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The role of retrieval inhibition in the associative memory impairment of schizophrenia

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Abstract

To examine retrieval-induced forgetting (RIF) in schizophrenia, subjects studied category-exemplar words taken from either strong or weak categories, and then practiced retrieval by completing category word-stems on half of the word pairs. Patients had reduced recall and recognition, but showed the expected RIF effect of better recall of unpracticed items from unpracticed categories than for unpracticed items from practiced categories. By contrast, patients and controls showed differing RIF for recognition as a function of categorical dominance: whereas controls showed RIF only for dominant category exemplar word pairs, patients showed RIF for both dominant and weak categories. Different patterns of baseline practiced retrieval for weak associate pairs in schizophrenia may explain this finding. The results failed to support faulty RIF in the associative memory impairment of schizophrenia.

Keywords

retrieval-induced forgetting; recognition memory; categorical dominance

1. Introduction

Bleuler (1911) first identified schizophrenic discourse as often marred by intrusions of dominant but contextually-inappropriate word associations, as illustrated by his patient listing her family members as "father, son, and Holy Ghost" Is such disturbance related to a failure to suppress highly active but irrelevant representations from consciousness? In computational and neuropsychological models of cognition, inhibitory processes play an important role in both memory retrieval and selective attention (e.g., Anderson & Spellman, 1995;Collins & Loftus, 1975;Roediger et al., 2001). In associative memory models, in particular, a retrieval cue, such as a category (e.g., FRUIT) activates a network of associates from which the to-beremembered target is isolated and selected. Activation spreads from a category node (e.g., FRUIT) along network members, even if only one item is sought (e.g., ORANGE). For the desired target to be retrieved, some inhibitory mechanisms are thought to be necessary to

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suppress activated, interfering alternatives (Anderson & Spellman, 1995). These inhibitory mechanisms would serve to deactivate the representation of a competing item in associative memory (Anderson & Spellman, 1995).

We used a newly-developed, retrieval-induced forgetting (RIF) paradigm to examine the mnemonic mechanisms by which a common category cue activates competition among exemplars for access to conscious recollection (Anderson et al., 1994). This gives rise to a phenomenon known as retrieval-induced forgetting whereby encoding and retrieving some associates of a category cue leads to the suppression of other competing and interfering associates during recall. An inhibitory process suppresses the competing category members, leading them to be forgotten. The RIF paradigm is based on the assumption that repeated encoding and retrieval of an item will strengthen the ease of recall of that item, while at the same time leading to the loss of retrieval access of other related items. Thus, the RIF paradigm is of particular interest to the study of the associative memory impairment of schizophrenia because it provides a means to isolate retrieval inhibition from other potential mechanisms of retrieval interference in the disease-related associative disturbance.

The RIF paradigm involves three phases: learning or encoding, retrieval-practice, and delayed category-cued recall. For encoding, subjects study 36 experimental words from six dissimilar categories, each presented as category-exemplar pairs (e.g., FRUIT-BANANA, FRUIT-ORANGE; METALS-IRON, METALS-ALUMINUM). For retrieval-practice, subjects complete category-plus-exemplar stem cue tests (e.g., FRUIT OR_____) for only half of the categories and exemplars. For example, subjects complete stem cue tests for FRUIT-ORANGE but not for FRUIT-BANANA and METALS-IRON. Following a 20-minute interval, subjects are presented with each category name from the encoding phase, and instructed to recall as many exemplars of that category that they remembered during anytime in the experiment (see Anderson et al., 1994).

Practiced category-exemplar pairs (e.g., FRUIT-ORANGE) are recalled best, but surprisingly the benefit of practice does not extend to related unpracticed associates of the same category (e.g., FRUIT-BANANA). In fact, even though they are studied for the same amount of time, the related unpracticed items (e.g., FRUIT-BANANA) have a lower rate of recall than the unrelated, unpracticed items (e.g., METALS-IRON) Anderson et al. (1994) termed this pattern of cued recall [e.g., FRUIT-ORANGE>METALS-IRON>FRUIT-BANANA] as the RIF effect. They proposed that retrieval practice of some of the members of a category results in retrieval inhibition of associated, unpracticed members. This pattern of cued recall has been replicated by other studies (Anderson & Spellman, 1995;Butler et al., 2001;Smith & Hunt, 2000; but see Williams & Zacks, 2001). Moreover, several studies have suggested that the effect may be localized to the recall stage, as only retrieval but not encoding manipulations result in forgetting of related material (Anderson et al., 2000;Bäuml, 1996,1997;Ciranni & Shimamura, 1999).

