

Serotonin Levels Influence Patterns of Repetition Priming

E. Darcy Burgund
Washington University School of Medicine

Chad J. Marsolek and Monica Luciana
University of Minnesota

Repetition priming in a word-stem completion task was examined in a group of control subjects and in a group of experimental subjects under conditions of acute tryptophan depletion (T⁻) and tryptophan augmentation (T⁺). Experimental subjects ingested amino acid compounds that depleted or loaded the body with tryptophan, and word-stem completion priming performance was measured. Results indicate differential effects of T⁻ and T⁺ manipulations on word-stem completion priming. In the control group, both specific-visual and amodal priming were observed. Conversely, in the T⁺ condition, specific-visual priming, but no amodal priming, was observed, whereas in the T⁻ condition, amodal priming, but no specific-visual priming, was observed. The authors conclude that serotonin (5-hydroxytryptamine) plays a critical role in repetition priming by helping to modulate which neural systems contribute to priming effects.

A growing amount of evidence suggests that the neuro-modulator serotonin (5-hydroxytryptamine, or 5-HT) plays a critical role in learning and memory. However, the exact relationship between 5-HT and these cognitive functions remains unclear. Results from animal studies suggest that increases in serotonergic activity impair learning and memory (Altman & Normile, 1988; McEntee & Crook, 1991) whereas decreases enhance these functions (Altman & Normile, 1986; Sirviö, Riekkinen, Jäkälä, & Riekkinen, 1994). Conversely, in humans, deficits in 5-HT transmission

have been associated with severe memory impairments, such as Alzheimer's and Korsakoff's diseases (Altman & Normile, 1988; Halliday, Cullen, & Harding, 1994; McEntee & Crook, 1991; Wenk, 1988), as well as with milder impairments, such as those observed in depressed patients (Brand, Jolles, & Gispen deWied, 1992) and in chronic users of ecstasy (methylenedioxymethamphetamine; Morgan, 1999).

Recently, researchers have begun to examine the effects of 5-HT on learning and memory in normal healthy adults by altering global 5-HT synthesis through dietary tryptophan manipulations (Luciana, Burgund, Berman, & Hanson, 2001; Park et al., 1994; Riedel, Klaassen, Deutz, van Someren, & van Praag, 1999; Rogers et al., 1999; Schmitt et al., 2000; Shansis et al., 2000). These studies yield a mixed pattern of results. Increases in tryptophan have been shown to decrease working-memory performance (Luciana et al., 2001), whereas decreases in tryptophan appear to leave working memory intact (Park et al., 1994; Riedel et al., 1999; Schmitt et al., 2000). With respect to long-term memory, impairments have been observed under conditions of tryptophan depletion (Park et al., 1994; Riedel et al., 1999; Schmitt et al., 2000); however, to our knowledge, the effects of tryptophan augmentation on long-term memory performance have not been examined. Moreover, examinations of long-term memory have tested performance on measures of explicit memory (e.g., free recall and recognition; Graf & Schacter, 1985) but ignored possible effects of tryptophan on indirect measures of memory, such as repetition priming (e.g., Tulving & Schacter, 1990).

In the present study, we examine the effects of tryptophan depletion and augmentation on repetition priming using a word-stem completion task (e.g., Graf, Mandler, & Haden, 1982). In this task, subjects complete three letter stems (e.g., "mar_") to the first word that comes to mind (e.g., "marble," "market," "marathon"). Repetition priming is measured as a

E. Darcy Burgund, Department of Neurology, Washington University School of Medicine; Chad J. Marsolek and Monica Luciana, Department of Psychology, University of Minnesota.

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Correspondence concerning this article should be addressed to E. Darcy Burgund, Department of Neurology, Washington University School of Medicine, 4525 Scott Avenue, St. Louis, Missouri 63110. E-mail: darcy@npg.wustl.edu

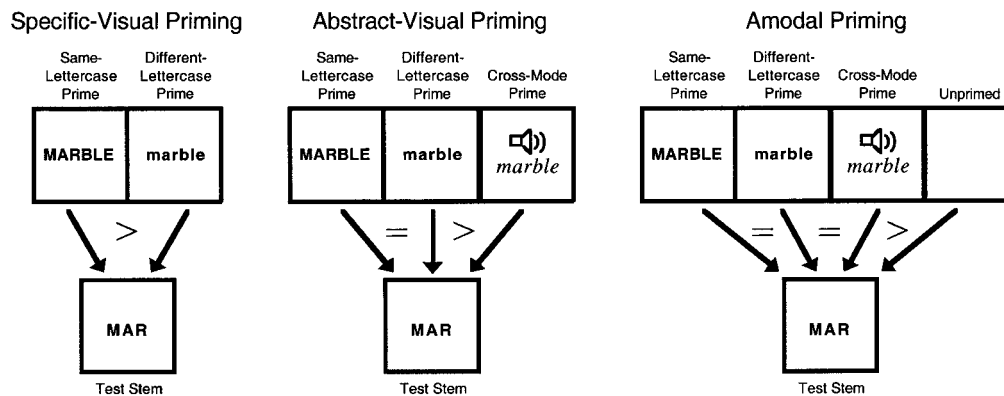


Figure 1. Different types of priming that may be measured in word-stem completion tasks. Specific-visual priming is measured as greater performance for same-lettercase primed stems compared with different-lettercase primed stems. Abstract-visual priming is measured as greater performance for same- and different-lettercase primed stems compared with cross-mode primed stems. Amodal priming is measured as greater performance for same-lettercase, different-lettercase, and cross-mode primed stems compared with unprimed stems.

