Deregulated semantic cognition contributes to object-use deficits in Alzheimer’s disease: A comparison with semantic aphasia and semantic dementia

Faye Corbett¹, Elizabeth Jefferies², Alistair Burns³ and Matthew A. Lambon Ralph¹

¹Neuroscience and Aphasia Research Unit (NARU), School of Psychological Sciences, University of Manchester, UK
²Department of Psychology, University of York, UK
³Faculty of Medical and Human Sciences, Institute of Brain, Behaviour and Mental Health, University of Manchester, UK

Executive control is impaired from the early stages of Alzheimer’s Disease (AD) and this produces deregulated semantic cognition (Corbett, Jefferies, Burns, & Lambon Ralph, 2012; Perry, Watson, & Hodges, 2000). While control deficits should affect semantic retrieval across all modalities, previous studies have typically focused on verbal semantic tasks. Even when non-verbal semantic tasks have been used, these have typically employed simple picture-matching tasks, which may be influenced by abnormalities in covert naming. Therefore, in the present study, we examined 10 patients with AD on a battery of object-use tasks, in order to advance our understanding of the origins of non-verbal semantic deficits in this population. The AD patients’ deficits were contrasted with previously published performance on the same tasks within two additional groups of patients, displaying either semantic degradation (semantic dementia) or deregulation of semantic retrieval (semantic aphasia; Corbett, Jefferies, Ehsan, & Lambon Ralph, 2009). While overall accuracy was comparable to the scores in both other groups, the AD patients’ object-use impairment most closely resembled that observed in SA; they exhibited poorer performance on comprehension tasks that placed strong demands on executive control. A similar pattern was observed in the expressive domain: the AD and SA groups were relatively good at straightforward object use compared to executively demanding, mechanical puzzles. Error types also differed: while all patients omitted essential actions, the SA and AD groups’ demonstrations also featured unrelated intrusions. An association between AD patients’ object use and their scores on standard executive measures suggested that control deficits contributed to their non-verbal semantic deficits. Moreover, in a task specifically designed to manipulate executive demand, patients with AD (and SA) exhibited difficulty in thinking flexibly about the non-canonical uses of everyday objects, especially when distracted by semantically related
Semantic cognition encompasses the processes and representations that support the storage and controlled use of our factual knowledge, including information about the meanings of words, pictures, objects, faces, sounds, and events. Direct comparisons of different semantically impaired patient groups have revealed that semantic cognition is supported by at least two interacting components: (1) a repository of transmodal semantic representations and (2) regulatory control processes (Corbett, Jefferies, Ehsan, & Lambon Ralph, 2009; Jefferies & Lambon Ralph, 2006). Qualitatively distinct semantic deficits follow damage to these different components. Patients with semantic dementia (SD) show gradual degradation of conceptual knowledge in the context of relative sparing of other aspects of cognition, following atrophy focussed on the anterior temporal lobe bilaterally (ATL; Davies et al., 2009; Galton et al., 2001; Mummery et al., 2000; Snowden, Goulding, & Neary, 1989). The multimodal, yet highly consistent nature of SD patients’ deficits supports the view that the ATL forms central semantic representations, which underpin semantic processing across the full range of semantic tasks – patients show impairment in their understanding of spoken and written words, pictures and environmental sounds, and in the production of meaningful words and actions (Bozeat, Lambon Ralph, Patterson, Garrard, & Hodges, 2000; Jefferies & Lambon Ralph, 2006; Lambon Ralph & Patterson, 2008; Lambon Ralph, Sage, Jones, & Mayberry, 2010). Multimodal semantic deficits are also exhibited by some aphasic patients following a stroke (‘semantic aphasia’ – SA: Jefferies & Lambon Ralph, 2006). Unlike SD, however, SA follows damage to the left prefrontal (PFC) and/or temporoparietal cortex. In a case-series comparison, Jefferies and Lambon Ralph (2006) found that semantic impairments in patients with SA differed qualitatively from those in SD. Conceptual knowledge did not appear to have been lost in SA; however, a failure of executive-control processes resulted in deregulated semantic retrieval, which was dominated by strong associations even when these were irrelevant for the task at hand. Consequently, SA patients’ level of conceptual impairment was dependent on the degree of control required by a particular task. A further comparison of these two patient groups revealed that their distinct profiles of semantic impairment extended from word comprehension/production into the non-verbal domain (differentially affecting tasks such as picture matching and object use), consistent with the view that in both groups core components of semantic cognition are damaged (Corbett, Jefferies, Ehsan, et al., 2009).

Alzheimer’s disease (AD) is also characterized by semantic impairment from the very early stages of the disorder (Ahmed, Arnold, Thompson, Graham, & Hodges, 2008; Hodges, Erzinclioglu, & Patterson, 2006; Hodges & Patterson, 1995). While a large body of research has examined these deficits in the verbal domain, a relatively limited number of studies have examined non-verbal conceptual knowledge through object use. Among these studies there is, nonetheless, general consensus that patients with AD frequently exhibit everyday action disorders which result at least in part from their disrupted semantic knowledge (Chainay, Louarn, & Humphreys, 2006; Dumont, Ska, & Joanette, 2000; Mack, Eberle, Frolich, & Knopf, 2005; Ochipa, Rothi, & Heilman, 1992). The multimodal nature of AD patients’ conceptual deficits suggests damage to a core component of semantic cognition (Dumont et al., 2000; see also Glosser, Wiley, & Barnoski, 1998). A small number of AD patients, however, appear to show impaired object use in the context of relatively preserved verbal conceptual knowledge (Moreaud,
Charnallet, & Pellat, 1998; Ochipa et al., 1992). These cases have been interpreted as evidence for a separate ‘action semantic system’ that can be damaged independently of more general semantic knowledge in the verbal domain.

