Dexamphetamine enhances explicit new word learning for novel objects

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Abstract
Past research suggests that dexamphetamine (Dex) can facilitate learning and memory in healthy individuals and after a neurological lesion. This study investigated the effects of Dex on the learning of names for new objects in young healthy adults (n = 37) within an explicit learning paradigm by using a double-blind, placebo-controlled between-subjects design. Participants received 10 mg Dex or a placebo each morning over five consecutive days before viewing 100 novel objects with non-word names plus matched fillers. Compared to the placebo, Dex enhanced both the rate of learning and the retention of the words 1 wk and 1 month later. The improved word learning correlated with baseline attention and memory scores for participants in the Dex group only. No correlations were observed between word-learning success and sustained attention, mood or cardiovascular arousal. It was concluded that the improved explicit word learning may have reflected dexamphetamine-induced changes in short-term memory and/or memory consolidation.

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Introduction
Converging evidence from animal and human paradigms shows that learning and memory can be modulated by pharmacological agents (Breitenstein et al., 2004; Izquierdo, 1994; Knecht et al., 2001; Kumari et al., 1997; Martinez et al., 1991; Riedel et al., 1995). Of these agents, dexamphetamine (Dex) has been found to enhance associative and list-based word learning in healthy individuals (Breitenstein et al., 2004; Soetens, et al., 1993, 1995), and linguistic and motor recovery after a cerebrovascular accident (Walker-Batson et al., 1995, 2001). To date, no studies have investigated the effects of Dex on the learning of names for new objects in healthy adults. Further, it has been recently proposed that new word learning may provide a model for word re-learning after neurological damage (Basso et al., 2001; Breitenstein and Knecht, 2002), providing additional motivation for this study.

One of the earliest studies to investigate the effects of Dex on word learning was conducted by Soetens et al. (1993) who found that Dex improved word list retention during a free recall task compared to a placebo for up to 3 d post-learning in a group of healthy males. A subsequent study found that Dex improved word list recognition up to 1 wk post-learning (Soetens et al., 1995). As Dex did not improve performance immediately after learning, Soetens et al. (1995) concluded that the drug acted by enhancing memory consolidation, rather than arousal or short-term memory processes. However, even though both study tasks required short-term memory, participants were required to learn lists of real words, which allowed the use of existing phonological representations of the words within long-term memory (Gathercole, 1999). Thus, the results may have reflected the effects of Dex on the activation of words in long-term memory, rather than short-term memory processes. New word learning may provide a means of circumventing this issue, as during new word learning, there is no existing phonological representation of the word. Instead, the learner is required to hold the new word form temporarily in short-term memory until a more permanent representation is established in long-term...
memory (Baddeley et al., 1988, 1998; Gupta and MacWhinney, 1997; Martin and Gupta, 2004; Service and Craik, 1993).

Indeed, Breitenstein et al. (2004) demonstrated that the facilitatory effects of Dex can extend to new word learning. Participants received Dex (0.25 mg/kg) or a placebo before learning new names for familiar objects over five consecutive days. The new names were learnt by implicit associative learning mechanisms, a process that involved subconsciously comparing the relative occurrences of ‘correct’ and ‘incorrect’ picture-to-new word pairings. At the end of the fifth training session, participants were required to translate the words into their native language (German). The Dex group showed enhanced new word learning compared to the placebo group, with the difference maintained 1 wk and 1 month later.

Unlike most word learning studies, Breitenstein et al. (2004) investigated new word learning within an implicit associative learning paradigm. Broadly defined, implicit learning involves the acquisition of information without conscious awareness, while explicit learning involves the conscious acquisition of information (Church and Schacter, 1994; Cohen et al., 1997; Squire et al., 1993; Ullman, 2004; Zacks et al., 2000). Thus far, the role of each memory system in lexical learning remains contentious. The study by Breitenstein et al. (2004) involved implicit learning, however, the words were retrieved in an explicit memory-based task, which suggested that participants may have had some explicit knowledge about the words. Consequently, Breitenstein et al. (2004) suggested that both the explicit and implicit memory systems may be involved in word learning. In contrast, Ullman (2004) proposed that lexical learning may be linked exclusively to the explicit (declarative) memory system. Therefore, given our current level of knowledge about memory systems, it is unknown whether the effects of Dex on new word learning observed by Breitenstein et al. (2004) are exclusive to implicit word learning or extend to other types of learning. As the study by Breitenstein et al. (2004) involved learning new names for familiar objects, similar results may not be observed when learning names for unfamiliar objects, given evidence from bilingual speakers (e.g. Kroll and Stewart, 1994).

