Title: Successful short-term re-learning and generalization of concepts in semantic dementia.

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Abstract

Background: Patients with semantic dementia (SD) can rapidly and successfully re-learn word labels during cognitive intervention. This new learning, however, usually remains rigid and context-dependent. Conceptual enrichment (COEN) training is a therapy approach aimed to produce more flexible and generalizable learning in SD. In this study we compare generalisation and maintenance of learning after COEN with performance achieved using a classical naming therapy (NT). **Method:** The study recruited a 62-year-old woman with SD. An AB_1ACAB_2 experimental design was implemented, with naming performance assessed at baseline, post- intervention, 3 and 6 weeks after the end of each treatment phase. Three generalisation tasks were also assessed pre- and post-intervention. **Results:** Naming post-intervention improved significantly following both therapies, however, words trained using COEN therapy showed a significantly greater degree of generalisation that those trained under NT. In addition, only words trained with COEN continued to show significant improvements compared with baseline performance when assessed 6 weeks after practice ceased. **Conclusions:** Therapies based on conceptual enrichment of the semantic network facilitate relearning of words and enhance generalisation in patients with SD.

Keywords: semantic dementia, cognitive therapy, conceptual enrichment, generalization of learning.

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INTRODUCTION

Semantic dementia (SD) is a variant of Primary Progressive Aphasia characterised by a progressive deterioration of semantic memory, which affects both verbal and non-verbal conceptual knowledge. The impact on language results in impaired naming, single-word comprehension and conceptual knowledge, in the context of fluent speech, relatively preserved grammar and motor production (Gorno-Tempini et al., 2011). In the non-verbal domain, marked impairments may also be found in understanding objects, sounds and faces (Bozeat, Lambon Ralph, Patterson, Garrard, & Hodges, 2000; Garrard & Carroll, 2006; Hsieh, Hornberger, Piguet, & Hodges, 2011). Despite the significant impacts upon language and semantic knowledge, episodic memory and other cognitive functions remain spared over years. This unique cognitive profile is associated with bilateral anterior temporal lobe atrophy, particularly marked on the left (Davies et al., 2009).

While no medical treatments are currently available to treat SD, rehabilitation efforts have mostly focused on word retraining interventions, in an attempt to delay the progression of the disease and maintain patients' independence as long as possible (Dressel et al., 2010; Fratali, 2004, 2001; Graham, Patterson, Pratt, & Hodges, 1999; Green Heredia, Sage, Lambon Ralph, & Berthier, 2009; Henry, Beeson, Rapcsak, 2008; Jokel & Anderson, 2012; Jokel, Rochon, & Anderson, 2010; Jokel, Rochon, & Leonard, 2002, 2006; Mayberry, Sage, Ehsan, & Lambon Ralph, 2011; Savage, Ballard, Piguet, &Hodges, 2013; Senaha, Brucki, & Nitrini R, 2010; Snowden & Neary, 2002; Suarez-Gonzalez et al., 2014). Results suggest that patients with SD may benefit from these strategies and not only re-learn vocabulary but potentially maintain these gains over periods of 3 to 6 months after the end of the therapy (Green Heredia et al., 2009; Jokel, Rochon, & Leonard, 2010; Savage, Piguet & Hodges, 2014). However, despite these positive results, the generalisation of this learning appears limited. For items that the patient can no longer name or understand, the information relearned is often rigid and context-dependent, and when generalisation is achieved, this is usually modest (Green Heredia et al., 2009; Mayberry et al., 2011; Snowden & Neary, 2002). As a result, a patient trained to re-learn the label "banana" using an image of the whole banana may be unable to name this item when seeing it peeled and sliced, because a general

understanding of the object has not accompanied the learning. This is a major issue as the translation of rehabilitation outcomes into everyday life is a final clinical goal.