The exact relationship between verbal and non-verbal conceptual deficits is likely to depend on which aspect of semantic cognition (control or representation) has been damaged in AD. Thus, apparent dissociations between modalities can be difficult to interpret. Studies examining semantic impairment in AD through language-based tasks have identified two possible causes of patients’ deficits: while some have suggested that semantic knowledge is degraded in this condition (Chertkow & Bub, 1990; Chertkow, Bub, & Caplan, 1992; Garrard, Lambon Ralph, Patterson, Pratt, & Hodges, 2005; Hodges, Salmon, & Butters, 1992), others have argued that knowledge remains intact but patients have difficulty accessing information (Bayles, 1991; Nebes, 1989; Nebes & Halligan, 1995, 1996). A more recent study has argued that the nature of semantic impairment in AD is not stable but subject to qualitative changes over the course of the disease. We extended Jefferies and Lambon Ralph’s case-series comparison of SA and SD to examine mild versus severe stage AD patients (Corbett et al., 2012). The semantic impairment exhibited by mild AD patients most closely resembled the pattern of deregulated knowledge previously observed in SA; specifically these patients showed: (1) an association between scores on semantic and executive tasks, (2) poorer performance on a semantic association task when distractor responses were more difficult to reject, and (3) an influence of cueing and miscuing on picture naming. By later stages of the disease, the already deregulated semantic system became exacerbated by the addition of degraded semantic representations. In common with SD patients, severely impaired AD cases exhibited an increasingly consistent deficit across tasks, a greater sensitivity to frequency/familiarity and reduced cueing effects.

The three-way contrast between patients with SD, SA, and AD provided by Corbett et al. (2012) examined the comprehension of words, pictures and environmental sounds, but did not provide data on object use. In the present study, we collected object-use data for a sample of AD patients, allowing direct comparison with previously published data from SD and SA (Corbett, Jefferies, Ehsan, et al., 2009). This study therefore permitted an exploration of the underlying causes of previously reported object-use deficits in AD. The novel comparative design allowed us to which aspects of the AD object-use impairment are likely to follow from degradation of amodal conceptual representations (i.e., similarities with SD), and which are more likely to follow from damage to processes that control semantic retrieval (i.e., similarities with SA). Evidence from the verbal domain suggests that semantic cognition is deregulated from the earliest stages of AD. If this hypothesis is correct, then AD patients should mirror the patterns of impaired object use observed previously in SA and thus exhibit the following key characteristics:

1. AD patients, like SA cases, are expected to show relatively good performance in item-matching tasks, which involve feature matching across modalities for the same items (e.g., matching the word ‘scissors’ to a picture or an action of this concept). In contrast, they should show poorer performance on attribute-matching tasks (e.g., matching different objects with a shared function/action), since these judgements involve items that are not globally related. Item-matching tasks have relatively low executive demands since the stimuli themselves provide the basis for a match. Attribute-matching tasks, on the other hand, require that semantic retrieval is constrained by top-down goals which specify the basis for each judgement.
2. In addition to these problems on matching tasks, AD patients, like SA cases, are predicted to show impaired use of objects on expressive tasks, particularly when these place high demands on problem solving and planning (i.e., tasks with strong executive demands such as solving mechanical puzzles). In contrast, AD and SA patients might be relatively intact at retrieving the correct way of holding and moving objects, compared with patients with SD, since the physical presence of a tool has a highly constraining influence on semantic retrieval. In line with this prediction, Corbett, Jefferies, and Lambon Ralph (2011) found that SA patients were unable to mime the correct use of an object when their output was unconstrained but they showed better retrieval of the correct action features when given either a picture of the recipient or the object itself.

3. Object-use deficits in AD, like SA, should not relate to item frequency. SD patients are highly sensitive to frequency, since the ATL is thought to acquire stronger representations to frequently encountered concepts and these are subsequently more robust to damage. In contrast, the store of amodal semantic knowledge is thought to be intact in SA patients, minimizing positive effects of frequency. SA patients show little effect of frequency or even reverse frequency effects in some contexts – that is, less accurate semantic judgements for more frequent items (Hoffman, Jefferies, & Lambon Ralph, 2011; Hoffman, Rogers, & Lambon Ralph, 2011; Almaghyl et al., 2012). This might reflect the fact that frequent words and objects are encountered in a greater range of contexts and have a wider range of associations, increasing their control demands. AD patients might resemble those with SA, particularly at the early stages if the disease, if their object-use deficits are linked to executive dysfunction and not loss of conceptual knowledge.

4. Finally, we predicted an association between AD patients’ ability to perform object-use matching tasks and the executive difficulty of those tasks, which resembles the pattern previous reported for SA (Corbett et al., 2011). Patients should show a relationship between accuracy and the strength of distractors for example.

Method

Participants
This study was approved by local health authority ethics committees and informed consent was obtained for all participants. We recruited ten patients with AD from memory services in the Manchester area, United Kingdom. All cases were diagnosed by an experienced Old Age Psychiatrist (AB) with respect to the standard, international consensus criteria. Patients with a history of stroke or other neurological conditions were excluded from the AD group. Eight of the group exhibited mild-moderate levels of impairment on the Mini-Mental State Examination (mean MMSE = 18/30; Folstein, Folstein, & McHugh, 1976), while two patients (AW and LA) were more severely impaired (see Table 1 for individual scores).