greater tendency to complete a test stem to a particular word when that word was encoded previously (e.g., primed test stem) than to complete a test stem to that word when the word was not encoded previously (e.g., unprimed test stem). The word-stem completion task is a particularly useful measure because it can be used to examine different types of priming by manipulating the relation between the encoded word and the test stem. For example, *specific-visual priming* can be measured as greater priming for stems presented in the same lettercase as their corresponding prime words than for stems presented in the different lettercase compared with their corresponding prime words (see left side of Figure 1). *Abstract-visual priming* can be measured as equivalent priming for stems presented in the same or different lettercase compared with their corresponding prime words. Critically, to be considered visual, the priming in same- and different-lettercase conditions must be greater than the priming obtained with visual stems after processing auditory prime words for those stems (see middle of Figure 1). Finally, *amodal priming* can be measured as equivalent priming for stems presented in the same lettercase, different lettercase, and different perceptual modality (visual stems following auditory words) compared with their corresponding prime words. Critically, all three conditions must produce priming per se, in that stems in all three of the primed conditions must be completed to primed words at a greater rate than unprimed stems are completed to those critical words (see right side of Figure 1).¹

Data from brain imaging, lesion, and divided-visual-field studies converge to suggest that these types of priming are supported by relatively independent neural subsystems. Functional imaging studies suggest that visual priming is supported by bilateral regions in the extrastriate cortex, most notably Brodmann's Area 19 (Buckner et al., 1995; Schacter, Alpert, Savage, Rauch, & Alpert, 1996; Squire et al., 1992), whereas amodal priming has been associated with other regions including the left posterior parietal, left

superior temporal, anterior prefrontal (Badgaiyan, Schacter, & Alpert, 1999; Schacter, Badgaiyan, & Alpert, 1999), and left medial temporal cortex (Blaxton et al., 1996). Evidence from brain-damaged patients corroborates these dissociations between visual priming and amodal priming (Gabrieli, Fleischman, Keane, Reminger, & Murrell, 1995; Keane, Gabrieli, Mapstone, Johnson, & Corkin, 1995). Moreover, brain lesion (Gabrieli et al., 1995; Vaidya, Gabrieli, Verfaellie, Fleischman, & Askari, 1998) and divided-visual-field studies (Marsolek, Kosslyn, & Squire, 1992; Marsolek, Schacter, & Nicholas, 1996; Marsolek, Squire, Kosslyn, & Lulenski, 1994) suggest that specific-visual priming, but not abstract-visual priming, is supported by a subsystem that operates more effectively in the right hemisphere than in the left. Hence, it is possible that 5-HT levels affect the sub-

¹ Many researchers have suggested an important distinction between perceptual and conceptual priming (e.g., Roediger & McDermott, 1993). It is important to note that specific-visual priming effects and abstract-visual priming effects, as defined in the text, both reflect what is typically termed *perceptual* priming (although we prefer the term *visual* priming to help specify the modality and localization). The commonality between the two is that they must involve visual-form representations because the priming effects require maintaining the same visual modality for stimuli between encoding and test. In addition, amodal priming effects, as defined in the text, reflect what we term *postvisual* priming. We prefer the term *postvisual* over *conceptual* priming because amodal priming could be supported by phonological representations (Badgaiyan et al., 1999; Rueckl & Mathew, 1999; Schacter et al., 1999), semantic-conceptual representations (Bassili, Smith, & MacLeod, 1989; Blaxton et al., 1996), explicit memory representations (Badgaiyan et al., 1999; Jacoby, Toth, & Yonelinas, 1993; Schacter et al., 1999), or some combination (Curran, Schacter, & Galluccio, 1999; Schacter & Badgaiyan, 2001). The important commonality in all of these possibilities is that the priming effect does not benefit from maintaining the same visual modality for stimuli between encoding and test.

systems underlying distinct types of priming in different ways. For example, given that 5-HT innervation is especially great in the visual cortex (e.g., Morrison & Foote, 1986; Varnäs, Hall, Bonaventure, & Sedvall, 2001), 5-HT may be especially important for supporting specific-visual priming effects.

To test this possibility, we measured amodal, abstract-visual, and specific-visual priming in the word-stem completion task under conditions of acute tryptophan depletion and augmentation across two sessions in the same group of subjects. Baseline levels of priming performance also were obtained across two sessions in a separate group of control subjects.²

Method

Subjects

Sixteen volunteers (10 men and 6 women with a mean age of 22.00 years \pm 4.56) from the University of Minnesota community participated in the experimental protocol. Experimental subjects were psychiatrically normal, as determined by a structured diagnostic interview (*Structured Clinical Interview for DSM-IV, Patient Version*; First, Spitzer, Gibbon, & Williams, 1997). Individuals were excluded from participation if they reported current or past histories of Axis I psychopathology, including affective disorders, psychosis, substance abuse or dependence, anxiety disorders, or eating disorders. In addition, experimental subjects were medically screened. Exclusions for pregnancy, oral contraceptive use during the previous 4 months, current prescribed or nonprescribed medication use, menstrual irregularities, endocrinopathies, neurological disease, and other clinical conditions were applied. Women were studied during the early to midfollicular phase (Days 1–10) of the menstrual cycle.