Generalisation at its most successful occurs when some conceptual knowledge of the treated items exists, indicating that the amount of remaining knowledge about an item plays an important role in the generalisation of newly acquired learning. Indeed, there is a growing body of evidence showing the importance of the integrity of semantic representations in successful vocabulary re-learning (Hoffman et al., 2015) and maintenance in SD (Jokel et al., 2010, 2006; Snowden & Neary, 2002). In a recent study we suggested an alternative approach to enhance generalisation for items that the patient can no longer name or recognise (Suarez-Gonzalez et al., 2014). This approach assumes that the rigidity of the new learning is proportional to the deterioration in links between the target item and the rest of the semantic network. By manipulating the encoding to promote greater links, it may be possible to achieve flexible learning and generalisation. The training goal of this conceptual enrichment therapy (COEN) is thus to restore concepts by boosting the semantic network of an item enough to make it functional again. The fundamental steps include:

1) Selection of an item which the patient can no longer name or recognise (target item),
2) placement of the item in a personally meaningful temporal and spatial context through the use of co-targets (drawing upon strengths in episodic memory to form associations),
3) improvement of the semantic connections of the target item by anchoring the new learning to well consolidated memories and inducing generalisation.

Results from a previous case study suggest that COEN therapy may be more useful than naming therapy (NT) when relearning items where meaning has been lost (Suarez Gonzalez et al., 2014). The current study aimed to replicate and extend upon these findings by examining differences between COEN and NT in naming, generalisation, and in the maintenance of learning in a further participant. We predicted that COEN therapy would outperform NT in all three generalisation tasks. In addition, because remaining semantic knowledge has been shown to facilitate items labels retention, we

also predicted that those items trained with COEN would show higher rates of maintenance over time than those trained with NT.

CASE REPORT

The participant, CC, was a 62-year-old right-handed, native Spanish speaker, who worked as freelance craftswoman painting and selling handmade fans. She completed 10 years of formal education. She was seen in the Memory Disorders Unit of the University Hospital Virgen del Rocio in 2012 where she presented with a 2-year history of word finding and comprehension difficulties. Common daily difficulties comprised poor understanding of films as a result of diminished vocabulary, limited culinary skills due to loss of knowledge for food (she stopped using many ingredients because she could no longer recognise them), increasing difficulties in recognising objects (e.g a pack of cards or a hammer) and frequent misunderstandings in conversations, with tip-of-the tongue phenomenon. Her children also noticed changes in CC's manners, in become more garrulous, over-reliant on using proverbs, and repetitive in her speech (e.g. "that was a long, long, long, long time ago", "not right now, now, now, now"). She was also observed to reply to questions using song choruses. Her relatives and friends described her as more disinhibited (e.g. dropping inappropriate comments in social situations) and more prone to obsession over minor issues. Otherwise daily function was described as normal. She continued to travel successfully for work and did not make mistakes with her finances or in the organisation of her business. Neurological examination was within normal limits and visual inspection of her magnetic resonance imaging brain scan revealed bilateral atrophy of the temporal pole greater on the left than the right, together with left hippocampus atrophy (see Figure 1). She was diagnosed with semantic dementia (SD) (Gorno-Tempini et al., 2011) with a moderate degree of semantic impairment (Pyramid & Palm Tree Test: 37/52 pictures, 40/52 written words). Results from her cognitive testing showed good verbal attention, repetition, executive and visuoperceptual function but poor verbal memory for words and semantic knowledge (additionally impacting naming and comprehension) (Table 1). CC was considered a suitable candidate to take part in this study given her overall preservation of cognitive function, good level of independence in daily life and absence of disruptive behaviour.

**** insert Figure 1 and Table 1 ****

METHOD

Research Design

A single case experimental design (AB_1 AC AB2) was implemented to investigate and compare two therapies (COEN and NT), with respect to naming and generalization of learning. Here, A refers to baseline, B_1 to the COEN therapy (using an initial list of words), C to a naming therapy (NT) that does not focus on boosting existing semantic links and B_2 to a repeated version of COEN therapy using a second list of words. For each of the treatment phases, B_1, C and B_2, a different but matched word list was trained. Treatment phases were interspersed with wash-out periods (A) of one month to avoid carryover effect. COEN therapy was introduced twice in order to rule out any impact of order effects of the therapies– either due to a facilitator effect of having conducted NT beforehand –(in the situation of B2) or due to fatigue or waning interest that may occur for later applied therapies (thereby artificially elevating the performance of NT). Each intervention involved a 1-hour session each day, over seven consecutive days, conducted under the supervision of a clinician at the Memory Disorders Unit.