The AD patients were compared with data previously reported by Corbett, Jefferies, Ehsan, et al. (2009) from two other groups of semantically impaired patients (cases with SD and SA). These patients had multi-modal semantic deficits which had qualitatively different effects on object use. The data from Corbett et al. included seven SA patients with semantic impairment in the context of chronic (>1 year post onset) stroke aphasia, recruited from stroke clubs and speech and language therapy services around Manchester, United Kingdom. They were selected on the basis that they showed significant
| Table 1. Background neuropsychological assessments |
|-----------------------------------------------|
|                                                |
|                                                |
| **Diagnostic**                                 |
| **ACE**                                        |
| 100                                           |
| 17 (9.4)                                      |
| 52                                            |
| 22                                            |
| 38                                            |
| 46                                            |
| 53                                            |
| 53                                            |
| 55                                            |
| 55                                            |
| 57                                            |
| 62                                            |
| 75                                            |
| **MMSE**                                      |
| 30                                            |
| 17 (9.4)                                      |
| 18                                            |
| 7                                             |
| 9                                             |
| 14                                            |
| 15                                            |
| 19                                            |
| 19                                            |
| 20                                            |
| 21                                            |
| 24                                            |
| 28                                            |
| **Executive/attentional**                     |
| Raven’s coloured progressive matrices (percentile score) |
| -                                             |
| -                                             |
| 87 (10.0)                                     |
| 31 (23.2)                                     |
| 42 (33.3)                                     |
| 10                                            |
| 10                                            |
| 10                                            |
| 55                                            |
| 25                                            |
| 25                                            |
| 80                                            |
| 82.5                                          |
| 25                                            |
| 95                                            |
| **WCST (no. categories)**                     |
| 6d                                            |
| 7                                             |
| 4.5 (1.97)                                    |
| 6.6                                           |
| 1                                             |
| 0f                                            |
| 0f                                            |
| 0f                                            |
| 6                                             |
| 6                                             |
| 7                                             |
| 6                                             |
| 7                                             |
| 7                                             |
| 6                                             |
| 6                                             |
| 7                                             |
| Elevator counting (no. categories)            |
| 2d,e                                          |
| 10                                            |
| 2.3 (3.39)                                    |
| 2.9                                           |
| 0f                                            |
| 0f                                            |
| 0f                                            |
| 1                                             |
| 8                                             |
| 4                                             |
| 1                                             |
| 3                                             |
| 10                                            |
| **Semantic**                                  |
| **PPT words**                                 |
| 51.1 (1.1)                                    |
| 52                                            |
| 40 (8.1)                                      |
| 42 (5.0)                                      |
| 43                                            |
| 33f                                           |
| 39f                                           |
| 39f                                           |
| 51                                            |
| 49                                            |
| 45f                                           |
| 40f                                           |
| 46f                                           |
| 47f                                           |
| 45f                                           |
| **PPT pictures**                              |
| 51.2 (1.4)                                    |
| 52                                            |
| 39 (7.8)                                      |
| 41 (7.8)                                      |
| 40                                            |
| 36f                                           |
| 32f                                           |
| 29f                                           |
| 49                                            |
| 40f                                           |
| 42f                                           |
| 37f                                           |
| 37f                                           |
| 47f                                           |
| 43f                                           |
| 44f                                           |
| **Naming**                                    |
| 62.3 (1.6)                                    |
| 64                                            |
| 22 (24.2)                                     |
| 21 (22.0)                                     |
| 46                                            |
| 32f                                           |
| 42f                                           |
| 52f                                           |
| 57f                                           |
| 39f                                           |
| 57f                                           |
| 45f                                           |
| 49f                                           |
| 42f                                           |
| 49f                                           |
| **WPM**                                       |
| 63.7 (3.5)                                    |
| 64                                            |
| 40 (20.8)                                     |
| 49 (12.9)                                     |
| 56                                            |
| 48f                                           |
| 52f                                           |
| 48f                                           |
| 63                                            |
| 56f                                           |
| 61f                                           |
| 58f                                           |
| 57f                                           |
| 50f                                           |
| 63                                            |
| **CCT words**                                 |
| 60.7 (2.06)                                   |
| 64                                            |
| 40 (5.0)                                      |
| 36 (12.0)                                     |
| 46                                            |
| 28f                                           |
| 47f                                           |
| 42f                                           |
| 47f                                           |
| 46f                                           |
| 43f                                           |
| 44f                                           |
| 53f                                           |
| 53f                                           |
| 52f                                           |
| **CCT pictures**                              |
| 58.9 (3.1)                                    |
| 64                                            |
| 49 (5.0)                                      |
| 34 (14.0)                                     |
| 37                                            |
| 28f                                           |
| 28f                                           |
| 37f                                           |
| 42f                                           |
| 32f                                           |
| 43f                                           |
| 30f                                           |
| 41f                                           |
| 39f                                           |
| 46f                                           |
| **Category fluency**                          |
| 95.7 (16.5)                                   |
| -                                             |
| 23 (27.9)                                     |
| 14 (9.6)                                      |
| 32                                            |
| 0f                                            |
| 28f                                           |
| 21f                                           |
| 22f                                           |
| 33f                                           |
| 50f                                           |
| 35f                                           |
| 31f                                           |
| 41f                                           |
| 54f                                           |
| **Letter fluency**                            |
| 44.2 (11.2)                                   |
| -                                             |
| 13 (13.9)                                     |
| 8 (8.8)                                       |
| 23                                            |
| 0f                                            |
| 15f                                           |
| 10f                                           |
| 15f                                           |
| 39                                            |
| 60                                            |
| 20f                                           |
| 10f                                           |
| 17f                                           |
| 48                                            |

**Note.** In all figures and tables, AD patients are arranged in order of their scores on the Mini-Mental State Examination (MMSE; Folstein et al., 1976) and Addenbrooke’s cognitive examination (ACE; Mioshi, Dawson, Mitchell, Arnold, & Hodges, 2006). SA data from Corbett, Jefferies, Ehsan, et al. (2009), N = 7. SD patients from Bozeat et al. (2002), N = 8. Data only available for n = 2 participants. Data only available for n = 6 participants. Data only available for n = 6 participants; one SA case with very limited speech production was not tested. "denotes normal cut-off; "normal cut-off for participants aged 65–80." denotes impaired performance (at least two standard deviations below the control mean, or below normal cut-off). PPT = Pyramids and Palm Trees task (Howard & Patterson, 1992); CCT = Camel and Cactus task (Bozeat et al., 2000). WCST = Wisconsin Card Sorting Task.
impairment on both verbal and non-verbal semantic assessments within a screening phase (i.e., they scored below the normal range on both the word and picture judgements within the Camel and Cactus semantic association task (CCT; Bozeat et al., 2000). They were not selected specifically on the basis of their object-use performance. While all of the SA cases had a shared multimodal semantic deficit, these deficits occurred in the context of a variety of aphasia classifications: four cases had transcortical sensory aphasia (i.e., semantic difficulties despite fluent speech and good repetition), two had additional impairment of speech fluency and/or repetition, and one had global aphasia with very limited speech output. Corbett, Jefferies, Ehsan, et al. (2009) also examined four indicators of hemiplegia/limb equivalence in the SA group: limb coordination, strength, proprioception and skin sensation. However, since there was no association between limb equivalence and object use, this factor was not considered further. Multimodal semantic deficits in the SA group were associated with lesions to left frontoparietal and posterior temporal areas (see Corbett, Jefferies, Ehsan, et al., 2009, for full details).

The AD cases were also compared with data from eight cases with SD recruited through the Memory and Cognitive Disorders Clinic at Addenbrooke’s Hospital, Cambridge (previously described by Bozeat, Lambon Ralph, Patterson, & Hodges, 2002). The SD cases showed bilateral atrophy of the ATL and met published consensus criteria for a diagnosis of SD (Hodges, Graham, & Patterson, 1995; Hodges, Patterson, Oxbury, & Funnell, 1992). Therefore, in this study, we were able to compare three groups of patients who all presented with a multimodal semantic deficit, but for different underlying reasons. The SA and SD groups were comparable in age (mean age in years: SA = 62; SD = 64; t(13) < 1) but, as is typical for these varying aetiologies, the AD patients were older than both other groups (AD = 81; t(16) = 3.9–5.7, \( p < .0001 \)). All three groups had received an equivalent number of years in education (AD = 10.5; SA = 10.7; SD = 10.5; t(13–16) < 1).