An additional 16 volunteers (8 men and 8 women with a mean age of 20.00 years \pm 1.57), recruited from the same subject pool as the experimental subjects, participated in the control protocol to provide baseline results with which results from the experimental group were compared. There were no significant differences between the experimental and control groups in age and gender. All subjects in experimental and control groups had normal or corrected-to-normal vision and normal hearing, and all gave informed consent in accordance with the guidelines set forth by the Research Subjects' Protection Program at the University of Minnesota and by the Scientific Advisory Committee of the General Clinical Research Center.

Materials

Stimuli were 96 medium frequency words (mean frequency = 88 occurrences per million; Francis & Kucera, 1982), ranging from four to seven letters in length, and their three-letter beginnings (i.e., stems). They were selected from *Webster's Vest Pocket Dictionary* (1989), with the constraints that the initial three letters (i.e., the stem) of each word were unique among the set of words chosen and could be completed to form at least 10 words in the dictionary. To enhance the possibility of observing specific-visual priming effects, we chose words for which all of the stems were composed of letters in the set ABDEFGHLMNQRT, as these are the 13 letters with the most dissimilar lowercase versus uppercase visual forms (from ratings and cluster analyses reported in Boles & Clifford, 1989). The 96 words were divided into eight lists of 12 words each. Lists were equated such that they did not differ

significantly from each other in terms of mean frequency, the number of words that could be completed from the stem of each word, and the unprimed probability that the stem of each word would be completed to form that word according to pilot measurements. Within-subjects conditions were created by crossing prime type (same-lettercase primed vs. different-lettercase primed vs. cross-mode primed vs. unprimed) with experimental session (Session 1 vs. Session 2), and each of the word lists was rotated through those eight conditions across subjects for counterbalancing purposes. Thus, each cell in the design was represented by 12 trials per subject.

Stimuli were presented on a Macintosh PowerBook 1400cs using the PsyScope software package and button box (Cohen, MacWhinney, Flatt, & Provost, 1993). During the encoding phase, words were presented either visually on the computer screen or auditorily through the computer speakers. Visually presented words appeared in either all uppercase letters or all lowercase letters in 24-point black Helvetica bold font against a white background, and each letter subtended approximately .65° of visual angle. Auditorily presented words were prerecorded and were played at a level that was easy for each subject to hear. During the test phase, three-letter word stems were presented visually in all uppercase letters in black Helvetica 24-point font against a white background. A 2-mm dot (subtending 0.23° of visual angle) served as the central fixation point. Finally, a chin rest was used to keep subjects' eyes approximately 50 cm from the computer screen.

Procedure

All subjects performed the word-stem completion task during two experimental sessions, separated by at least 1 week. Each experimental session had an encoding phase and a test phase.

During the encoding phase, subjects encoded a list of 36 words (plus five filler words, three at the beginning and two at the end, to attenuate primacy and recency effects). Each trial began with the presentation of a warning signal in the form of a fixation point, which appeared at the center of the display for 500 ms. Subjects were instructed to focus on this fixation point. On visual trials, a word was presented in the center of the screen for 3 s immediately after the fixation point disappeared. On auditory trials, the fixation point remained on the screen for 3 s and the auditory word was presented in the middle of the 3-s time period. After this 3-s time period, subjects pressed a number key from 1 to 5 on the computer keyboard to indicate how much they liked or disliked that word. For these judgments, subjects were asked to consider the meanings

² Ideally, it would have been preferable to test baseline, tryptophan depletion, and tryptophan augmentation in the same group of experimental subjects rather than using a separate group of control subjects to assess baseline performance. We did not test baseline performance in our experimental subjects, however, to minimize the number of necessary sessions per experimental subject and because sufficient stimuli that adhered to our constraints were not available. As it was, subject recruitment and retention was difficult because of the time commitment required. Therefore, by decreasing the amount of time needed for each subject's participation, we maximized the number of potential subjects that were willing and able to complete the study. Furthermore, if anything, between-subjects comparisons provide less opportunity to observe significant effects than within-subjects comparisons because of inflated error in these designs. Nonetheless, because we observed significant differences between control and experimental groups, we do not believe that the use of separate subject groups compromised our results.

associated with the words as opposed to how they sound or what they look like. This encoding task has been used in many versions of the word-stem completion task and is known to produce robust priming effects (e.g., Graf, Shimamura, & Squire, 1985; Marsolek et al., 1992).

During the test phase, subjects were presented with 48 three-letter stems and instructed to verbally complete each stem with the first English word that comes to mind (excluding proper nouns). One fourth of the stems had been primed by words appearing in the same lettercase, compared with encoding (same-lettercase primed). One fourth of the stems had been primed by words appearing in the different lettercase, compared with encoding (different-lettercase primed). One fourth of the stems had been primed by words presented auditorily during the encoding phase (cross-mode primed), and one fourth of the stems had not been primed; that is, they could not be completed to form any of the words presented during the encoding phase (unprimed). A test trial began with the presentation of the fixation point at the center of the display for 500 ms. Subjects were instructed to focus their attention on the fixation point. Immediately after the fixation point disappeared, a stem appeared in the center of the computer screen for 183 ms. A blank screen followed and remained until the subject verbally completed the stem. Subjects' verbal responses were recorded by the experimenter.