Naming performance was assessed in each study phase. In the baseline and post-intervention periods, both trained and control items were tested, such that the patient served as her own control. Generalization was assessed after each study phase only for trained items.

Item selection and lists of words

Prior to baseline, a naming assessment was conducted to facilitate item selection for the matched sets of training and control lists. Stimuli from the Snodgrass and Vanderwart's (1980) databank and Boston naming test (Goodglass et al., 2000) were used for this purpose. 122 items that CC could no longer name nor recognize (that is, she was unable to produce any semantic information about them) were assigned to three sets (see Table 2).

Item sets were matched for word frequency using the BuscaPalabras database (Davis & Perea, 2005), with no significant differences across the three sets (total word frequency lists B_1, C and B_2, Kruskal-Wallis test - χ^2 (2) = 0.47, p = 0.82) or between therapy and control items.

**** insert Table 2 ****

COEN training materials

As described by Suárez-González et al. (2014), to construct COEN training slides, suitable images of co-targets have to be identified and displayed alongside the target item (see Supplementary Figure A for an example of the arrangement). Co-targets consist of pictures of objects or scenes semantically related to the target item that are familiar and well understood by the participant. The correct selection of items is important as the utility of the co-targets relies upon providing a familiar semantic framework on which to anchor the target concepts.

The clinician, CC, and a family member worked together to select the appropriate images for co-targets. CC was presented with as many potential co-targets as needed until she identified two which were meaningful. For example, to create the training slide for "sheep" we firstly selected a standard view of a sheep as a target item and placed the written label below. Based on this picture alone, CC was only able to recognize the sheep as "a little animal". As CC came from a farming family, we presented a picture of a sheep that was being sheared (to try to evoke meaningful memories), however, CC could not comprehend this picture. We presented a picture of wool but again CC failed to recognize this. We then asked CC's son to suggest pictures that may be meaningful. He suggested a photograph of a sheep being milked, as they used to produce homemade sheep's cheese when he was small. CC immediately recognized the meaning of this picture, and this was added as the first co-target. For the second co-target we followed the same procedure and after a number of attempts a picture of a herd of sheep in the countryside was selected (as CC could remember a protest conducted by shepherds against the central government involving the blocking of the main streets of Madrid with herds).

Two training slides were then created for each item. The first slide comprised only the target picture. The second slide included the same target picture, together with the written label and two co-targets. While not part of the training slides, the clinician also made a note of the connecting links between the target and co-targets in the form of a short description. This description was then used when introducing the materials to the participant during an induction session (see COEN training method below). This process was repeated for each of the 41 COEN items (21 in phase B1 and 20 in phase B2).

COEN training method

Induction session

Prior to commencing the training, a half hour induction was conducted with CC to explain the procedures of the therapy. CC was told that she was going to be shown a picture of an object, selected from those that she could no longer recognize or understand, and she would be asked to name it if she could. Whether she could name it or not, she would then move to the next slide, where she would see the target item now with the label below and with two co-targets. She was told that the co-targets in each of the slides were the same items that were discussed with her when constructing the materials. To confirm that she understood the link between the co-targets and the target item in each slide, she was shown each slide, one at a time and was verbally provided with the linking description as indicated in Appendix 1 and 2 (with no variations in these descriptions or extra verbal information given).

Procedure of the therapy:

The therapy was delivered via two simple steps:

- Step 1: the target picture was displayed on a slide and CC was asked to say the name, if she knew, but not to guess.
- Step 2: on the next slide, CC was presented with the same picture (target picture) together with its co-targets and corresponding written label below the target picture.

CC was told to read the word and look at the co-targets before moving on to the next item (see Supplementary Figure A).