Control data were available from 10 participants from the subject panel of the MRC Cognition and Brain Sciences Unit Cambridge who were matched in age and education to the SD cases (Bozeat et al., 2002).

**Background neuropsychological assessments**

**Attentional/executive tasks**

All patients were examined on Raven’s Coloured Progressive Matrices (RCPM) test of non-verbal reasoning (Raven, 1962). The AD and SA patients were also examined on the Wisconsin Card Sorting Task (Milner, 1964; Stuss et al., 2000) and the Elevator counting task, with and without distraction, from the Test of Everyday Attention (Robertson, Ward, Ridgeway, & Nimmo-Smith, 1994).

**Semantic background tests**

Patients were assessed on both word and picture versions of the Pyramids and Palm Trees semantic association task (PPT; Howard & Patterson, 1992). This task requires participants to select which of the two items is most closely related to a probe item (e.g., PYRAMID \( \rightarrow \) PALM TREE or PINE TREE). We also used the Cambridge semantic battery to assess knowledge of the same 64 items across three different semantic tasks, including: (1) naming black and white line drawings (taken from Snodgrass & Vanderwart, 1980); (2) spoken word-picture matching (WPM) with nine semantically related distractors; and (3)
word and picture versions of the CCT semantic association task in which participants had to match a probe item (e.g., camel) with the most closely related associate (e.g., cactus) from a choice of four possible responses. Fluency was assessed for six categories (animals, tools, vehicles, fruit, household items, and birds) and three letters (F, A, S). Participants were given one minute to generate as many exemplars from a given category as possible.

**Object-use assessments**

*Mechanical puzzles task (Ochipa et al., 1992)*

This task required both motor control and problem solving but minimized the contribution of semantics through the use of unfamiliar tools. Participants were required to remove a wooden block from a Perspex cylinder using one of a choice of four tools. Nine different cylinders were presented on separate trials. Each trial was scored for tool selection and application. One point was awarded if the correct tool was selected on the participant’s first attempt (total possible score of nine). Tool use was awarded a score of two if the wooden block was removed from the cylinder immediately and a score of one was achieved if the block was removed after a period of trial and error (total possible score of eighteen).

*Cambridge object-use battery (Bozeat et al., 2002)*

Four tasks in this battery assessed knowledge relating to the same 36 household items drawn from three categories (tools, stationery, and kitchen implements). Knowledge was assessed in four ways:

**Attribute-matching tasks.** Three picture–picture-matching tasks were used to probe knowledge relating to specific attributes of the 36 items (their recipients, functions and actions). Colour photographs were used to present the probe item and four possible response options (the target response and three semantically/visually related foils).

(a) **Matching to recipient:** Participants were required to match the probe item with its canonical recipient (e.g., garlic press → garlic clove).

(b) **Matching by function:** In this task, participants were required to match the probe item with a target that shared a common function (e.g., garlic press → pestle and mortar).

(c) **Matching by action:** Participants had to select the object that required the same action as the probe item (though the two objects might be held differently). For example, the garlic press would be matched with the secateurs because they both require a ‘squeezing’ action that would not be appropriate for the foil responses (corkscrew, bottle opener, and compass).

**Cross-modal item-matching tasks.**

(a) **Word–picture matching:** Participants were asked to match the picture of an item to its spoken label. Eight pictures were presented on each trial (the target and seven foils that were drawn from the same category).
(b) **Action–picture matching:** Participants were required to select the picture of the object that corresponded to a mime of the object’s use delivered by the experimenter. As above, the target item was presented alongside seven foils from the same category.

**Naming.** Real objects were presented one at a time for the participant to name.

**Single object use.** Each object was presented one at a time and the participant was asked to demonstrate how it would normally be used. The demonstrations were videotaped and later scored against a set of target features extracted from control participants’ demonstrations (Bozeat *et al.*, 2002). Each demonstration was scored with respect to hold (including grasp and position on the object), movement and orientation. Points were lost from the overall score if an essential feature of the object’s use was omitted from the demonstration.

The scoring system developed by Bozeat *et al.* (2002) captured the demonstrations given by patients with SD, which were dominated by omissions of key aspects of an object’s normal use. In addition to omissions, Corbett, Jefferies, Ehsan, *et al.* (2009) noted that SA patients’ demonstrations were frequently interrupted by erroneous intrusion errors that were not related to the target object. When demonstrating the use of a wallpaper scraper, for example, one participant used the correct hold and orientation for the tool but, in addition to the expected scraping motion, also rocked the head of the tool towards and away from the body. In the present study, as well as using Bozeat *et al.*’s original scoring system, we also scored the AD group’s object-use demonstrations for the presence of intrusion errors. Each component of object use (i.e., hold/movement/orientation) was analysed for this combination of omission and intrusion errors.

**Judgements of canonical and non-canonical tool use**

The effect of executive difficulty on object-use knowledge was further probed with an object-use judgement task (Corbett *et al.*, 2011). Participants were asked to decide which of six objects (presented as colour photographs) would be most suitable for performing an everyday task (e.g., ‘kill a fly’, depicted both verbally and using a picture of the recipient – in this example, the fly). Executive demand was increased by making it more difficult to select the correct response and reject the distracting responses. Selection was considered to be easy if the canonical object (i.e., the object most commonly used for completing the probe task) was present in the array of possible responses (e.g., ‘kill a fly’ → fly swat). Selection was more difficult when the canonical object was not present but a plausible, non-canonical alternative constituted the correct response (e.g., ‘kill a fly’ → magazine). Rejecting the foil items was made harder by including distractors that were semantically related to the canonical item (e.g., ‘kill a fly’ → fishing net/mouse trap).

We used a $2 \times 2$ design to explore the impact of canonicity and distraction in four conditions: (1) canonical object with unrelated distractors; (2) canonical object with semantically related distractors; (3) non-canonical object with unrelated distractors; and (4) non-canonical object with semantically related distractors. Three of the five foils were semantically related in the highly distracting condition and the remaining two foils were unrelated objects. All 37 trials were assessed in each of the conditions in separate testing sessions. The four conditions were interleaved in a pseudorandom order. The AD patients’
performance on this task was compared with that of eight SA cases (previously reported by Corbett et al., 2011). Control data from healthy participants were available for the two most difficult conditions of this task (non-canonical selection with related and unrelated distractors).