In summary, previous research has found that Dex can facilitate word learning in list-based and implicit associative learning contexts. However, the effect of Dex on the learning of names for unfamiliar objects within an explicit learning paradigm remains unknown. Additionally, no research has examined the effects of Dex on new word learning with semantic information. It might be expected that providing semantic information in conjunction with a phonological form would facilitate word learning compared to when only a phonological form is provided, given that deeper processing of information has been found to improve learning (Craik and Tulving, 1975; Maestu et al., 2003). As a consequence, the aims of the present study were to (a) determine whether the effects of Dex on word learning extend to explicit new word learning, and (b) examine whether Dex boosts new word learning in the presence of additional semantic information. By including mood, cognitive, and cardiovascular assessments, we were able to investigate whether learning was related to mood or other cognitive functions, or cardiovascular arousal. Overall, it was predicted that Dex would improve both the rate of new word learning and the retention of the new words. In addition, it was predicted that the inclusion of extra semantic information would further improve new word learning, compared to when only a phonological form was provided. Finally, it was predicted that new word learning would be related to baseline learning and memory skills, and changes in mood and cardiovascular arousal, reflecting dopaminergic or adrenergic mechanisms (Breitenstein et al., 2004; Knecht et al., 2001).

Methods

Participants

The participants were 37 right-handed native English-speaking adults (11 males, 26 females) aged between 18 and 34 yr. Participants were randomly assigned to the Dex (M 5, F 14) or placebo (M 6, F 12) groups in a between-subjects, double-blind design (see Table 1 for the demographic characteristics of each group). There were no significant differences between the Dex and placebo groups in terms of age, body weight, cigarette consumption, or baseline neuropsychological scores (all \( p > 0.10 \)) (see Table 1 for a summary of the pre-test neuropsychological scores). Participants possessed hearing and visual abilities (with or without corrective devices) within normal limits. All participants completed a medical review with a doctor, including an electrocardiogram, prior to participation in the study. Exclusion criteria included pregnancy or any psychiatric, neurological, cardiac, metabolic, degenerative condition, or motor disorders or diseases. Any individuals with a history of substance abuse (any substance), as determined by a government registry of individuals with a known history of substance abuse, were excluded.
Participants were requested to abstain from alcohol, caffeine, and food for at least 6 h before each session. Written informed consent for participation in the study was obtained from each participant. All participants received monetary reimbursement for participation. In order to encourage participants to attend to the task, there was an additional monetary bonus for the participant with the highest accuracy score at the end of the five learning sessions.

**Stimuli**

The same stimulus items were viewed by participants in the Dex and placebo groups. Each of the stimulus items consisted of a black-and-white line drawing of an object and a randomly assigned non-word name (e.g. barve, dreint, peam) with/without a fictitious description of the object’s function (e.g. a tool used for digging trenches) written below. The stimulus items consisted of a combination of critical and filler items.

In total, participants viewed 240 stimulus items during the sessions. There were 50 critical items with a drawing of an unfamiliar object, a non-word name and a description of the object’s function, and 50 critical items with a drawing of an unfamiliar object, a non-word name but no description of the object’s function. There were 10 matched fillers for each of the two types of unfamiliar critical items. There were 120 additional items consisting of drawings of familiar objects paired with non-words for a companion study.

The drawings of the unfamiliar objects had been used in an earlier experiment by Laine et al. (2003) and were used with permission from the author. The non-word names for all items were obtained from the Australian Research Council (ARC) non-word naming database (Rastle et al., 2002), and consisted of combinations of consonants and vowels that adhered to the rules of written English. Homophones and words that closely resembled real words in English were excluded. In addition, only non-words that had...
a one-to-one phoneme–grapheme correspondence were selected. The length of the non-words ranged from four to six letters.