Steps 1 and 2 were repeated for each item for up to one hour with a break of 5 minutes every 15 minutes (45 minutes of effective therapy and 10 minutes break in total). Therapy sets were organized into three different randomized orders of presentation, which were alternated during the session to avoid rote learning the order of the words. Thus after completing the first order of presentation (plus a break), the second order of presentation was used, and then the third.

The session was conducted with the therapist during one hour for seven days (first five consecutive, a gap of two days of no therapy and two more days). A full list of the items, co-targets and the induction descriptions are shown in the Appendix 1 and 2.

It was not part of the training procedure to repeat the description of the items; however, on a rare occasion during the first session of training, some descriptions were repeated on request, to help orient CC to the training slide.

Naming therapy (NT) training materials

To construct the NT training slides, the target picture and written label were assembled onto the slides – again with the first slide comprising only the target picture, and the second slide including both the target picture and the written label (see Supplementary Figure A for an example).

NT training method

Induction session

Similar to training with COEN, a half hour induction was provided for NT prior to training. CC was told that a target picture would firstly be displayed and she should try to say the name of the item, if known. She would then see the same picture on the next slide, accompanied by the written label below. She was told she should read the target word out aloud. In order to make both procedures (COEN and NT) comparable, CC was then shown each of the slides, one at a time, together with a brief verbal description of each item (individually tailored to CC's understanding, Appendix 3).

Procedure of the therapy:

The 20 therapy items allocated to the NT approach were trained with the "look and say" method (Dressel et al., 2010; Green Heredia et al., 2009; Jokel & Anderson 2012; Snowden & Neary, 2002, Suarez-Gonzalez et al., 2014). This involves two simple steps:

- Step 1: the target picture was displayed on a slide and CC was asked to say the name, if she knew, but not to guess.
- Step 2: on the next slide, CC was presented with the same picture with the written label below. CC was told to read the word before moving on to the next item (see Supplementary Figure A).

Steps 1 and 2 were repeated for up to one hour with a break of 5 minutes every 15 (45 minutes of effective therapy and 10 minutes break in total). Again, items were organized into three different randomized orders of presentation, which were alternated during the session to avoid rote learning the order of the words (e.g. 1st set, then 2nd set, then 3rd set).

The session was conducted with the therapist during one hour for seven days (first five consecutive, a gap of two days of no therapy and two more days). Again, it was not part of the training procedure to repeat the description of the items; however, if this was requested during the first session of training to aid orientation to the slide, this was permitted. In practice, this rarely, if ever occurred.

In summary, COEN and NT were matched for the number of steps involved in training and the total amount of therapy time. The key difference in procedure was that COEN therapy contained co-targets, otherwise training procedures were identical. To see a comparison of differences and similarities between both therapies see Supplementary Material 1 and Supplementary Figure A for an example of the training material for each therapy.

Assessment

Naming performance

To compare naming performance under NT and COEN, the three sets of items were tested at baseline (both therapy and control items), and immediate post-training (seven days later) using a fixed order of items that differed from the three orders used during

the training. Progress during the training phases was also monitored, with naming of trained items assessed at the end of every session (with items presented using a random order).

Generalisation

At baseline and then at the end of each treatment phase (B_1, C and B_2), generalisation of knowledge was assessed using three tasks:

1) Naming visually-dissimilar-pictures (dissimilar exemplars of trained items). CC was asked to correctly name visually dissimilar pictures of the trained items (COEN list 1 [21 items], NT [20 items] and COEN list2 [20 items]). The new exemplars were rated for typicality by three independent raters (where a score of '1' point was assigned for an atypical appearance of the trained item and zero for exemplars which were deemed typical of the trained item). Only items with full inter-rater agreement of atypicality were included in this generalization task and therefore presented to CC for naming.