The details of the tryptophan manipulation in the experimental protocol are described elsewhere (see Luciana et al., 2001); however, a summary follows: Experimental subjects adhered to a low-tryptophan diet for 48 hr prior to each session and fasted from midnight the previous night. Each session began at 10:00 a.m. with the insertion of an intravenous catheter into the nondominant forearm of each subject. Soon after, subjects consumed an amino acid mixture that would cause tryptophan depletion (T⁻; or that would cause tryptophan augmentation, T⁺) during the first session and opposite during the second session (in a double-blind manner) and then fasted with the exception of water and several glasses of fruit juice throughout the day. Between 10:30 a.m. and 5:30 p.m., blood was drawn, and plasma tryptophan, serum prolactin, and serum cortisol were measured. Subjects remained recumbent throughout the day except from 2:30–4:30 p.m., when they completed a battery of cognitive tests (see Luciana et al., 2001), including the word-stem completion task. The tasks were administered in five different orders such that the word-stem completion priming task, which lasted about 20 min, began at approximately 2:30 p.m., 2:50 p.m., 3:10 p.m., 3:50 p.m., or 4:10 p.m. The task orders were balanced across subjects, and each subject participated in the same task order on both the T⁻ and T⁺ condition testing sessions. A schematic of the study protocol is depicted in Figure 2.

Results

Plasma Tryptophan, Serum Prolactin, and Serum Cortisol Levels

Plasma tryptophan, serum prolactin, and serum cortisol levels in the experimental subjects were analyzed separately in a two-way analysis of variance (ANOVA) in which tryptophan manipulation (T⁻ vs. T⁺) and time of blood sampling (10:30 a.m., baseline, vs. 3:30 p.m., for plasma tryptophan; 10:30 a.m., baseline, vs. 1:30 p.m. vs. 3:30 p.m. vs. 5:30 p.m., for serum prolactin and cortisol) were within-subjects independent variables. Results from these analyses are reported in Table 1.

The analysis of plasma tryptophan revealed a significant interaction of Tryptophan Manipulation \times Time of Blood

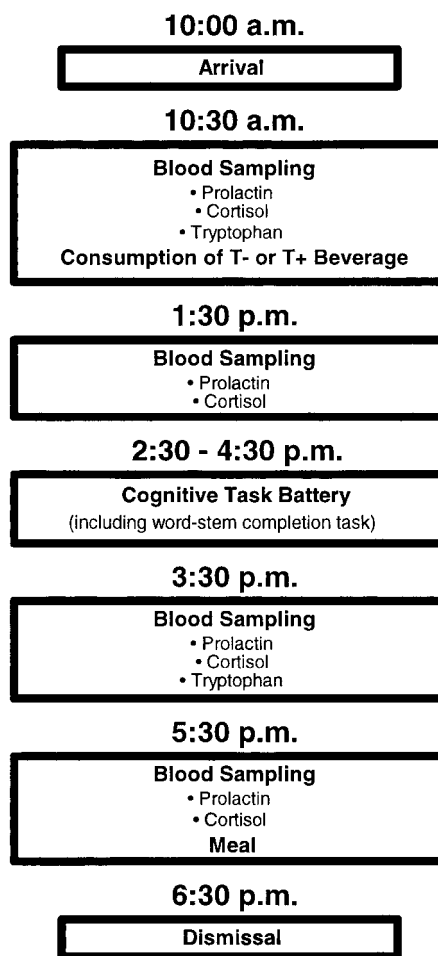


Figure 2. A schematic of the protocol used in the present study. Greater detail regarding this protocol has been published elsewhere (see Luciana et al., 2001). T⁻ = tryptophan depletion; T⁺ = tryptophan augmentation.

Sampling, $F(1, 15) = 221.11, p < .01, MSE = 5187.77$. Paired t -tests indicated that plasma tryptophan increased relative to baseline in the T⁺ manipulation condition, $t(15) = 14.10, p < .01$, and decreased relative to baseline in the T⁻ manipulation condition, $t(15) = -15.88, p < .01$. Thus, the tryptophan manipulation was successful; the T⁺ beverage caused plasma tryptophan levels to rise, and the T⁻ beverage caused plasma tryptophan levels to fall. In addition, the main effects of tryptophan manipulation, $F(1, 15) = 214.52, p < .01, MSE = 5312.15$, and time of blood sampling, $F(1, 15) = 173.74, p < .01, MSE = 4525.86$, were significant.