Experimental design

The study was conducted in accordance with the Declaration of Helsinki. Ethical clearance was obtained from the University of Queensland Medical Research Ethics Committee. The study was divided into one pre-test session, five learning sessions, and two post-test sessions. Participants did not receive a tablet during the pre-test or post-test sessions. During the pre-test session, participants completed a series of formal and informal tests designed to assess learning, attention, memory (immediate, delayed, visuospatial, auditory, numeric, and linguistic), word suppression, reading, vocabulary, and executive function (Burgess and Shallice, 1997; Cambridge Cognition, 2004; Nelson and Willison, 1991; Randolph, 1998; Reynolds and Bigler, 1994; Wagner et al., 1999; Woodcock, 1998) (see Table 1 for a summary of the tests and results). During the learning sessions, participants attended five 3–3.5 h learning sessions over five consecutive mornings. Each learning session consisted of a tablet ingestion phase, a waiting phase, an initial learning phase, and then a short test phase.

At the start of each learning session, the participants were given either two 5 mg Dex tablets or two placebo tablets. There was a 2-2.5 h wait between tablet ingestion and commencement of the learning tasks each session. This time-period was selected so that optimal Dex plasma levels were reached during the learning tasks (Angrist et al., 1987; Asghar et al., 2003).

During the learning phase, each object was seen with its corresponding non-word name once for 5 s. The order of the items was randomized. A break was provided after each block of 60 items. Participants were not required to respond to the stimuli when viewing them at the start of each learning session. At the end of each learning session, participants completed recall and recognition tasks, which are described below. The post-test sessions involved recall and recognition tasks and were conducted 1 wk and 1 month after participants had completed the learning sessions. E-prime software (Psychology Software Tools, Pittsburgh, PA, USA) was used for all of the learning tasks.

Recall task

During the recall task, participants viewed each of the 120 pictures of the critical unfamiliar items one-by-one on the computer screen without non-word names or descriptions. The objects were presented in random order, with the order of the items differing between each session. Participants were instructed to type the non-word name of each object. For a response to be recorded as correct, participants had to type all of the letters of the non-word name in the correct order.

Recognition tasks

After completing the recall task each session, participants then completed two recognition tasks: a name recognition task and a description recognition task. The order of the two recognition tasks was randomized each session.

Name recognition task

During the name recognition task, participants saw the 120 critical unfamiliar objects with a single non-word written below. The non-word was either the ‘correct’ non-word name of the object or an ‘incorrect’ non-word name. The ‘incorrect’ names consisted of (a) non-words that differed from the ‘correct’ names by 2–3 letters, (b) the names of other objects seen during the session, or (c) non-words that had not been seen by the participants previously. The correct/incorrect pairings of the non-words and objects were randomized in order to reduce expectancy effects, however, half of the object/non-word pairings were correct each session.

Participants were required to indicate whether the non-word was the ‘correct’ or ‘incorrect’ name of the object by pressing either a ‘yes’ or ‘no’ button on a SRB200 response box (Psychology Software Tools). Participants were encouraged to respond to the stimuli as quickly as possible. The accuracy (correct/incorrect) and response latency (in milliseconds) of participants’ responses were automatically recorded by E-prime.

Description recognition task

The description recognition task was included so that participants would attend to the descriptions of the items’ functions. The task was only conducted with the 50 items that included descriptions of the objects’ functions. The description recognition task was the same as the name recognition task described above, however participants were required to indicate which description matched an item rather than a non-word name. Data from the task was not included in the analyses.

Physiological measures

To provide an indication of the effects of Dex on physiological functioning, each participant’s blood
pressure (diastolic and systolic) and heart rate were measured at the start of each learning session before tablet ingestion and then at half-hourly intervals throughout the session.

Rapid Visual Information Processing (RVIP) task

To examine the effects of Dex on sustained attention, participants completed a computerized RVIP task during the middle learning session. The task was based on similar experiments used by researchers to investigate the effects of pharmacological agents on information processing (Wesnes and Warburton, 1983, 1984). During the RVIP task, participants viewed a series of digits (1–9) presented one-by-one at a rate of 100 digits per minute for a total of 10 min. The digits appeared in black font against a white background and were pseudo-randomized so the same digit never appeared successively. Participants were instructed to press a response button as soon as they saw three consecutive even or odd digits in a row. The time limit for responding to an item was 1500 ms. The number of correct responses, misses, and false alarms, and response times were automatically recorded.