2) Description-to-naming: CC was required to provide her own description of each item named by the examiner (mere recall of the induction description was not credited). For each list ($COEN_1$, NT and $COEN_2$) description of the corresponding training items was tested after completion of the phase. Responses were recorded and accuracy was assessed by two independent raters, with respect to meaningfulness of content and adequate dissimilarity from the description provided during induction. Only responses that were scored favorably by both raters were deemed correct (for a transcription of example responses see Supplementary Material 2);

3) Naming-to-description: In this task, CC was asked to provide the correct item name after listening to a verbal description, where references to visual attributes of the item are avoided as much as possible. For each list ($COEN_1$, NT and $COEN_2$) naming of the corresponding training items was tested after completion of the phase. Descriptions provided for sets 1 and 3 ($COEN_1$ and $COEN_2$) also aimed to avoid mention of the co-target items (see Supplementary Material Appendix List 1 and List 2).

Maintenance of performance

To compare performance over time, naming of therapy and control items from all three sets of words were also tested at 3 and 6 weeks following the end of B1 (COEN list 1) and C (NT) training phases. For B2 (COEN list 2), the final assessment occurred at 3 weeks post training, as the patient was not available for testing at 6 weeks. These assessments were conducted using a fixed order of items.

Statistical analysis

The McNemar's test for related samples was used to compare naming performance across time points (baseline, immediate post-training, and at three and six weeks post-intervention), and to compare pre- and post-intervention performances on generalization tasks. Chi-squared and Fisher exact tests were used to make comparisons across sets (i.e. across therapy approaches) and among the three generalization tasks.

RESULTS

Naming

Significant baseline to immediate post-training improvements in naming were observed for each of the training lists (all $p < 0.001$): $COEN_1$ (90%), $COEN_2$ (90%) and NT (80%). Performances on the control lists remained unchanged (all $p > .05$). Improvements in naming were similar across therapies, with no differences in naming performance found among the sets ($\chi^2(2) = 1.24$, $p = 0.53$). Changes observed during the therapy phase occurred quickly, with significant improvements observed at day 3 of COEN ($COEN_1$ McNemar test, $p = 0.002$ and $COEN_2$ $p = 0.031$) and at day 2 for NT (McNemar test, $p = 0.016$). See Supplementary Material Table-e.

Generalisation

At baseline, CC was unable to correctly answer any items on the three generalisation tasks (description-to-naming, naming-to-description and naming visually-dissimilar-pictures). After COEN, performance on all 3 generalisation tasks significantly improved (McNemar tests, all $p < .0001$) and to a similar extent (by approximately 60-70%). In

comparison, after NT, only naming of visually-dissimilar-pictures improved compared with baseline (45%, McNemar test p=.004). Significant differences were found across therapies in description-to-naming and naming-to-description but not in naming visually dissimilar pictures (see these results displayed in Figure 2).

**** insert Figure 2 ****

Maintenance

Naming performance at 3 weeks post-intervention, remained significantly above baseline for $COEN_1$ (McNemar test, $p = 0.002$), $COEN_2$ (McNemar test, $p = 0.004$) and NT (McNemar test, $p = 0.008$), indicating a significant level of retention. However, at 6 weeks post-intervention, naming performance dropped and only remained significantly above baseline for $COEN_1$ (McNemar test, $p = 0.031$), and not for NT (McNemar test, $p = 0.12$). There were, however, no significant differences in the direct comparison among therapy sets for each of the time points: naming at immediate post-treatment $\chi^2(2)= 1.24$, $p = 0.53$; naming at 3 weeks $\chi^2(2)= 0.64$, $p = 0.72$, or naming at 6 weeks post-intervention $\chi^2(1)= 0.40$, $p = 0.53$).). See Figure 3.

**** insert Figure 3 ****

DISCUSSION

In this study we have not only replicated previous results (Suarez-Gonzalez et al., 2014) in a new patient but have been able to directly test the COEN approach versus a standard naming therapy of the same therapy dose under controlled conditions, while taking into account the order of therapy (i.e. showing that COEN is superior whether it is administered before or after a standard naming therapy). We also extended previous findings by conducting a comparative follow-up assessment at 3 and 6 weeks post-intervention to look at short-term retention. As found in previous studies, fast and significant improvements in naming can occur in SD following word training. In agreement with our previous participant VC (Suarez-Gonzalez et al., 2014), CC correctly named a significantly higher number of items after both COEN and NT, with no differences in the level of improvement attained between the two approaches at

immediate post-intervention. Despite this similar initial improvement in naming, training based on conceptual enrichment of the semantic network (COEN) resulted in greater ability for CC to transfer her learning to other tasks (i.e. generalization of knowledge by both improving her ability to name items in a different context - in response to a verbal description of the item - and complete non-trained tasks, such as providing verbal descriptions of items). While declines in naming did occur once training ceased, encouragingly, CC could still correctly name a significantly higher number of words at 6 weeks compared with baseline for COEN, but not for NT. No significant differences, however, were found in the direct comparison of performance between therapies at 6 weeks.