**Results**

**Background neuropsychology**

**Attentional/executive tasks**

The AD cases exhibited impairment across a range of attentional/executive tasks (see Table 1). Seven of the ten AD cases scored below the normal cut-off on at least one attentional/executive assessment. Of the remaining three cases with preserved performance, two were the most mildly impaired patients on the MMSE screening test (EMO and EMA). As a group, the AD patients’ scores were equivalent to the SA patients’ on all executive measures ($t(14–15) < 1$) except Elevator Counting without distraction on which the SA group were more impaired ($t(5) = 2.55, p = .05$). There was little variation in the scores of the AD group on the Wisconsin Card Sort Test and six of the ten patients scored 0, which might have at least partially reflected difficulty understanding the complex instructions for this task. However, all but one of these patients (case MO) showed additional weakness on the other executive tests, suggesting genuine impairment in this domain. The SD group scored significantly better than both other groups on the RCPM test ($t(7–11) = 4.08–5.88, p < .002$), showing that this group had more preserved non-verbal reasoning skills.

**Semantic memory assessments**

Like the SA and SD groups, all AD cases exhibited impairment across multiple semantic assessments (see Table 1). AD patients performed comparably with the other two groups in most tasks, with the following exceptions: category fluency (AD > SA; $t(15) = 2.71, p = .02$), WPM (AD > SD; $t(8) = 2.1, p = .03$) and naming (AD > SA and SD; $t(7–8) < 2.89, p = .02$). The two AD cases with the most severe deficits on the ACE and MMSE (AW and LA) were still above chance on these comprehension tests, suggesting that, despite their severity, they had understood the instructions. Unlike the AD and SD groups, two of the patients with SA had impaired speech production even in a non-semantic context (see case description): they performed relatively poor on picture naming, and one of these cases was also unable to produce item names in the category fluency task. Nevertheless, the SA group clearly showed evidence of their semantic dysfunction on picture naming and two SA cases performed very poorly at picture naming even though their spontaneous speech output was fluent.

**Object-use tasks**

**General praxis – meaningless gesture imitation**

All AD patients attained accuracy scores of 70% or greater on this task. Five of the seven SA cases scored 85% or more. The remaining two SA patients made less precise imitations of the gestures, which meant their scores were impaired (10 and 30% respectively). The SD patients scored comparably with controls on this task ($t(16) = 1.5, n.s$; Bozeat et al., 2002).
Mechanical puzzles task

All three patient groups scored below the control mean on both selection and use components of this task (see Figure 1). The SD group performed significantly better than both other groups (compared to AD: $t(16) = 3.29, p = .005$; compared to SA: $t(13) = 2.4, p = .03$), perhaps reflecting this group’s superior non-verbal reasoning abilities. The SA and AD groups obtained equivalent scores ($t(15) < 1$), in line with our prediction that their executive deficits would disrupt object use even in a non-semantic context. Two of the AD cases with the most severe deficits on the MMSE (LA, EA) were barely above chance on initial tool selection but they were able to complete the puzzles at an above-chance level, showing that they had understood the goal of this assessment.

Attribute-matching tasks

All groups were most accurate when matching objects with their recipients, but still obtained scores well below the control mean on this task (see Figure 2). In a $3 \times 3$ repeated-measures ANOVA, there was a main effect of task type (function/action/recipient: $F(2,38) = 32.64$, $p < .001$), no main effect of group (AD/SA/SD: $F(2,19) = 2.44$, $p = .11$) and no interaction between the two ($F(4,38) < 1$). Three SD cases were unable to comprehend the action-matching task and were excluded from the analysis. While all of the AD cases were able to attempt the task, one of the more impaired cases (EA) showed below chance performance for all three judgment types, and several others in the group (AW, LA, TA, MO, EMA) showed performance around or below chance level on function and/or action judgements. Basic abilities to comprehend verbal instructions and make a selection are unlikely to entirely explain the AD patients’ deficits (since all but one of the patients was above chance at the easier recipient-matching task which had an identical format). However, the function and action tasks might have been harder to comprehend as well involving more difficult judgements for similar reasons: unlike the recipient-matching task, these decisions involved identifying a match between items that are not commonly found and used together.

![Figure 1](image-url)  
**Figure 1.** Performance on the mechanical puzzles task. **Note.** Error bars denote SE.
Cross-modal item-matching tasks

All three patient groups fell below the control mean in both WPM and action–picture matching (APM; see Figure 3). Data for the APM task were not included for one SD case, who was unable to comprehend the task. While SA and SD groups displayed no significant difference between the two tasks, the AD group performed significantly better in WPM than APM (t(9) = 10.82, p < .001). In a 3 × 2 repeated-measures ANOVA, there was a significant main effect of task type (WPM > APM: F(1,21) = 29.37, p < .0001), no main effect of group (F(2,21) = 2.53, n.s.) and a significant interaction between group and task type (F(2,21) = 9.49, p = .001). The AD group scored significantly more poorly than the SA group in APM (t(15) = 3.99, p = .001) and showed somewhat better performance than the SD group in WPM; this difference approached significance (t(10) = 2.1, p = .06). These findings show that the AD patients had less substantial semantic impairment when they had to match pictures with their verbal labels (WPM); however, they showed more severe deficits when the task required less dominant action features of concepts to be retrieved (APM).

Naming

All patient groups were impaired in their ability to name the individual objects. Four cases in the SD group were unable to name any of the items. One SA patient was not examined on this task due to very poor spoken output. The AD group named more objects than the SD patients (t(16) = 2.16, p = .05) and showed no difference when compared with SA patients (t(14) < 1; see Figure 3).

Object-use demonstrations

Accuracy: All three groups scored below the control mean, with overall performance following the pattern AD > SA > SD (see Figure 4). In a 3 × 3 repeated-measures ANOVA, there were main effects of component of object use (hold/movement/orientation:
(2,44) = 47.41, p < .0001) and group (SA/SD/AD: F(2,22) = 6.29, p = .007) as well as a significant interaction between the two (F(4,44) = 6.15, p = .001). The AD group obtained significantly higher scores than SD patients on object movement and orientation as well as overall object use (t(8–9) = 2.53–3.34, p < .03). They were also more accurate than SA on object hold and movement (t(15) = 2.71–2.77, p < .02), but not orientation (t(15) = <1) or total object use, though this comparison approached significance (t(15) = 2.1, p = .053). The AD and SA groups obtained significantly poorer scores for movement than both other components of use (AD: t(9) > 4.73, p < .001; SA: t(6) > 4.68, p < .003). The SD group showed significant differences across all task comparisons (hold>orientation>movement: t(7) > 2.75, p < .03).