Mood rating scales

To measure the effects of Dex on mood, participants completed the Mood Rating Scale (Bond and Lader, 1974) twice during each learning session: once immediately before tablet ingestion and then 2 h after tablet ingestion. The timing of the second measure was selected to correspond with peak plasma Dex levels, as identified in previous studies (Angrist et al., 1987; Asghar et al., 2003; Mattay et al., 2000). The Mood Rating Scale consists of a 16-item visual analogue scale designed to measure drug effects. Each scale represented a continuum between positive and negative feelings (e.g. alert–drowsy, troubled–tranquil).

Data analysis

Analyses were conducted with the independent variable ‘group’ (dexamphetamine, placebo) and the dependent variables ‘accuracy’ (for the recall and recognition tasks) and ‘response time’ (for the recognition tasks only). In order to equalize variance, an arc sine transformation was applied to data that involved proportions (i.e. the accuracy data from the recall and recognition tasks). A log transformation was applied to the mood rating scale data to reduce skewness.

Data from the learning sessions were analysed using a series of repeated-measures ANOVAs with ‘session’ (1–5) and ‘description’ (description, no description) as within-subjects factors, and ‘group’ (dexamphetamine, placebo) as a between-subjects factor. For the data pertaining to blood pressure and heart rate, ‘time’ (baseline, 2 h post-tablet ingestion) was added as an additional within-subjects factor. The difference in self-reported feelings between baseline and 2 h post-tablet ingestion each session, as measured by the mood rating scales, was analysed using linear mixed models with ‘group’ (dexamphetamine, placebo), ‘subject’, and ‘session’ (1–5) as factors. Data from the 1 wk and 1 month post-tests were analysed using independent-samples t-tests.

Spearman’s correlation coefficients were used to analyse the effect of different variables (e.g. mood, baseline neuropsychological characteristics, and changes in blood pressure and heart rate) on training success and changes in response latency over the five learning sessions. As in Breitenstein et al. (2004), training success was measured by calculating the difference in accuracy scores between sessions 1 and 5 on the recall and recognition tasks. In order to minimize the risk of Type I errors due to multiple comparisons, an α-level of 0.01 was employed for analyses involving correlations. An α-level of 0.05 was employed for all other analyses.

Preliminary analyses indicated that there were no significant correlations between body weight and training success or response time, or between gender and training success or response time (all p > 0.10). As a consequence, body weight and gender were not included as factors in subsequent analyses.

Results

Learning data

Recall

Both groups improved in terms of accuracy on the recall task over the five learning sessions [main effect – session, linear trend: F(4, 32) = 60.559, p < 0.001)], however, the Dex group was consistently more accurate than the placebo group during each session [interaction – session × group: F(4, 32) = 6.858, p < 0.001] (see Figure 1). The difference in accuracy scores between the two groups was still apparent 1 wk and 1 month after the completion of the learning sessions, with the Dex group still performing significantly more accurately on the task than the placebo group [t(35) = 2.997, p = 0.005 and t(35) = 3.400, p = 0.002 respectively].

Participants responded more accurately to items that did not include a description of the object’s function compared to items that included a description
[main effect – description: $F(1, 35) = 19.048, p < 0.001$] (see Figure 2), but this pattern was not affected by drug. Participants’ recall of both sets of items increased each session, however, items without a description were recalled more accurately each session than items that included a description [interaction – session × description: $F(4, 32) = 2.755, p < 0.05$].

Correlations with pre-test neuropsychological measures

There were no significant correlations between training success on the recall task and any of the pre-test neuropsychological measures for either the Dex or placebo groups (all $p > 0.01$).

Name recognition

Accuracy

The accuracy of participants in both groups on the name recognition task improved over the five learning sessions [main effect – session, linear trend: $F(4, 32) = 80.505, p < 0.001$] (see Figure 3). However, the Dex group consistently performed more accurately during each session than the placebo group [interaction – session × group: $F(4, 32) = 7.424, p < 0.001$], with the difference remaining significant 1 wk and 1 month later [(35) = 4.109, $p < 0.001$ and (35) = 3.395, $p = 0.002$ respectively] (see Figure 3). Overall, participants performed more accurately on items that did not include a description of the object’s function [main effect – description: $F(1, 35) = 5.436, p = 0.026$]. Whilst participants’ accuracy scores increased each session, participants were consistently more accurate each session on items that did not include a description [interaction – session × description: $F(4, 32) = 3.005, p = 0.033$] (see Figure 4).