We recently examined RIF in patients with chronic schizophrenia (Nestor et al., 2005). In two experiments, patients with chronic schizophrenia showed significantly overall reduced delayed cued recall. However, patients and controls showed similar RIF for unrelated categories (e.g., FRUIT-ORANGE, METALS-IRON), as reflected by lowest recall for members of a practiced category in comparison to members of an unpracticed category. These results pointed to intact within-category inhibition for patients. Kissler and Bäuml (2005) have demonstrated a similar finding using a part-list cuing paradigm. In a second experiment, we examined RIF for word-pair exemplars from both related and unrelated categories (e.g., COTTON-SHIRT, LEATURE SKIPT).

LEATHER-SKIRT). Here the results failed to demonstrate RIF for either controls or patients, but instead pointed to a significant decline in cued recall for related but not unrelated category-

exemplars for patients in comparison to controls (Nestor et al., 2005; Experiment 2) The results suggested faulty specificity/distinctiveness for encoding and retrieval, but not abnormal RIF may contribute to the associative memory disturbance of schizophrenia (Nestor et al., 2005).

In the current study, we examined the role of RIF in recall and recognition in patients with chronic schizophrenia. The associative disturbance of schizophrenia is often characterized by difficulties overriding prepotent, dominant responses, as illustrated in the foregoing Bleuler example (see Han et al., 2003; Nestor et al, 1998; Nestor et al., 2002) We therefore manipulated associative strength word pair exemplars taken from strong and weak categories to examine the effect of categorical dominance on RIF for both recall and recognition in patients with chronic schizophrenia.

2. Method

2.1. Participants

Eighteen right-handed male patients with chronic schizophrenia recruited from the VA Boston Healthcare System – Brockton Division had a mean age of 42.59 years (SD=9.91), a mean parental socioeconomic status of 3.25 (SD=1.07), a mean length of illness of 18.50 years (SD=10.54), a mean educational level of 12.47 years (SD=2.00) and a mean chlorpromazine equivalent of 422.53mg (SD=275.69) (Stoll, 2003). All patients were part of an ongoing comprehensive, longitudinal study of schizophrenia. The Structured Clinical Interview for DSM-IV Axis I Disorders-Patient Edition (SCID-P) (First et al., 1997), along with chart review, ascertained the diagnosis of schizophrenia. Eighteen right-handed male control subjects recruited from the community had a mean age of 45.88 years (SD=7.51) and a mean level of education of 15.88 years (SD=2.26). All subjects were native speakers of English, without histories of ECT, neurological illness, head trauma, and without alcohol or drug abuse in the past 5 years, as assessed by the Addiction Severity Index (McLellan et al., 1992). All subjects had normal or corrected-to-normal vision.

2.2. Materials

Eight semantic categories (e.g., FRUITS) paired with six representative exemplars for each category (e.g., BANANA) served as the target stimuli for each phase (see Table 1). No two categories were semantically related to another (Anderson et al., 1994;Marshall & Cofer, 1970). Four dominant categories and four weak categories were used (Battig & Montague 1969;Shapiro & Palermo 1970) as well as two filler categories with 12 exemplars to control for primacy and recency effects during learning, practice and recall phases.