Erroneous intrusion errors. As previously observed for the SA group, the AD patients made several erroneous intrusion errors in all aspects of their object-use demonstrations (see Figure 5). While the SA patients made more intrusions in their object movement compared to orientation (t(6) = 5.45, p = .002), no differences were observed for the AD group (t(9) < 1.41, n.s.). The AD and SA cases did not differ from one another in their rate of erroneous intrusions for any aspect of object use (t(15) < 1.56, n.s.).

Cross-task comparisons
In their case-series comparison of object use in SA and SD, Corbett, Jefferies, Ehsan, et al. (2009) found that SD patients exhibited a highly stable deficit whereas SA patients’ performance varied across tasks in line with their differing executive demands. We therefore contrasted AD patients’ performance on straightforward cross-modal item-matching tasks against the more executively demanding attribute-matching tasks. In a 3 × 2 repeated-measures ANOVA, we observed a significant main effect of task type.
(item/attribute matching: $F(1,22) = 39.85, p < .0001$; see Figure 6a), no main effect of
group (AD/SA/SD: $F(2,22) = 2, n.s.$) and a significant interaction between the two ($F$
$(2,22) = 7.85, p = .003$). As expected, the SA and AD groups obtained significantly higher
scores in item matching than attribute matching (SA: $t(6) = 5.2, p = .002$; AD: $t(9) = 8.02,$
$p < 0.0001$) whereas the SD group scored equivalently across these tasks ($t(7) < 1$).

We also examined patients’ performance across two expressive tasks – object-use
demonstrations and the mechanical puzzles task (using overall accuracy scores). Although
both of these tasks required object use, the mechanical puzzles task placed particularly
large demands on executive problem-solving skills and minimized the role of semantic
information compared to real object use. When the tasks were examined in a $3 \times 2$
repeated-measures ANOVA, we found no main effect of task (object-use demonstrations
vs. mechanical puzzles: $F(1,22) = 2.78, n.s.$; see Figure 6b) or group (AD/SA/SD: $F$
$(2,22) < 1$) yet a significant interaction between these two factors ($F(2,22) = 20.82,$

![Figure 4](image-url)  
**Figure 4.** Hold, movement, and orientation scores for object-use demonstration. Note. Error bars denote SE.

![Figure 5](image-url)  
**Figure 5.** Rate of erroneous intrusion errors in object use. Note. Errors bars denote SE.
The SD and AD groups exhibited opposite differences across these tasks (SD: puzzles > object-use demonstrations; $t(7) = 5.06, p = .001$; AD: object-use demonstrations > puzzles; $t(9) = 5.67, p < .0001$), while the SA cases did not show a task difference ($t(6) = 1.59, \text{n.s.}$). Compared to SD patients, the AD patients were more impaired at the mechanical puzzles task ($t(16) = 3.29, p = .005$), possibly reflecting their executive and non-verbal reasoning deficits. In contrast, the AD patients did better than the SD cases when asked to demonstrate object use for real items, perhaps because their knowledge of the actions associated with the objects was less degraded ($t(16) = 3.33, p = .004$). The SA and AD groups did not differ significantly from each other on either of these tasks ($t(15) < 2.1, p < .053$).

Figure 6. Cross-task comparisons. Note. Error bars denote SE.
Object-use battery summary
All three groups exhibited impaired performance across various different aspects of object knowledge and use. This suggests that damage to a core component of semantic cognition underlies multimodal semantic impairment in AD as well as SA and SD. We focussed on the AD patients’ pattern of performance across tasks. In common with the SA patients, the AD group found it substantially easier to match the same item presented in different modalities compared to matching different items with a shared attribute. In contrast, the SD group performed comparably across the two types of task. In the expressive domain, both SA and AD groups obtained particularly impoverished scores on the executively demanding mechanical puzzles task even though conceptual knowledge was minimized by the use of unfamiliar tools in this assessment. In contrast, the SD patients’ more intact problem-solving skills supported relatively good novel tool use while their ability to demonstrate everyday object use was comparatively much poorer. These results suggest that like SA, a failure of regulatory control processes underlies semantic impairment in our sample of patients with AD. In the following analyses we investigate this possibility further.

Item frequency and object use
Bozeat et al. (2002) observed a significant correlation between SD patients’ overall object use and the frequency with which they encountered those objects ($r = .39, p = .01$). This is consistent with the fact that familiarity/frequency effects appear to be a core feature of degraded semantic representations (Jefferies & Lambon Ralph, 2006; Warrington & Cipolotti, 1996; Warrington & Crutch, 2004). We explored the relationship between object-use scores and the frequency with which those items are normally encountered (rated on a six point scale by control participants). As observed for SA patients, the AD group exhibited no association between their overall use scores and object frequency (SA: $r = .12$, n.s; AD: $r = .2$, n.s.). In addition, the rate of erroneous intrusion errors did not correlate with frequency for either group (SA: $r = -.10$, n.s; AD: $r = .01$, n.s.).

Inter-task correlations
Corbett, Jefferies, Ehsan, et al. (2009) assessed the relationship between standard semantic tasks, object-use tests and executive assessments for SA and SD patients. The SD group showed strong associations on all semantic tasks, irrespective of whether knowledge was assessed through verbal or non-verbal modalities. The SA patients exhibited some associations between standard semantic assessments and tasks assessing object-use knowledge, especially if they had similar task demands. However, unlike the SD group, the SA patients also displayed a relationship between their performance on the RCPM test and object-use tasks, suggesting that non-verbal as well as verbal semantic deficits were associated with impairments of non-verbal reasoning. In the sections below, we examine correlations for the AD patients (i) between different types of tasks within the semantic domain; and additionally between object use and (ii) semantic impairment, (iii) executive performance and (iv) visual spatial skills.