Correlations with pre-test neuropsychological measures

For the Dex group, there was a significant positive correlation between training success on the name recognition task and the RBANS attention index score.
psychological measures for the placebo group (all the name recognition task and the pre-test neuropsychological measures for the Dex group). There was no significant difference between the two groups (Final measurement – Dex group: mean = 104.00, S.D. = 2.48; placebo group: mean = 102.97, S.D. = 0.85) (p > 0.05).

There were no differences in diastolic blood pressure between the Dex or placebo groups at baseline (Dex group: mean = 68.78, S.D. = 2.50; placebo group: mean = 70.04, S.D. = 3.34) (p > 0.05). The change in diastolic blood pressure between the initial and final measurements each session did not differ significantly between the groups (Final measurement – Dex group: mean = 69.37, S.D. = 1.75; placebo group: mean = 68.79, S.D. = 2.25) (p > 0.05).

There was no difference in baseline heart rate (Dex group: mean = 72.04, S.D. = 3.36; placebo group: mean = 70.97, S.D. = 2.89) (p > 0.05), or in the change in heart rate between initial and final measurements each session (final measurement – Dex group: mean = 74.76, S.D. = 4.21; placebo group: mean = 70.97, S.D. = 2.89) (p > 0.05) for either the Dex or placebo groups.

RVIP task
There were no differences between the Dex or placebo groups on the RVIP task with respect to the proportion of correct positive hits, misses, false alarms, or the response latency of correct positive hits (all p > 0.10) (see Table 3). In addition, there were no significant correlations between the proportion of correct positive hits or response latency on the RVIP task and training success or response latency on the recall or recognition tasks for either group (all p > 0.01).

Mood rating scales
Four mood ratings were not available for four different participants (i.e., one record sheet for each of the four participants was unavailable on four separate days).

Table 2. Mean reaction times on the name recognition task in milliseconds

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean</th>
<th>S.D.</th>
<th>Mean</th>
<th>S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamphetamine</td>
<td>1720.28</td>
<td>458.89</td>
<td>1478.01</td>
<td>367.50</td>
</tr>
<tr>
<td>Placebo</td>
<td>1596.52</td>
<td>361.22</td>
<td>1294.97</td>
<td>287.17</td>
</tr>
<tr>
<td>1 month post-test</td>
<td>1258.68</td>
<td>265.71</td>
<td>1155.28</td>
<td>248.55</td>
</tr>
<tr>
<td>1 wk post-test</td>
<td>1313.86</td>
<td>336.01</td>
<td>1115.48</td>
<td>152.34</td>
</tr>
<tr>
<td>5</td>
<td>1275.81</td>
<td>229.61</td>
<td>1008.39</td>
<td>150.32</td>
</tr>
<tr>
<td>4</td>
<td>1281.37</td>
<td>300.26</td>
<td>1087.34</td>
<td>212.11</td>
</tr>
<tr>
<td>3</td>
<td>1525.19</td>
<td>290.31</td>
<td>1183.65</td>
<td>238.73</td>
</tr>
<tr>
<td>2</td>
<td>1596.52</td>
<td>361.22</td>
<td>1294.97</td>
<td>287.17</td>
</tr>
<tr>
<td>1</td>
<td>1720.28</td>
<td>458.89</td>
<td>1478.01</td>
<td>367.50</td>
</tr>
</tbody>
</table>

(r = 0.652, p = 0.002, all other p > 0.01). There were no significant correlations between training success on the name recognition task and the pre-test neuropsychological measures for the placebo group (all p > 0.01).

Response time
Statistical analyses were conducted only on correct ‘yes’ responses. Participants responded increasingly faster on the name recognition task over the five learning sessions [main effect – session, linear trend: F(4, 32) = 36.014, p < 0.001], however, there was no significant difference between the two groups (p > 0.10) (see Table 2). At the 1 wk post-test, participants in the placebo group responded to the stimuli in the name recognition task significantly faster than the Dex group [(t(35) = 2.229, p < 0.05), although the difference was no longer significant at the 1 month post-test (p > 0.10). There was no significant difference between items that included a description of the object’s function and items without a description for participants in either group (p > 0.10).

Correlations with pre-test neuropsychological measures
For the Dex group, the change in response times between session 1 and 5 was negatively correlated with the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) immediate memory index score (r = -0.583, p = 0.009) and RBANS delayed memory index score (r = -0.598, p = 0.007, all other p > 0.01). In contrast, there were no significant correlations between the change in response times between sessions 1 and 5 and the pre-test neuropsychological measures for the placebo group (all p > 0.01).