The analysis of serum prolactin revealed a marginally significant interaction of Tryptophan Manipulation \times Time of Blood Sampling, $F(3, 45) = 2.78, p < .06, MSE = 50.67$. Paired t tests indicated that serum prolactin was increased marginally at 1:30 p.m. relative to baseline in the T⁺ manipulation condition, $t(15) = 2.10, p < .06$, and decreased marginally at 3:30 p.m. relative to baseline in the T⁻ manipulation condition, $t(15) = 1.83, p < .09$. Changes

Table 1
Plasma Tryptophan, Serum Prolactin, and Serum Cortisol Levels

Assay	Tryptophan manipulation							
	T-				T+			
	10:30 a.m.	1:30 p.m.	3:30 p.m.	5:30 p.m.	10:30 a.m.	1:30 p.m.	3:30 p.m.	5:30 p.m.
Plasma tryptophan ($\mu\text{mol/l}$)	54 \pm 10		8 \pm 5		53 \pm 11		534 \pm 142	
Serum prolactin ($\mu\text{g/l}$)	13 \pm 8	14 \pm 7	10 \pm 7	13 \pm 10	14 \pm 10	22 \pm 20	11 \pm 7	11 \pm 7
Serum cortisol ($\mu\text{g/dl}$)	15 \pm 4	10 \pm 3	11 \pm 5	13 \pm 7	16 \pm 5	12 \pm 7	13 \pm 5	11 \pm 8

Note. Values represent means \pm standard deviations. T- = tryptophan depletion; T+ = tryptophan augmentation.

in prolactin are believed to indicate central nervous system alterations in 5-HT synthesis (e.g., Luciana, Collins, & Depue, 1998; Murphy, Aulakh, Mazzola-Pomietto, & Briggs, 1996). Although the effects of the tryptophan manipulation on serum prolactin levels did not reach significance in the present group of subjects, the effects were in the predicted direction. Furthermore, in analyses of prolactin data that included 3 additional subjects who did not complete the priming tasks (see Luciana et al., 2001), these effects were significant. Thus, results from the prolactin assays suggest that the T- and T+ manipulations used in the present study induced significant changes in central nervous system neurochemistry. In addition, the main effects of tryptophan manipulation, $F(1, 15) = 4.60, p < .05, MSE = 122.07$, and time of blood sampling, $F(1, 15) = 5.77, p < .01, MSE = 50.86$, were significant.

The analysis of serum cortisol revealed a main effect of time of blood sampling, $F(3, 45) = 4.16, p < .05, MSE = 30.24$, but this effect did not interact with the tryptophan manipulation variable, $F(3, 45) = 1.11, p > .35, MSE = 21.15$.

Word-Stem Completion

A completion for a word stem was scored as correct only if the reported word was exactly the same as the corresponding word on one of the experimental word lists. No plural forms, past-tense forms, or other changes were accepted. Percent correct completion rates for the control and experimental groups were analyzed separately and together.

Control group. Word-stem completion rates across all conditions for the control group are presented in Table 2. Data from the control group were analyzed in a two-way repeated measures ANOVA, in which prime type (same-lettercase primed vs. different-lettercase primed vs. cross-

mode primed vs. unprimed) and experimental session (Session 1 vs. Session 2) were within-subjects independent variables.

Most important, percent correct completion rate was greatest for same-lettercase primed stems, followed by different-lettercase primed stems, followed by cross-mode primed stems, followed by unprimed stems, $F(3, 45) = 18.75, p < .01, MSE = 433.93$, for the main effect of prime type (see Figure 3A). Simple effect contrasts indicated that priming was obtained in each of the three primed conditions (all $ps < .01$, for comparisons between the primed conditions and the unprimed condition). Moreover, the simple effect contrast comparing completion rates for same-lettercase primed stems with different-lettercase primed stems indicated that specific-visual priming was obtained, $F(1, 45) = 6.69, p < .05, MSE = 433.93$, and the simple effect contrast comparing completion rates for cross-mode primed stems with unprimed stems indicated that cross-modality priming was obtained, $F(1, 45) = 12.75, p < .01, MSE = 433.93$. However, the difference between completion rates for different-lettercase primed stems and cross-mode primed stems, although in the predicted direction, was not significant, $F(1, 45) = 1.47, p > .20, MSE = 433.93$; thus, significant abstract-visual priming was not observed.

In addition, a significant interaction was observed between prime type and experimental session, $F(3, 45) = 3.00, p < .05, MSE = 322.51$. Tests of the simple effects revealed significant priming in each of the primed conditions at each session (all $ps < .05$, for comparisons between the primed conditions and the unprimed condition, with the exception of the cross-mode primed condition in Session 1, $p < .11$). For same-lettercase primed stems, completion rates increased from Session 1 to Session 2, $F(1, 60) = 7.67, p < .01, MSE = 319.34$, for the simple effect contrast. However, completion rates did not differ across session for the other test conditions (all $ps > .14$). The main effect of experimental session did not reach significance ($p > .15$).

Experimental group. Word-stem completion rates across all conditions for the experimental group are presented in Table 3. Data from the experimental group were analyzed in a three-way repeated measures ANOVA in which prime type (same-lettercase primed vs. different-lettercase primed vs. cross-mode primed vs. unprimed) and tryptophan manipulation (T- vs. T+) were within-subjects

Table 2
Word-Stem Completion Rates (%) for Control Subjects

Session	Prime type			
	Same-lettercase primed	Different-lettercase primed	Cross-mode primed	Unprimed
1	50 \pm 19	43 \pm 22	36 \pm 19	25 \pm 18
2	68 \pm 21	48 \pm 25	42 \pm 21	16 \pm 18

Note. Values represent means \pm standard deviations.