2.3. Procedures

Procedures followed the Anderson et al (1994) study, and are outlined in Figure 1 adapted from Butler et al (2001). Subjects were tested individually in a quiet room, and were told that they would be participating in a test of memory. Before the experiment began, subjects were told their task was to remember as many items as they could. They were then given a learning booklet to study, containing 48 pages, each with a single category-exemplar pair printed in large bold font in the center of the page. Each pair was read by the examiner and presented for five seconds. After the completion of the study phase of the experiment, subjects performed retrieval practice, which consisted of completing a category-exemplar word stem with a word that was shown during the study phase (e.g., FRUIT-OR____). Each stem along with a category label was presented in a 45 page retrieval-practice booklet, one category-cued word stem per page. The booklet contained half of the experimental categories (3) and members (3), each practiced three times, along with the filler categories (2), and half of their members (3), each

had studied in their learning booklets. They were given 10 seconds to respond. These items are referred to as retrieval-practiced (RP+). Following a 20 minute delay in which subjects performed unrelated tasks (e.g., vocabulary and block design tests), a category-cued recall test was then administered in booklet form, one page for each of the six studied categories. Subjects were asked to recall and write down all the examples of the category they could remember. Category-cued recall rates were computed for retrieval-practiced items (RP+, e.g., FRUIT-ORANGE), unpracticed items from retrieval-practiced categories (RP–, e.g., FRUIT-BANANA), and non-retrieval practiced items (Nrp, e.g., METALS-IRON).

Last, subjects completed a recognition test, which consisted of the 48 target pairs that were initially learned and 48 novel pairs (Table 2). Twenty-four of the novel word pairs comprised of target categories paired with novel exemplars and an additional 24 novel pairs included novel categories paired with novel exemplars

3. Results

3.1. Retrieval practice category-plus-stem completion

A mixed-model ANOVA with one between-subject factor of group (schizophrenia, normal control) and one within-subject factor of associative strength (strong, weak) revealed significant effects for group, F(1, 34) = 17.33, p < .001, and for the interaction of group by associative strength, F(1, 34) = 5.59, p < .05. Controls completed 87% of word stems in contrast to 67% for the patient group. In addition, the significant group by associative strength interaction indicated that the groups differed on stem completion rates for strong and weak associates. That is, stem completion rates for weak associates in comparison to strong associates declined by 27% for patients and by 10% for controls, $t_{34} = 2.36$, p < .05. Overall, schizophrenic subjects completed fewer strong (M = 79.62, SD = 16.60; $t_{34} = 2.51$, p < .05) and weak (M = 53.08, SD = 23.91; $t_{34} = 4.14$, p < .001) category plus stem exemplar pairs correctly than did normal controls (strong pairs: M = 91.96, SD = 12.83; weak pairs: M = 81.77, SD = 17.14).

3.2. Delayed category-cued recall

A mixed-model ANOVA with one between-subject factor of group (schizophrenia, normal control) and two within-subject factors of associative strength (strong, weak) and item (RP+, RP-, NRP) revealed a significant effect for group, F(1, 34) = 12.64, p = .001, item, F(2, 33) = 35.42, p < .001, and associative strength, F(1, 34) = 30.86, p < .001. There were no significant two-way or three-way interactions of group, associative strength and item. Patients with schizophrenia recalled fewer category-exemplar pairs (M = 33.92, SD = 15.66) than did normal controls (M = 50.48, SD = 14.41). Both groups demonstrated RIF, as reflected by better recall for unpracticed exemplars in unpracticed categories than in practiced categories (NRP>RP-). Subjects with schizophrenia recalled more retrieval-practiced (RP+) than NRP items ($t_{17} = 3.21$, p < .01) as well as RP-items ($t_{17} = 4.51$, p < 001) (see Table 3). Importantly, fewer RP- item words were recalled than NRP item words for schizophrenic patients (14% difference, $t_{17} = 3.52$, p < .01), demonstrating the retrieval induced forgetting effect. Normal control subjects showed similar effects of retrieval practice and the retrieval induced forgetting effect to schizophrenic patients, with a significant difference between NRP and RP- recall (12%, $t_{17} = 2.36$, p < .05).

Furthermore, given divergent baseline differences, relative RIF computations were made accordingly: (NRP-RP–)/NRP*100. With reference to the NRP baseline, subjects with schizophrenia demonstrated a 29% (SD = 58.65) decline in recall of related associates. Normal comparison subjects, in relation to the NRP baseline, evidenced a smaller decline of 15% in

recall of related associates (SD = 53.42). Thus, subjects with schizophrenia demonstrated increased rates of decline of associate recall or RIF compared to control subjects, though this difference was not statistically significant.