Correlations within the semantic domain
We assessed the relationships among six semantic assessments: picture naming (average score for the 64-item and object-use battery), WPM (64-item/object-use battery average
score), PPT (word/picture average), category fluency, APM and an attribute-matching score (function/action/recipient average score). The results reveal a multi-modal semantic deficit in AD. Of fifteen pair-wise comparisons, nine associations were significant for the AD group ($r = .62–.96$, $p < .03$; all correlations are one-tailed) with exceptions occurring for naming, which failed to correlate with all other tasks (except WPM), as well as category fluency and PPT/APM.

Correlations between object use and semantic processing

Next, we examined the relationship between the six semantic tasks examined above and all three components of object use (hold/movement/orientation) plus overall object use. Our findings were consistent with the proposal that impaired object use in AD follows from impaired semantic cognition. PPT, WPM, and attribute-matching tasks correlated significantly with all components of object use ($r = .61–.85$, $p < .03$). APM correlated with all components of object use except hold ($r = .6–.71$, $p < .04$). The remaining associations arose between category fluency and object hold as well as naming and object orientation ($r = .58–.7$, $p < .04$).

Correlations between object use and executive tests

To examine the hypothesis that the degree of non-verbal semantic impairment in AD is related to executive deficits, correlations between the RCPM test of non-verbal reasoning and eleven assessments from the object-use battery were computed (including: WPM, APM, object hold/movement/orientation/total, function/recipient and action matching, object naming, and mechanical puzzles). Like the SA patients examined by Corbett, Jefferies, Ehsan, et al. (2009), the AD group displayed significant associations between RCPM and aspects of the object-use battery, namely correlations with WPM, APM, overall object use, object orientation, object movement, function matching and recipient matching ($r = .59–.89$, $p < .04$). In addition, correlations approached significance for RCPM and object hold ($r = .46$, $p = .09$) as well as action matching ($r = .50$, $p = .07$).

Correlations between object use and visuospatial skill

Patients with AD sometimes exhibit visuospatial deficits in addition to semantic impairment (Caine & Hodges, 2001). We examined the relationship between AD patients’ performance on the object-use battery and their visuospatial skill. A score for visuospatial function was derived from five subtests of the ACE (Addenbrooke’s Cognitive Examination; Mioshi et al., 2006): overlapping pentagon drawing, clock drawing, cube drawing, dot counting and letter identification. Although visuospatial skill was associated with performance on attribute and item-matching tasks as well as overall object use and object movement ($r = .56–.75$, $p < .05$), the same was not true for object naming, hold or orientation ($r = .09–.45$, n.s.). This suggests that visuospatial deficits can be ruled out as the sole cause of patients’ impaired object-use knowledge.

Ratings of executive demands and performance on semantic matching tasks

Previous studies have observed a relationship between SA patients’ performance on semantic association judgments and ratings of the executive difficulty of each trial. The same relationships were not found for SD patients (Corbett, Jefferies, Ehsan, et al., 2009;
We examined the relationship between executive difficulty and performance on five matching tasks from the object-use battery, namely the two item-matching tasks (WPM/APM), and three attribute-matching tasks (function/action/recipient). Seven control participants rated the trials from each task on two indicators of executive difficulty: (1) the ease with which the probe and target could be matched with one another, and (2) how easy it was to reject the distractor responses. We generated an overall executive difficulty score for every trial in each task based on the ratings from these two scales.

Simultaneous logistic regression was used to determine the extent to which item accuracy could be predicted by (a) the executive difficulty of each trial, (b) task type (item/attribute matching), and (c) individual task identity (WPM, APM, action/function/recipient matching) for the three patient groups (AD/SA/SD). We found that executive difficulty was a significant predictor of performance (Wald = 163.5, \( p < .0001 \)), alongside group (Wald = 58.12, \( p < .0001 \)) and patient identity (Wald = 33.68, \( p < .0001 \)). The influence of task type approached significance (Wald = 3.21, \( p = .073 \)) but there was no relationship between performance and individual task identity (Wald = 1.04, n.s.). Using an interactive term, we found a significant group by executive difficulty interaction (Wald = 7.27, \( p = .007 \)). Although executive difficulty was a significant predictor of performance for all three groups individually, this effect was greatest for the AD group (ExpB = 3.34), followed by the SA patients (ExpB = 2.15) and smallest for the SD group (ExpB = 1.71).

Judgements of canonical and non-canonical tool use
This experiment directly manipulated the executive demands of object use judgements to establish if SA and AD patients show comparable effects. We used a 2 x 2 design to explore the impact of type of distracters (related vs. unrelated) and canonicity (canonical tool use, e.g., kill a fly with a fly swat vs. non-canonical tool use, e.g., kill a fly with a magazine). Both groups exhibited similar levels of impaired performance relative to control participants but the two groups performed similarly across the different conditions (see Figure 7). We examined the effect of canonicity and distractor...
relationship for the two patient groups using repeated-measures ANOVAs. Both groups exhibited significant main effects of canonicity (AD: $F(1,9) = 85.48, p < .0001$; SA: $F(1,7) = 107.43, p < .0001$) and distractor relationship (AD: $F(1,9) = 73.86, p < .0001$; SA: $F(1,7) = 118.24, p < .0001$). The AD group also exhibited an interaction between canonicity and distractor type ($F(1,9) = 51.84, p < .0001$), which was attributable to their particularly poor performance when selecting non-canonical targets from an array of semantically related foil responses (see Figure 7).

Discussion

This study examined the status of non-verbal semantic knowledge in patients with AD. We employed a battery of tasks assessing knowledge of object use relating to 36 household items. Relative to control participants, AD patients exhibited impoverished knowledge, including difficulty naming objects, matching them on the basis of their identity and attributes (e.g., function/action/recipient), and demonstrating how they are normally used. These findings confirm that damage to a core component of semantic cognition underlies a multimodal semantic deficit in AD which affects object use.

In addition to patients with AD, multimodal semantic impairments are also exhibited by individuals with SA and SD (Bozeat et al., 2002; Coccia, Bartolini, Luzzi, Provinciali, & Lambon Ralph, 2004; Corbett, Jefferies, & Lambon Ralph, 2009; Jefferies & Lambon Ralph, 2006; Luzzi et al., 2007). Direct case-series comparisons of SD and SA have shown, however, that the nature of their deficits differs qualitatively as a result of damage to different core aspects of semantic cognition (Corbett, Jefferies, Ehsan, et al., 2009; Jefferies & Lambon Ralph, 2006). Degradation of the amodal semantic repository in the context of SD leads to a highly stable and consistent impairment across a range of verbal and non-verbal semantic tasks tapping different input and output modalities. In contrast, semantic representations appear to remain intact in SA but a failure of executive control causes semantic cognition to become deregulated. Consequently, SA patients perform more poorly on semantic tasks that place the greatest demand on executive-control processes, irrespective of other task factors, such as stimulus modality. This pattern can be seen both for standard semantic tasks employing pictures and words (Jefferies & Lambon Ralph, 2006) and within the highly non-verbal domain of object use (Corbett, Jefferies, Ehsan, et al., 2009).