A consistent finding across the previous and the current study was the equivalence of relearning found using both COEN and NT approaches. Regardless of method or order of therapy, CC's gains became significant within two to three days of training, in keeping with the rapid improvements in naming reported in other word retraining studies (Dressel et al., 2010; Graham et al., 2001; Henry et al., 2008; Jokel et al., 2006; Savage et al., 2013; Snowden and Neary, 2002). The current study, however, now provides evidence regarding the implications of the learning with respect to the application of knowledge and to maintenance over time. Consistent with our 2014 study, a greater degree of generalisation was demonstrated for those words trained under COEN than words trained using NT. Importantly, this was observed for both description-to-naming and naming-to-description tasks, where responses must draw from semantic knowledge, unaided by visual cues. Where pictures were provided, - naming visually dissimilar examples - no significant differences were found between the two approaches. This form of generalization, however, is limited and needs to be interpreted with caution. Improvements in naming pictures may be achieved by identifying overlapping visual attributes (even when using visually dissimilar exemplars) and do not necessarily reflect a change in conceptual knowledge, being less likely to translate into everyday communication – the ultimate goal of such an intervention.

In the COEN trained words, performances on each of the three generalization tasks were equally high (61-71% correct). This provides evidence that the concept of the item has been strengthened, as knowledge is demonstrated across a variety of tasks, involving

expressive and receptive language skills. This truer form of generalisation was not seen, however, for words trained under NT. By contrast, clear differences in performance across tasks occurred. While CC could now name approximately half of the items (45%), even when shown an alternative picture, the NT approach did not clearly assist CC in understanding the objects named (10%) or in being able to describe salient facts regarding the objects (25%). To explain the enhanced generalization effect under COEN compared with NT we would argue that use of co-targets, carefully selected from the participant's own episodic memories, used in combination with the target item facilitates and extends the item's semantic network by linking it with previous memories. For instance CC could no longer name or explain the use of a yoke. When displayed with co-targets of oxes wearing a yoke and pulling fair wagons in a very popular annual event in Andalusia, CC immediately recognized the scene and recalled: "I belong to a fraternity which owns one of this (pointing to the wagons and oxes) and I go inside to El Rocio. With many many other people, friends…every year...and I sing." The triggering of episodic memories thus provides additional contextual understanding and relevance to the person's life. This important interaction between episodic and semantic memory has been highlighted previously as a significant factor in recall and generalization of learning (Kumaran & McClelland, 2012). By contrast, therapy approaches which focus on a single aspect of semantic memory (e.g the definition of what is a yoke) may fail to encourage connections which link this learning with an individual's broader existing knowledge.

With regard to maintenance, naming performance of trained words remained significantly above baseline levels within the first month post-intervention, as reported in previous word retraining studies (Fratali et al., 2004; Graham et al., 2001; Snowden et al., 2002). Over the next few weeks, however, performances declined significantly such that at 6 weeks post-intervention, only words practiced using COEN remained above baseline levels. While variable rates of retention after the first month have been reported previously, in some studies, post-intervention performances have remained significantly above baseline 3-6 months later (Dressel et al., 2010; Jokel et al., 2006. Green Heredia et al., 2009; Jokel et al., 2010; Mayberry et al., 2011; Savage et al., 2015). Ongoing use, extension of the period of practice, remaining semantic knowledge and revision all play a major role in maximizing the retention of words in the medium to