3.3. Delayed recognition

A similar mixed-model ANOVA on delayed recognition memory revealed significant effects for item, F(2, 33) = 164.46, p < .001, and for the three-way interaction of group by associative strength by item F(2, 33) = 4.83, p < .05 (see Table 4). There were no significant effects of associative strength or two-way interactions. Results did indicate a marginal two-way interaction of set and associative strength, F(2, 33) = 3.18, p = .055. The main effect of item indicated highest recognition rates for retrieval-practiced, strong associates for both groups. The significant three-way interaction revealed that associative strength and item factors exerted different effects on delayed recognition for patients in comparison to control subjects. Controls and patients showed the RIF effect of better recognition of unpracticed items of unpracticed strong categories than for unpracticed items of practiced strong categories. However, for weak associates, only the patients showed the RIF effect. A mixed-model ANCOVA with one between-subject factor of group (schizophrenia, normal control) and two within-subject factors of associative strength (strong, weak) and item (RP+, RP-, NRP) covarying for overall retrieval practice rates was performed. Analyses revealed no significant main effects or interactions among variables. In addition, chlorpromazine levels in schizophrenia were negatively correlated with recognition rates of strongly associated category-exemplar pairs, r(15) = -.76, *p* < .001.

4. Discussion

This study examined the effects of category dominance on RIF in patients with schizophrenia. In relation to age-matched controls, patients showed overall reduced rates of both delayed cued recall and delayed recognition of associates of either dominant or weak categories. For recall, both groups showed a similar level of RIF for dominant and weak categories, as reflected by the absence of any significant two- or three-way statistical interaction of group by associative strength by item. However, for delayed recognition, the two groups showed a different pattern of performance as a function of category dominance. That is, only the patients showed the RIF effect for delayed recognition of associates belonging to weak categories.

For both groups, retrieval practice of the dominant category exemplar pairs (e.g, FRUIT-ORANGE) impaired later recall of other category members (e.g, FRUIT-BANANA), as did the retrieval-practice of weak category exemplar pairs (e.g., TREE-PALM) impaired later recall of other members of the same category (e.g., TREE-WILLOW). Butler et al (2001) also found similar RIF in cued recall for weak and dominant categories in their sample of healthy subjects. By contrast, Anderson et al (1994) found the RIF effect for dominant but not weak categories.

For patients, we had expected that category dominance would differentially affect RIF. However, our results indicated otherwise, and are consistent with a prior RIF study in patients with chronic schizophrenia (Nestor et al., 2005). Similarly, a recent study by Kissler and Bäuml (2005) found no difference in part-list cuing for strong and weak items between healthy controls and patients with schizophrenia. This result is relevant, because recently part-list cuing, like RIF, has been attributed to inhibitory processes as well (Bäuml & Aslan, 2004). These data suggested that the schizophrenic propensity for prepotent dominant categories cannot be attributed to failed inhibitory processes as indexed by RIF (Nestor et al, 2002). In contrast to delayed recall, for delayed recognition, the performance of the patient group diverged from that of age-matched controls, as reflected by the significant three-way interaction of group by associative strength by item. For dominant categories, both groups showed the RIF for delayed recognition, as reflected by better performance for unpracticed member of unpracticed categories than for unpracticed members of practiced categories. For example, similar to recall, retrieval-practice of DRINKS-BOURBON suppressed recognition

of its unpracticed associate, DRINKS-TEQUILIA, in comparison to an unpracticed and unrelated category exemplar pair of METAL-CHROME. However, the groups showed different patterns of recognition performance for the weak categories. Here the healthy controls did not show the RIF effect whereas patients did. In fact, the healthy controls showed a slight advantage for unpracticed members of practiced weak categories (e.g., DRINKS-TEQUILIA), in relation to unpracticed members of unpracticed categories (e.g., METAL-CHROME), an effect opposite to RIF.