Physiological measures
Systolic blood pressure
Baseline measurements indicated that there were no differences in systolic blood pressure between the Dex or placebo groups (Dex group: mean = 102.41, S.D. = 1.93; placebo group: mean = 103.37, S.D. = 2.32) (p > 0.05). The change in systolic blood pressure between the initial and final measurements each session did not differ significantly between the groups (final measurement – Dex group: mean = 104.00, S.D. = 2.48; placebo group: mean = 102.97, S.D. = 0.85) (p > 0.05).

Diastolic blood pressure
There were no differences in diastolic blood pressure between the Dex or placebo groups at baseline (Dex group: mean = 68.78, S.D. = 2.50; placebo group: mean = 70.04, S.D. = 3.34) (p > 0.05). The change in diastolic blood pressure between the initial and final measurements each session did not differ significantly between the groups (final measurement – Dex group: mean = 69.37, S.D. = 1.75; placebo group: mean = 68.79, S.D. = 2.25) (p > 0.05).

Heart rate
There was no difference in baseline heart rate (Dex group: mean = 72.04, S.D. = 3.36; placebo group: mean = 70.97, S.D. = 2.89) (p > 0.05), or in the change in heart rate between initial and final measurements each session (final measurement – Dex group: mean = 74.76, S.D. = 4.21; placebo group: mean = 70.97, S.D. = 2.89) (p > 0.05) for either the Dex or placebo groups.

RVIP task
There were no differences between the Dex or placebo groups on the RVIP task with respect to the proportion of correct positive hits, misses, false alarms, or the response latency of correct positive hits (all p > 0.10) (see Table 3). In addition, there were no significant correlations between the proportion of correct positive hits or response latency on the RVIP task and training success or response latency on the recall or recognition tasks for either group (all p > 0.01).

Mood rating scales
Four mood ratings were not available for four different participants (i.e., one record sheet for each of the four participants was unavailable on four separate days).
Table 3. Mean proportion of positive hits and reaction times in milliseconds on the rapid visual information processing task

<table>
<thead>
<tr>
<th>Measure</th>
<th>Group</th>
<th></th>
<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Dexamphetamine</td>
<td>Placebo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>Mean</td>
<td>S.D.</td>
<td>Mean</td>
<td>S.D.</td>
<td></td>
</tr>
<tr>
<td>Proportion of correct positive hits</td>
<td>0.46</td>
<td>0.15</td>
<td>0.48</td>
<td>0.12</td>
<td></td>
</tr>
<tr>
<td>Mean reaction time (ms)</td>
<td>580.00</td>
<td>70.00</td>
<td>550.00</td>
<td>80.00</td>
<td></td>
</tr>
</tbody>
</table>

Alertness

There were no significant differences in subjective alertness levels between the Dex or placebo groups at the start of each learning session (Dex group: mean = 5.25, S.D. = 0.08; placebo group: mean = 5.59, S.D. = 0.05) (p > 0.10). The difference in alertness between participants in the two groups between baseline and 2 h post-tablet ingestion was marginal, with participants in the Dex group feeling more alert than participants in the placebo group (Dex group: mean = 4.95, S.D. = 0.07; placebo group: mean = 5.49, S.D. = 0.03) [main effect: group, F(1, 30.391) = 3.831, p = 0.06]. There were no correlations between the change in alertness each session and training success or response time on the recall or recognition tasks for the Dex group (all p > 0.01).

Contentedness

The Dex and placebo groups did not differ in terms of subjective contentedness at baseline (Dex group: mean = 4.51, S.D. = 0.10; placebo group: mean = 4.76, S.D. = 0.02) or 2 h after tablet ingestion (Dex group: mean = 4.43, S.D. = 0.07; placebo group: mean = 4.74, S.D. = 0.06) (all p > 0.10).