longer term in SD. The current study involved a relatively short amount of practice - only seven days. Additional practice may have provided greater strengthening of the semantic network, to prevent decay in knowledge. In the case of CC, however, it was expected that her performance would show a level of decline post-intervention, given the poverty of her remaining knowledge for these trained items. Previous cases have clearly demonstrated that re-learning of items where verbal comprehension has been lost tend to fade quickly due to the weaker semantic network (Jokel et al., 2010, 2006). Conversely, previous studies have also demonstrated the potential advantage of using meaningful memories to anchor new learning in SD. For instance, Snowden and Neary (2002) demonstrated that patient CR was able to provide significantly more defining contextual information for items where meaningful definitions had been supplied (although her follow up data was confounded by having revised prior to the assessment).

The results of the current study are, however, encouraging. Despite declines, some benefit of naming persisted in the short-term following 7 days of COEN therapy, as compared to baseline performance. This same benefit did not continue at the 6-week follow up for words relearned using the NT approach, although no significant difference in naming performance arose when direct comparisons were made between therapies. This failure to detect a difference may in part be due to the use of small samples of words, with further studies required to confirm a relative advantage in retention of COEN over NT. Maintenance of results, however, is likely to be strongly influenced by disease stage, irrespective of training approach. Although it was not possible to obtain 6-week results for $COEN_{2,}$ the results at 3-weeks suggest a more precipitous forgetting rate. This coincides with worsening of CC's behavior during the last phase of the therapy, where she became more disinhibited, impulsive and perseverative (both within the therapy and in everyday living reported by her son). Thus disease progression may impact the degree to which a patient can engage and benefit from therapy over time. As studies using NT approaches are now emerging to suggest that retained benefits may be possible with revision (Savage et al., 2015), a similar or superior retention of learning using COEN with revision may also be found. Future studies which incorporate a longer initial practice and the opportunity for regular revision may provide important evidence to confirm whether there is superiority of COEN in the long term.

A limitation of the current study is that we did not test performance on the generalization tasks over time. This means we are only able to draw conclusions about the retention of knowledge regarding labels but not whether some of the trained concepts that the patient could no longer name at 3 and 6 weeks still remained meaningful. Thus future investigation should also test the participant's conceptual knowledge at these additional time points. Longer periods of follow up would also be advantageous in providing a more comprehensive understanding of the curve of forgetting to estimate the lasting effects of training. Finally, on a practical level, it must be acknowledged that the COEN approach does involve a significant investment of time by the clinician in the creation of the training materials. Once set up, however, successful therapy can be run fairly independently, as shown in the 2014 study, where VC practised at home. Future developments in software tools may help to further reduce the time burden for clinicians by allowing patients and their families to customize and auto-administer the therapy, while clinicians remotely monitor the intervention. Such approaches, of course, require testing to confirm efficacy.

In summary, this study extends on previous findings to reaffirm the advantage of conceptual enrichment therapy, as compared with naming therapies, when treating patients with SD. COEN not only facilitates significant relearning of words, but importantly, promotes greater rates of generalisation when re-learning items where conceptual knowledge has been lost. Further research, which incorporates schedules of revision over longer periods of time, will be important in confirming whether COEN also has the potential to produce more durable learning.

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Figure captions

Figure 1.
MRI coronal (A) and axial (B) slides. Note marked left anterior atrophy and shrinkage of the left hippocampus.

Figure 2.
Performances after COEN and NT therapy in the three generalisation tasks. P values are calculated across therapies for each task using Chi-squared test. * means statistically significant

Figure 3.
Percentage of accurate responses in naming at baseline, post-training, 3 and 6 weeks after intervention. BL indicates performances at baseline; Post-treatment indicates performances immediate post-training; 3 weeks indicates performances three weeks after the end of the intervention; 6 weeks indicates performances six weeks after the end of the intervention. P values showed no significant differences and were calculated across therapies for each task using Chi-squared test (for time-points at post-treatment and 3 weeks) and Fisher exact test for performances at 6 weeks.

Supplementary Figure A.
Picture A shows arrangement of slides and administration of Naming therapy
Picture B shows arrangement of slides and administration of COEN therapy