional discounting" process. Participants attribute some of their greater liking for the repeated items to their repeated exposure and to compensate for it they discount some of the liking from their liking scores. However, in the case of participants such as TGA patients, who are not aware of prior repetition of stimuli, attributional discounting does not happen, and the preference value of the stimuli therefore remains unaffected. This dissociation between the amnesic group and the control healthy group is in harmony with other instances of paradoxical functional facilitation in memory-impaired patients where competitive interaction between implicit and explicit memory systems has been postulated to underlie enhanced performance in amnesia (Kapur, 2011). It remains possible that a different pattern of results, and in particular more equivalent ME effects in patients and healthy participants, would have been found if we had used subliminal rather than a 3-second exposure. Using a 3-second exposure duration allowed for the possibility that the test and any effects could be more easily translated into clinical settings (cf. Guillery et al., 2001).

Brain imaging studies have shown that the ME effect is associated with increased activation in the lateral prefrontal area (Elliott & Dolan, 1998) and in the anterior insula, caudate nucleus, and putamen (Green, Baerentsen, Stodkilde-Jorgensen, Roepstorff, & Vuust, 2012). In association with TGA, transient brain changes have been found in the hippocampal formation (Bartsch et al., 2006; Bartsch & Deuschl, 2010).

Although our findings about the preservation of the mere exposure effect during the amnesic episode would seem to be consistent with observations that brain areas related to this effect are not significantly affected during TGA, it is worth noting that frontal lobe hypometabolism has been reported in TGA (Baron et al., 1994; Eustache et al., 1997). While some of this frontal involvement may have been secondary to limbic-diencephalic pathology, there may well be fractionation within the frontal lobe in terms of distinct contributions to mechanisms relating to TGA and to mere exposure.

In conclusion, our study has found evidence for preserved learning in TGA using the mere exposure paradigm and has extended the utility of this paradigm from earlier studies that have shown preserved ME in primary degenerative dementia (Willems et al., 2002; Winograd, Goldstein, Monarch, Peluso, & Goldman, 1999) and prosopagnosia (Greve & Bauer, 1990). In the case of clinical implications of our findings, it is possible that in certain therapeutic settings simply providing repeated exposure to stimuli may help to make them more acceptable and favored, and this may provide a rationale for policies such as having the same, named nurse looking after a patient. However, systematic studies need to be carried out before generalizing from experimental ME effects such as those found in this study.

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