Calmness

There were no differences in subjective calmness between the Dex or placebo groups at the start of each learning session (Dex group: mean = 3.56, S.D. = 0.08; placebo group: mean = 3.89, S.D. = 0.07) (p > 0.10). However, the difference in calmness levels between baseline and 2 h post-tablet ingestion differed between the groups. Participants in the Dex group reported reduced feelings of calmness (i.e. participants felt more tense and excited) ~2 h after drug ingestion compared to participants in the placebo group (Dex group: mean = 3.76, S.D. = 0.15; placebo group: mean = 3.90, S.D. = 0.10) [main effect: group, F(1, 17.607) = 7.340, p < 0.05]. However, the change in calmness each session for the Dex group did not correlate with training success or response times on the recall or recognition tasks (all p > 0.01). There was a significant difference in the change in calmness levels from baseline to 2 h later between the sessions [main effect: session, F(4, 132.610) = 4.769, p < 0.05], with paired-samples t tests indicating that there was less of a change in participants’ calmness levels from baseline to 2 h later during session 2 compared to session 1 [t(33) = 2.396, p < 0.05, for all other paired-samples t tests p > 0.05].

Discussion

The present study found that within an explicit learning paradigm, Dex significantly improved (a) the rate of word learning, and (b) the retention of the newly learnt words at follow-up. Irrespective of drug group, the inclusion of additional semantic information hindered new word learning. Baseline attention and memory skills were correlated with name recognition accuracy and response time for participants in the Dex group only. In contrast with Breitenstein et al. (2004), changes in subjective mood ratings did not correlate with new word learning success. The following discussion will centre on the mechanisms underlying the effects of Dex on new word learning observed in the present study.

Implicit learning mechanisms

As discussed previously, Breitenstein et al. (2004) found that Dex enhanced new word learning within an implicit associative learning paradigm. In contrast, the present study found that Dex improved new word learning within an explicit learning paradigm. Consequently, the results of the present study suggest that the facilitatory effects of Dex on new word learning are not solely due to implicit learning mechanisms.

Short-term memory and attention

Attention and memory, especially working memory (a subcomponent of short-term memory linked to the prefrontal cortex), are closely related to linguistic learning (Arnsten, 1998; Baddeley et al., 1998; Cornelissen et al., 2004; Duyck et al., 2003; Gupta, 1996; Gupta et al., 2004; Gupta and MacWhinney, 1997; Martin and Freedman, 2001; Schuchert, 2004; Service and Craik, 1993). In the present study, performance on the name recognition task correlated...
significantly (in a positive direction) with baseline attention levels for the Dex group only. Baseline attention levels in the present study were measured according to the R-BANS attention index (Randolph, 1998), a measure comprising of digit span and coding tasks, which are designed to measure short-term memory. Martin and Gupta (2004) argued that digit recall and lexical learning are closely related and that both are reliant on short-term memory. The results of the present study suggest that Dex further enhanced task performance in individuals who already had higher baseline short-term memory capacity. Interestingly, higher levels of dopamine have been associated with higher performance on learning and memory tests (Arnsten, 1998; Diamond et al., 2004; Knecht et al., 2004). Further, Knecht et al. (2004) found that there was a linear relationship between levodopa (a precursor of dopamine) and implicit associative word learning, with higher doses being linked to improved word learning. Thus, one possible explanation for the present data is that Dex acted through dopaminergic mechanisms by enhancing short-term memory, a cognitive skill that was critical for task success. It should be noted that the effects of dopamine have also been found to have an inverted U curve relationship with prefrontal working memory, with too little or too much dopamine leading to impaired functioning (Arnsten, 1998; Mattay et al., 2000); however, for the memory tests used in the present study this effect was not apparent.

Contrary to the findings of previous studies (Fillmore et al., 2005; Fleming et al., 1995; Rapoport et al., 1980), in the present study, there was no difference between the Dex or placebo groups in terms of accuracy or response times on the RVIP task, a measure of sustained attention. This finding suggested that the effect of Dex on learning was not secondary to any effects on sustained attention. However, the lack of difference between the groups on the task may have been due to the small dose (10 mg) of dexamphetamine. The dose may have been insufficient to make a significant difference, given the substantial cognitive demands of the RVIP task. The difference in cognitive demands between the new word learning and RVIP tasks may also explain why Dex improved new word learning, but not RVIP task performance.