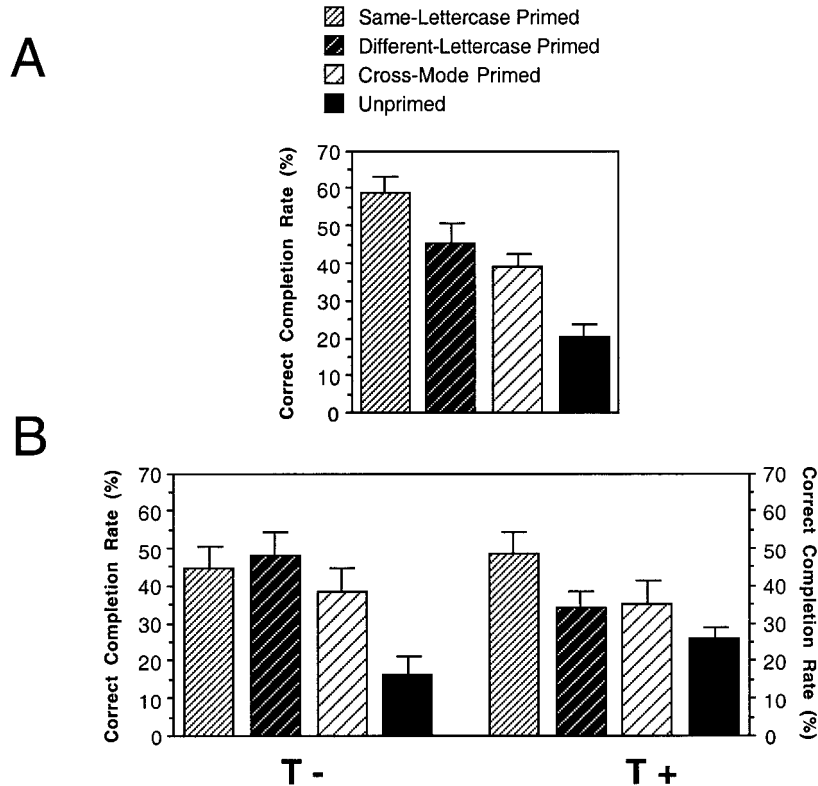


Figure 3. Results from the word-stem completion task for control (A) and experimental (B) subject groups. In A, percent correct completion rate is displayed as a function of prime type. In B, percent correct completion rate is displayed as a function of prime type and tryptophan manipulation. Error bars indicate standard errors of the mean. T- = tryptophan depletion; T+ = tryptophan augmentation.

independent variables. The session during which subjects consumed the T- beverage (Session 1 vs. Session 2) was included as a between-subjects variable.

Most important, this analysis revealed a significant interaction between prime type and tryptophan manipulation, $F(3, 42) = 3.75, p < .05, MSE = 252.42$ (see Figure 3B). Tests of simple effects revealed that in the T- condition, same-lettercase primed, different-lettercase primed, and cross-mode primed items were each completed at a greater rate than unprimed stems (all $ps < .01$). Moreover, completion rates in these three primed conditions did not differ from each other significantly (all $ps > .15$). This pattern of results reflects only cross-mode priming and not either of the other forms of priming. Conversely, in the T+ condition, same-lettercase primed stems were completed at a greater rate than unprimed stems ($p < .01$), but completion rates for different-lettercase primed stems and cross-mode primed stems did not differ significantly from unprimed stems (both $ps > .15$). In addition, completion rates were greater for same-lettercase primed stems than for different-lettercase primed stems ($p < .05$). However, completion rates for different-lettercase and cross-mode primed stems did not differ ($F < 1$). This pattern of results reflects only

specific-visual priming and not either of the other forms of priming.³ None of the effects including session reached significance (all $ps > .08$).

Combined group analysis. As illustrated by comparing Figures 3A and 3B, the patterns of priming observed under T- and T+ conditions in the experimental group were different from the pattern of priming observed in the control group. In particular, in the control group, both specific-visual priming and amodal priming were observed, whereas in the tryptophan group, only amodal priming was observed in the T- condition and only specific-visual priming was observed in the T+ condition. Very little, if any, abstract-

³ Some of the statistically insignificant differences seem to be numerically different enough to raise questions about whether we provided sufficient power to test these differences. For example, in the T+ condition, the different-lettercase primed (34%) and cross-mode primed (35%) completion rates seem fairly different from the unprimed rate (26%), yet the differences were not statistically significant. However, the comparison between different-lettercase primed and unprimed conditions was significant in our control group of subjects, and we had a 71% chance of obtaining an effect the size of that obtained in our control group (or larger) when

Table 3
Word-Stem Completion Rates (%) for Experimental Subjects

Session (T-)	Tryptophan manipulation							
	T-				T+			
	Same-lettercase primed	Different-lettercase primed	Cross-mode primed	Unprimed	Same-lettercase primed	Different-lettercase primed	Cross-mode primed	Unprimed
1	44 ± 23	49 ± 29	42 ± 22	21 ± 18	50 ± 22	36 ± 16	30 ± 21	23 ± 8
2	47 ± 27	47 ± 19	30 ± 30	7 ± 15	47 ± 22	30 ± 14	47 ± 32	33 ± 12

Note. Values represent means ± standard deviations. T- = tryptophan depletion; T+ = tryptophan augmentation.