Thus, for delayed recognition, retrieval-practice by completing word-stems appeared to facilitate rather than inhibit recognition memory of weak associates for control subjects. This pattern of recognition performance would be consistent with models of semantic priming and automatic spread of activation, according to which encoding and retrieval should facilitate related knowledge, not impair it. For healthy controls, recognizing previously-studied, weak associates may reflect both implicit and explicit mnemonic processes, the former influenced by familiarity and the latter by directed study and practice. Other studies of normal controls have also shown priming for implicit memory tests of recognition, instead of the RIF effect of worse performance for unpracticed items from practiced categories (Perfect et al., 2002).

By contrast, for patients with schizophrenia, retrieval-practice via word-stem completions continued to exert a similar RIF effect of suppression for delayed recognition of associates taken from either weak or dominant categories, a pattern of performance consistent with their delayed recall. The patients, unlike controls, did not show evidence of any priming effect for unpracticed associates of practiced, weak categories: simply studying pairs taken from weak categories failed to prime their subsequent recognition. This pattern suggested that the associative memory impairment of schizophrenia may be tied to abnormalities of priming of the response input stage, as opposed to retrieval-induced forgetting of the response output stage.

Several important caveats limit the interpretation of the different RIF pattern for recognition in the patient and control participants. First, the patient group showed an anomalous recognition pattern of best performance for non-retrieval practiced items taken from weak categories. This is clearly an unexpected and anomalous finding that may reflect measurement failure, and most importantly limits interpretation of the RIF effect shown by the patients for weak categories.

Second, our control participants showed RIF for recognition of dominant category exemplar word pairs. This finding stands in contrast to research when only recognition tests have been used (e.g., Veling & van Knippenberg, 2004). In the current study, the same items were tested on the recall and recognition tests. Thus, this study cannot rule an alternative interpretation that the observed interaction of group and categorical dominance on the recognition test reflected group differences in performance on the recall test. Likewise, the groups differed in retrieval practice performance, and such pre-existing differences limit interpretation of RIF in patients on subsequent tests of recall and recognition.

Third, the differences between control and patient groups on recognition of category-exemplar pairs according to strength condition may be partly explained by an influence of retrieval practice. Subjects with schizophrenia demonstrated significant impairment in their ability to complete category-plus-stem word pairs for weak associates in comparison to the control

group. Given reduced retrieval practice completion rates of weak exemplars in patients with schizophrenia, recognition and recall rates may be affected.

Overall, RIF belongs to a class of information processing procedures that are intended to reduce retrieval interference by inhibiting activated, competing associates Priming on the other hand belongs to a distinct class of information processing procedures that are intend to facilitate recall of related material. Associative memory may therefore reflect a balance of interference-reducing and activation-spreading procedures, and each may be initiated automatically as well as being under direct control. For the current study, the RIF effect observed in both controls and patients may have reflected an automatic form of inhibition, in contrast to a more directed, controlled form of inhibition. These two forms of inhibition have been shown to be neurologically dissociable with RIF deficits of automatic inhibition linked to temporal lobe lesions, and directed forgetting deficits of controlled inhibition linked to frontal lobe lesions (Conway & Fthenaki, 2003). Future studies are needed to examine these two forms of inhibition within the same group of patients with schizophrenia.

To summarize, schizophrenia is characterized by a marked susceptibility to interference that leads to impaired associative memory (Torres et al., 2001). The current results demonstrated clear evidence of associative memory impairment in schizophrenia, but no evidence of deficient RIF. Therefore, the bases of this associative memory deficit could not be attributable to disturbed automatic inhibitory processes, as index by RIF. Indeed, if anything, patients showed enhanced RIF. Whether this is an example of a disease-related abnormality of heightened automaticity is unknown (Callaway & Naghdi, 1982). Alternatively, the theory underlying RIF presupposes that repeated retrieval of a given item strengthens that item while simultaneously causing the loss of retrieval access to other related items. For patients with schizophrenia, however, repeated retrieval cues may have less potency, and pre-existing associative links may require greater priming. For patients, then, instead of being an index of preserved automatic inhibition, intact RIF may mask a failure to form enduring associative links among to-be-remembered items.