**Long-term memory, long-term potentiation, and memory consolidation**

Both the present study and the study by Breitenstein et al. (2004) found that Dex improved retention of the newly learnt words when tested off drug several days after the learning sessions ceased. Similarly, research by Soetens and colleagues (Soetens et al., 1993, 1995) found that Dex enhanced word list recall and recognition up to 1 wk after initial learning. Soetens et al. (1993) suggested that Dex acted by selectively enhancing the memory storage process (i.e. memory consolidation), rather than memory encoding. Animal studies have found that Dex can enhance memory consolidation (Carr and White, 1984; Martinez et al., 1980), with the improved memory retention being linked to dexamphetamine-induced effects on dopaminergic function (Carr and White, 1984). Furthermore, both Jones (2004) and Knecht et al. (2004) suggested that dopamine is involved in long-term potentiation associated with memory consolidation. Although the mechanisms underlying long-term memory remain contentious, dexamphetamine-induced neurophysiological changes may have contributed to enhanced new word learning and retention in the present study.

**Mood**

Recent research into the effects of emotion on memory has produced equivocal results (Arntz et al., 2005; Fenker et al., 2005). During the present study, Dex increased subjective levels of alertness and tenseness/excitability, however, the changes did not correlate with new word learning success. This finding contrasts with Breitenstein et al. (2004) who found that new word learning success was correlated with dexamphetamine-induced changes in positive feelings. One possible explanation for this difference is the use of two different learning methods (i.e. explicit vs. implicit associative learning), suggesting that explicit new word learning may be more reliant on mood-based mechanisms (but see Knecht et al., 2004) and that increased positive emotions do not drive improved new word learning under explicit learning conditions.

**Cardiovascular arousal**

Previous studies have found that Dex can increase blood pressure and heart rate, albeit not always significantly (Asghar et al., 2003; Brauer et al., 1996; Breitenstein et al., 2004; de Wit et al., 2002; Mattay et al., 2000). At a neurophysiological level, noradrenaline, a neurotransmitter that increases after Dex ingestion (de Wit et al., 2002; Kuczenski and Segal, 1997; Martinsson and Eksborg, 2004), has been implicated in the modulation of cardiovascular arousal (Arnsten, 1998; Brauer et al., 1996; Breitenstein et al., 2004; Knecht et al., 2004; Kuczenski and Segal, 1997;
Soetens et al., 1995). However, changes in motor/cardiovascular arousal have been found to be un-correlated with the effects of Dex on word learning (Breitenstein et al., 2004; Cooper et al., 2003). The present study supported these findings, as during the learning sessions, the Dex and placebo groups did not differ on measures of cardiovascular arousal, despite differences in the success of new word learning. The finding that Dex did not modulate explicit new word learning through cardiovascular mechanisms suggests that noradrenergic mechanisms were not chiefly responsible.

Effects of semantic information on new word learning

The inclusion of additional semantic information through descriptions of the objects’ functions did not facilitate new name learning in the present study. This finding resembles that of Gronholm and colleagues (2005) who used some of the same stimuli as the present study. Unlike Gronholm et al. (2005), the present study included tasks designed specifically to encourage participants to attend to both the phonological form and the semantic information, however, this did not result in superior learning for items with additional semantic material. The most straightforward explanation for the poorer performance in new word learning with vs. without a description in the present study is that the participants did not have sufficient time to read and subsequently learn the name and description for each item compared to the name alone. Participants may have found the semantic information easier to learn, and thus concentrated on learning the descriptions at the expense of the names. Dex did not appear to influence this process.

As a final note, it must be mentioned that during the present study all participants in the Dex group received a 10 mg dose of the drug irrespective of body weight. Despite the use of this uniform dose, behavioural effects (i.e. improved word learning) were observed with the drug and statistical analyses indicated that body weight did not influence drug outcomes.

Conclusion

In conclusion, the results of the present study show that Dex facilitates new word learning in an explicit learning paradigm. This finding is important for the development of relevant models of language rehabilitation and pharmaotherapy using healthy word learning, as explicit learning more closely resembles the type of relearning utilized during naming therapy in aphasia than implicit associative learning, which involves the repeated introduction of erroneous word forms. This study further elucidates the role of Dex in word learning by demonstrating enhanced learning and development of word-object mappings when competing pre-existing names are not present. Importantly, the data suggest that the facilitatory effects of Dex may be due to improved short-term memory and/or long-term potentiation, rather than alterations in general attention, mood, or cardiovascular arousal. These findings have important implications for the future use of pharmacological agents in the treatment of naming and learning disorders.

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Statement of Interest

None.

References

Dexamphetamine and word learning