visual priming was observed in either of the groups.⁴ To directly test whether amodal and specific-visual priming differed across groups as a function of tryptophan level, we conducted an additional ANOVA in which tryptophan level (T- vs. control vs. T+) was treated as a between-subjects variable. Difference scores representing amodal and specific-visual priming were the dependent measure. The difference score representing specific-visual priming was computed by subtracting the percentage correct in the different-lettercase primed condition from the percentage correct in the same-lettercase primed condition for each subject. The difference score representing amodal priming was computed by subtracting the percentage correct in the unprimed condition from the percentage correct in the cross-mode primed condition for each subject. Thus, priming type (specific-visual priming vs. amodal-visual priming) was a within-subjects independent variable.⁵

Results from this analysis are shown in Figure 4. Critically, the two-way interaction of Priming Type × Tryptophan Level was significant, $F(2, 45) = 4.33$, $p < .05$, $MSE = 438.56$. A significant contrast effect confirmed that specific-visual priming was greater in both the T+ and the control conditions than in the T- condition, $F(1, 90) = 9.54$, $p < .01$, $MSE = 496.41$. Thus, specific-visual priming was decreased by depleted levels of tryptophan and associated 5-HT levels in the central nervous system, compared against augmented or nonmanipulated levels. Conversely, a marginally significant contrast effect confirmed that amodal priming was greater in both the T- and the control group than in the T+ condition, $F(1, 90) = 3.82$,

$p < .06$, $MSE = 496.41$. Thus, cross-mode priming was decreased by augmented levels of tryptophan and associated 5-HT levels in the central nervous system, compared against depleted or nonmanipulated levels.

Discussion

In the present research, we investigated the effects of tryptophan depletion and tryptophan augmentation on repetition priming for words, in particular on word-stem completion priming. In the control group, amodal priming was exhibited by greater completion rates for cross-mode primed stems compared with unprimed stems. Specific-visual priming also was demonstrated by greater completion rates for same-lettercase primed stems compared with different-lettercase primed stems. This general pattern of results replicates previous work testing these priming conditions (e.g., Marsolek et al., 1992; Rajaram & Roediger, 1993). Results from the experimental group differed significantly from the control group. Amodal priming, but not specific-visual priming, was observed under conditions of

testing with 16 subjects in the T- or T+ conditions (according to power tables in Cohen, 1988). Despite this high power level, the difference was not significant in the T+ condition (it was significant in the T- condition), as we report. Also, the comparison between cross-mode primed and unprimed conditions was significant in our control group of subjects, and we had a 50% chance of obtaining an effect the size of that obtained in our control group (or larger) when testing with 16 subjects in the T- or T+ conditions (again, according to power tables in Cohen, 1988). Despite this high power level, the difference was not significant in the T+ condition (it was significant in the T- condition), as we report. For these reasons, we conclude that we provided sufficient power to test those differences, and it is safe to accept the null hypothesis of no differences in those comparisons.

⁴ Although completion rates for different-lettercase primed stems were numerically greater than completion rates for cross-mode primed stems, this difference was not significant. Therefore, strong evidence for abstract-visual priming was not obtained in this experiment. It is possible that this was due to the use of stems that were composed of letters with visually dissimilar lowercase and uppercase structures (e.g., a and A), which may have operated against finding a very strong abstract-visual priming effect.

⁵ It may be important to note why priming scores (i.e., difference scores) are necessary for comparing priming effects per se across treatment conditions. Although cross-mode primed completion rates were 35% and 39% in the T- and T+ conditions, respectively (see Figure 3), amodal priming effects (cross-mode primed minus unprimed performance) were 22% and 9% in the T- and T+ conditions, respectively (see Figure 4). Direct comparisons of individual means are not informative for testing different kinds of priming effects per se. On a related point, although the difference in unprimed completion rates between T- and T+ conditions (at least in part) presumably reflects noise of measurement, systematic differences may also be partly responsible for that difference. For example, decreased tryptophan may lead to a decreased ability to visually perceive the briefly presented stems, which could decrease unprimed completion rates. This possibility highlights why it is important to measure unprimed performance as a baseline against which to measure amodal priming per se.

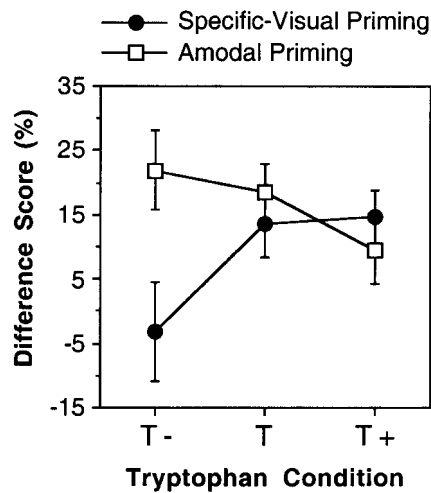


Figure 4. Results from the analysis of difference scores from control and experimental groups. Specific-visual priming difference scores were computed by subtracting the percentage correct in the different-lettercase primed condition from the percentage correct in the same-lettercase primed condition for each subject. Amodal priming difference scores were computed by subtracting the percentage correct in the unprimed condition from the percentage correct in the cross-mode primed condition for each subject. Difference scores are displayed as a function of tryptophan condition. Data for the tryptophan nonmanipulated (T) level are from the control subjects. Data for the tryptophan depletion (T-) and tryptophan augmentation (T+) levels are from the experimental subjects. Error bars indicate standard errors of the mean.

tryptophan depletion. In contrast, specific-visual priming, but not amodal priming, was observed under conditions of tryptophan augmentation. Thus, the results from this study support two major conclusions. First, 5-HT appears to play an important role in priming, a new result that warrants further investigation. Second, and more specifically, the direction of 5-HT manipulation appears to influence priming; 5-HT may help to modulate the types of priming observed, such that low levels of 5-HT decrease specific-visual priming and high levels decrease amodal priming effects.