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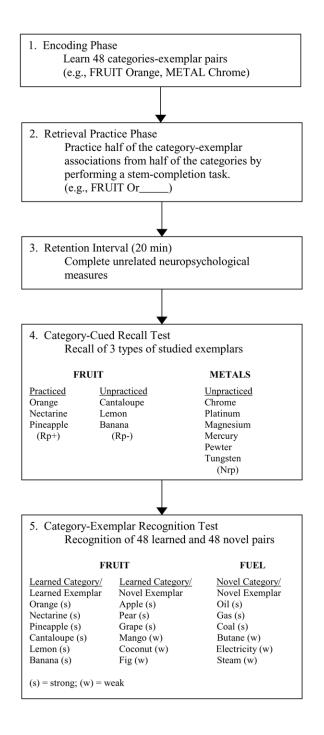


Figure 1.

A schematic depiction of the RIF paradigm with the addition of final recognition.

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Table 1

Target and filler category-exemplar word pairs (Anderson et al., 1994)

Туре	Category	Exemplars
Strong Category-exemplar Pairs	Fruits	Orange, Nectarine, Pineapple, Banana, Cantaloupe, Lemon
	Leather	Saddle, Gloves, Wallet, Shoes, Belt, Purse
	Drinks	Bourbon, Scotch, Tequila, Brandy, Gin, Rum
	Hobbies	Gardening, Coins, Stamps, Ceramics, Biking, Drawing
Weak Category-exemplar Pairs	Trees	Palm, Hickory, Willow, Poplar, Sequoia, Ash
	Professions	Tailor, Florist, Farmer, Critic, Grocer, Clerk
	Metals	Chrome, Platinum, Magnesium, Mercury, Pewter, Tungsten
	Weapons	Hammer, Fist, Lance, Rock, Arrow, Dagger
Filler Category-exemplar Pairs	Cities	London, Tokyo, Houston, Miami, Moscow, Atlanta
	Animals	Dog, Lion, Goat, Fox, Wolf

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Table 2

Recognition	phase	distractor	word	pairs
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Туре	Category	Strong Exemplars	Weak Exemplars
Target Category/Novel Exemplar Pairs	Fruits	Apple, Pear, Grape	Mango, Coconut, Fig
	Drinks	Wine, Beer, Vodka	Sherry, Vermouth, Port
	Metals	Iron, Copper, Steel	Nickel, Titanium, Bronze
	Trees	Oak, Maple, Pine	Cypress, Cottonwood, Magnolia
Novel Category/Novel Exemplar Pairs	Stone	Diamond, Ruby, Emerald	Zircon, Onyx, Amethyst
	Color	Blue, Red, Green	Beige, Maroon, Gray
	Fuel	Oil, Gas, Coal	Butane, Steam, Electricity
	Instrument	Piano, Drum, Trumpet	Triangle, Baritone, Fiddle

Table 3

Percent of category-exemplar word pairs recalled according to item factors. Standard deviations noted within parentheses.

		RP+	RP-	NRP
Control	Overall	70.8 (18.1)	35.6 (17.1)	47.7 (19.4)
	Strong	74.1 (20.8)	38.9 (17.1)	52.3 (21.2)
	Weak	67.6 (24.6)	32.4 (21.8)	44.4 (19.8)
Schizophrenia	Overall	47.2 (24.4)	20.4 (16.2)	34.0 (16.9)
	Strong	56.5 (230)	24.1 (23.7)	36.6 (20.0)
	Weak	38.0 (30.7)	16.7 (15.1)	31.5 (18.9)

Table 4

Percent of category-exemplar word pairs recognized according to item factors. Standard deviations are noted in parentheses.

		RP+	RP-	NRP
Control	Strong	95.4 (11.1)	64.8 (21.3)	80.1 (16.2)
	Weak	92.6 (11.7)	74.1 (20.0)	72.2 (24.3)
Schizophrenia	Strong	88.9 (17.2)	59.3 (36.7)	71.8 (18.8)
	Weak	75.1 (26.3)	63.9 (29.8)	77.3 (23.7)