Studies exploring semantic impairment in the context of AD have largely employed language-based tasks and there has been little consensus regarding the nature of the deficit (i.e., in terms of impairment to executive-semantic control processes and/or conceptual representations). Moreover, the relationship between verbal and non-verbal deficits in this disorder is inadequately understood. However, case-series comparisons of patients with AD against SD versus SA provides a potentially powerful way of tackling this issue given that the semantic deficits in SD and SA are qualitatively different and associated with deficits of semantic representation and control respectively. Motivated by this goal, Corbett et al. (2012) provided evidence showing that performance on a multimodal semantic battery (including word- and picture-based comprehension tasks) reflected deficits of semantic control from the very earliest stages of AD. In the present study, we extended these investigations by examining 10 AD patients on a battery of object-use tasks, which probed both comprehension of the actions and functions of objects, and overt demonstrations of object use. We compared the AD group with previously
published data for patients with SA and SD (from Corbett, Jefferies, Ehsan, et al., 2009) to examine the origins of non-verbal semantic deficits within the domain of object use, in which effects of covert naming are minimized.

We found that on comprehension tasks examining understanding of object use, the degree of AD patients’ semantic impairment was comparable to both SD and SA patients; however, the pattern of their deficits most closely resembled those observed in SA; patients’ performance varied in line with the executive demands of the tasks. While the AD and SA patients performed relatively well on comprehension tasks that required them to match the same items presented in different modalities, they found it substantially more difficult to match different items with a common attribute (e.g., shared function/action). In contrast, the SD group performed consistently across the tasks, presumably reflecting the fact that they employed the same concepts, despite their differing executive demands.

Important group differences were also observed in the expressive domain. All groups exhibited poorer object use than control participants due to frequent omission errors. A number of findings suggested, however, that the patients were failing this task for different reasons. The SD group gave the poorest demonstrations for items that they were least familiar with, in line with the frequency-graded course of semantic degradation in this condition (Bozeat et al., 2000, 2002). The SA and AD groups did not show an effect of frequency in object use but did exhibit erroneous intrusion of actions that were unrelated to the target actions; these errors were not a prominent feature of the SD patients’ demonstrations. Patients’ performance across different expressive tasks revealed further distinct sources of their object-use impairments. The SD group found it difficult to give accurate demonstrations of real household objects, reflecting their highly degraded semantic representations, but scored within the normal range when using novel, meaningless tools which minimized the contribution of semantics. The reverse pattern was true of the SA and AD patients; both groups performed relatively well in straightforward object use but they showed much poorer performance on the mechanical puzzles task, which placed a substantial demand on executive, problem-solving skills.

A number of additional analyses were used to probe the relationship between object-use knowledge and executive skill. We collected a measure of executive difficulty for each trial within five matching tasks in the object-use battery by asking control participants to rate how easy it was to select the correct response and reject the foil options. Item-by-item performance on these matching tasks was predicted by their executive difficulty rating for all three groups but this effect was particularly strong for the AD and SA patients. In addition, we designed an object-matching task that specifically manipulated the requirement for regulatory control. We found that both SA and AD patients were relatively good at matching objects with the tasks they are canonically used for. Accuracy declined substantially, however, when participants had to think flexibly in order to select objects for non-canonical purposes and when they were required to reject semantically related distractor objects. The AD patients’ impairments on the object-use battery are consistent with the view that a failure of core regulatory control processes is a major cause of multimodal semantic deficits in this condition. Consistent with this hypothesis, we observed an association between patients’ performance on object-use tasks and assessment of executive skill. This mirrors the association found for the SA patients.

We also observed an association between the AD patients’ performance on standard verbal semantic tasks (e.g., object naming) and those assessing non-verbal object use. This indicates a common source of impairment in these two domains. Some previous studies examining semantic impairment in AD have claimed that verbal and non-verbal semantic
impairments can occur independently of one another, which has been taken as evidence for a separate ‘action semantic system’ (Moreaud et al., 1998; Ochipa et al., 1992). Based on the results from the present study, however, it is possible that variable performance across verbal and non-verbal semantic tasks in previous studies could have reflected different levels of executive demand rather than a true dissociation between different types of semantic knowledge. For example, one previous study reported cases of AD who appeared to exhibit deficits in object use despite intact verbal semantic knowledge (Ochipa et al., 1992). While a large assessment battery was used to probe object use, verbal semantic knowledge was examined using a straightforward WPM task with only three foil responses per trial. It is possible that a more comprehensive and demanding range of semantic tasks would have revealed the truly multimodal nature of the semantic impairment in these patients.

Our previous investigation of word and picture semantic tasks in AD (Corbett et al., 2012) found that semantic impairment in the mildest cases was qualitatively similar to that in SA, indicating that executive-semantic deficits are apparent even from an early stage of the disease. However, in a more severely impaired sample of AD patients, there was evidence of additional degradation of conceptual knowledge, consistent with the view that damage is likely to encroach on the inferolateral ATL as the disease progresses. In the current investigation, given that object-use data are only available for only ten AD patients (broadly comparable to the sample size in the SD and SA groups), it is not possible to directly test this account. Nevertheless, the patients’ scores on MMSE/ACE suggested 8/10 of our sample had mild-to-moderate deficits, while the remaining two cases (AW and LA) were severely impaired. These two more severe cases showed a pattern largely consistent with poor control over semantic retrieval: they showed more severe impairment of non-verbal reasoning, semantic performance and object use overall, they showed poorer performance on attribute than identity matching tests like other AD cases, and they showed a strong influence of the strength of the targets and distracters when making judgements about canonical and non-canonical tool use. For this reason, the 10 AD patients are examined as a group in this case-series comparison.

In summary, the present study has provided converging evidence for the idea that semantic cognition is supported by the interaction of two core components: an amodal semantic repository and regulatory control processes. Damage to the executive-control component of this system appears to underlie multimodal semantic impairment in AD from an early stage. This study uniquely demonstrates the impact of this deregulated semantic cognition on the highly non-verbal domain of object use.

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