The modulatory effects of 5-HT on information flow within neural systems have been described by several researchers (Buhot, 1997; Coull et al., 1995; Spoont, 1992). In general, the role of 5-HT is hypothesized to be one of neural and behavioral constraint. That is, increased 5-HT may constrain the flow of information within a given system to maintain task-appropriate signal-to-noise ratios within that system. In line with this hypothesis, previous evidence indicates that 5-HT agonists selectively reduce attentional distractibility, via modulation of the visual signal, especially when distractions are weak (e.g., Boulenguez, Foreman, Chauveau, Segu, & Buhot, 1995). Specific-visual priming requires encoding of visual details in the extrastriate visual cortex, which may be enhanced by effective attentional allocation or selectivity in the visual cortex. Furthermore, specific-visual priming occurs in the relatively early occipital-temporal cortex (Buckner et al., 1995; Schacter et al., 1996; Squire et al., 1992), in which 5-HT innervation is especially dense—even

more so than in the later visual cortex (e.g., Morrison & Foote, 1986; Varnäs et al., 2001). Therefore, when 5-HT levels are normal or high, attentional selectivity in the early visual cortex may be sufficient to produce specific-visual priming.

In addition, greater attentional selectivity in the early visual cortex may lead to less opportunity for amodal priming, which is supported by different, more anterior, neural regions (Badgaiyan et al., 1999; Blaxton et al., 1996; Schacter et al., 1999). For example, during trials in which stem completion occurs in early stages of processing in the visual cortex, no opportunity exists for the completions to take place in efferent subsystems downstream. Therefore, the higher the 5-HT levels in the early visual cortex, the lesser the opportunity for priming in later stages. In contrast, when 5-HT levels are low, there is a greater opportunity for priming to be tapped in any subsequent (to visual) processing subsystems, especially postvisual subsystems of the sort that must support cross-modal priming. Thus, 5-HT levels may modulate repetition priming by helping to modulate which subsystems underlie the priming effects.

As noted earlier, evidence from tryptophan depletion studies (e.g., Park et al., 1994; Riedel et al., 1999; Schmitt et al., 2000) and studies testing Alzheimer's (Ergis, van der Linden, & Deweer, 1995; Fennema-Notestine, Butters, Heindel, & Salmon, 1994; Nakamura, Nakanishi, Hamonaka, Nakaaki, & Yoshida, 2000) and Korsakoff's patients (Graf et al., 1985; Schacter, Cooper, & Treadwell, 1993) suggest that decreased levels of 5-HT produce decrements in explicit memory. In the present studies, we observed decrements in implicit memory for one sort of priming (specific-visual priming) but not for another sort (amodal priming) after tryptophan depletion. Moreover, after tryptophan augmentation, we observed decrements in amodal priming but not in specific-visual priming. This difference between the present results (in implicit memory) and previous results (in explicit memory) may reflect actual differences in the manner in which 5-HT influences implicit compared with explicit memory. Alternatively, it is possible that previous studies examining explicit memory revealed decreases in memory with depleted 5-HT levels because those studies only examined memory for test stimuli that were identical to encoded stimuli (and not memory for cross-mode items). Of course, research that directly compares implicit and explicit memory is needed to investigate this possibility properly. However, the issue highlights the importance of including multiple memory-type conditions (e.g., including cross-mode memory) in addition to identical stimulus conditions (e.g., same-lettercase memory), as in the present research. In both the T- and T+ conditions, stem-completion performance was greater for same-lettercase primed stems (identical stimulus) than for unprimed stems. Thus, if only these two conditions had been included, we would not have detected the interesting differences in specific-visual and amodal priming across tryptophan level and would have concluded that 5-HT level does not affect implicit memory.

Furthermore, the inclusion of the tryptophan augmentation condition, in addition to the tryptophan depletion condition, was an uncommon strength of the present study. Most studies examining the effects of tryptophan on mem-

ory have focused primarily on tryptophan depletion rather than tryptophan augmentation (for a review, see Reilly, McTavish, & Young, 1997). In the present study, we observed a decrease in amodal priming in the tryptophan augmentation condition, compared with the tryptophan depletion and tryptophan nonmanipulated conditions. Because amodal priming in the tryptophan depletion and tryptophan nonmanipulated conditions did not differ, we would not have detected the effects of tryptophan on amodal priming had we not included the augmentation condition.

Finally, previous research indicates that task and stimulus demands affect which neural subsystems are evidenced in priming experiments (e.g., Burgund & Marsolek, 1997; Marsolek, 1999; Marsolek & Burgund, 2002; Marsolek & Hudson, 1999). It is unclear, however, what mechanisms play a role in causing one or another subsystem to be evidenced in a particular task or with a particular kind of stimulus presentation. An interesting possibility given the present results is that 5-HT plays a mechanistic role in determining whether specific-visual priming or amodal priming is exhibited and hence may help to control the expression of memory storage in different subsystems through neuromodulatory effects.

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