

The degraded concept representation system in semantic dementia:
Damage to pan-modal hub, then visual spoke

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Word count (main text): 5859

Running header: Damaged concepts in semantic dementia

Acknowledgements

We are grateful to Beth Jefferies and Hannah Gardner for their help with data collation, and to Alistair Burns and Roland Zahn for referring patients to us. The research was supported by MRC programme grants (G0501632 & MR/J004146/1) and an NIHR senior investigator grant to MALR.

Abstract

The core clinical feature of semantic dementia (SD) is a progressive yet selective degradation of conceptual knowledge. Understanding the cognitive and neuroanatomical basis for this deficit is a key challenge for both clinical and basic science. Some researchers attribute the deficit to damage to pan-modal conceptual representations that are independent of any particular sensory-motor modality and are represented in the ventrolateral anterior temporal lobes. Others claim that damage to modality-specific visual feature representations in the occipitotemporal ‘ventral stream’ is responsible. In the present study, we tested the hypothesis that concept degradation in SD involves a combination of these pan-modal and modality-specific elements. We investigated factors influencing knowledge of object concepts by analysing 43 sets of picture naming data from SD patients. We found a strong influence of two pan-modal factors: highly familiar and typical items were named more accurately than less familiar/typical items at all stages of the disorder. Items associated with rich sensory-motor information were also named more successfully at all stages, and this effect was present for sound/motion knowledge and tactile/action knowledge when these modalities were studied separately. However, there was no advantage for items rich in visual colour/form characteristics; instead, this factor had an increasingly negative impact in the later stages of the disorder. We propose that these results are best explained by a combination of (a) degradation of modality-independent conceptual representations, which is present throughout the disorder and is a consequence of atrophy focused on the ventrolateral anterior temporal lobes and (b) a later, additional deficit for concepts that depend heavily on visual colour/form information, caused by the spreading of atrophy to posterior ventral temporal regions specialised for representing this information. This explanation is consistent with a graded hub-and-spoke model of conceptual knowledge, in which there is a gradual convergence of information along the temporal lobes, with visual attributes represented in the posterior cortex giving way to pan-modal representations in the anterior areas.

Keywords: conceptual knowledge; hub-and-spoke; ventral stream; anterior temporal lobe

Introduction

The goal of this study was to improve our understanding of the nature of conceptual knowledge impairment in semantic dementia (SD), a neurodegenerative disorder in which conceptual knowledge progressively degrades but other cognitive functions remain largely intact (Hodges and Patterson, 2007, Warrington, 1975). SD is a highly selective disorder, at least in its early stages, both in terms of the cognitive deficit and the brain regions affected by atrophy. For this reason, SD has been influential in shaping theories of concept representation, making an understanding of this disorder important from both theoretical and clinical perspectives. In particular, this group of patients has been the inspiration behind what has become known as the hub-and-spoke theory of conceptual knowledge (Patterson *et al.* , 2007, Pobric *et al.* , 2010a, Rogers *et al.* , 2004a). The “spokes” in this model refer to a distributed network of brain regions that are specialised for representing conceptual information arising in different sensory-motor modalities. So, for example, the shape of a banana is thought to be coded in areas of the ventral temporal cortex specialised for representing the visual forms of objects (Chao *et al.* , 1999, Martin *et al.* , 1995, Thompson-Schill *et al.* , 1999), the actions required to peel it in frontoparietal regions specialised for coding object manipulation (Buxbaum and Saffran, 2002, Goldberg *et al.* , 2006, Ishibashi *et al.* , 2011, Kellenbach *et al.* , 2003) and its gustatory properties in orbitofrontal cortex (Goldberg *et al.* , 2006). There is a broad consensus that such a network of modality-specific knowledge regions exists (Barsalou, 2008, Binder and Desai, 2011, Kiefer and Pulvermuller, 2012, Martin, 2007, Patterson *et al.* , 2007). Damage to particular spoke regions has been proposed as an explanation for category-specific semantic disorders (e.g., Capitani *et al.* , 2003, Caramazza and Shelton, 1998, Warrington and Shallice, 1984). For example, damage to inferior parietal regions involved in representing actions disproportionately affects processing of tools and other manipulable manmade objects (Buxbaum and Saffran, 2002).

The hub-and-spoke model also posits the existence of a pan-modal integrative “hub” region, which receives inputs from the spoke regions and uses them to form transmodal conceptual representations that capture the deeper patterns of coherent variation across all sensory-motor and verbal modalities. These integrated representations are thought necessary because similarity in any single sensory-motor domain is, at best, only a partial guide to true conceptual similarity (Lambon Ralph *et al.* , 2010). For example, apples and bananas have different colours and shapes but are conceptually very similar. The proposal of a transmodal hub was motivated by the pan-modal, pan-category conceptual deficits experienced by patients with SD. SD patients display poor conceptual knowledge in every modality tested, including written and spoken words (Jefferies *et al.* , 2009), pictures (Bozeat *et al.* , 2000), non-verbal sounds (Goll *et al.* , 2010), smells (Luzzi *et al.* , 2007), tastes (Piwnica-Worms *et al.* , 2010) and object manipulation (Hodges *et al.* , 2000). In addition, all categories of object are affected (Lambon Ralph *et al.* , 2007) as are all types of word (Hoffman and Lambon Ralph, 2011, Hoffman *et al.* , in press). These knowledge deficits are correlated with cortical atrophy and hypometabolism centred on the ventrolateral, anterior temporal lobes (Mion *et al.* , 2010, Nestor *et al.* , 2006), suggesting that the pan-modal knowledge deficit is due to damage to a single, neuroanatomically constrained region. This view is now supported by converging evidence from a number of other methodologies. Distortion-corrected fMRI (Binney *et al.* , 2010, Visser and Lambon Ralph, 2011), PET (Sharp *et al.* , 2004, Vandenberghe *et al.* , 1996), MEG (Marinkovic *et al.* , 2003) and transcranial magnetic stimulation (Pobric *et al.* , 2007, Pobric *et al.* , 2010b) have all revealed involvement of the anterior, ventrolateral temporal lobes in processing various kinds of concept presented in a number of different modalities.

We refer to this perspective as the pan-modal view of SD because it emphasises the involvement of verbal and non-verbal information from all sensory modalities in the

conceptual breakdown. The hub-and-spoke model attributes this deficit to damage to a transmodal hub region that makes a critical contribution to all types of concept. In contrast, other researchers have highlighted the disproportionate loss of visual-perceptual knowledge in SD (Bonner *et al.* , 2009, Breedin *et al.* , 1994, Pulvermuller *et al.* , 2010). Initial evidence for this assertion came from studies that probed knowledge for particular object features (Breedin *et al.* , 1994, Lambon Ralph *et al.* , 1999, Lambon Ralph *et al.* , 2003, Tyler and Moss, 1998). For example, when SD patients are asked to define objects, their descriptions lack much of the information that healthy controls provide. Lambon Ralph *et al.* (2003) subdivided their responses according to the type of information provided (perceptual, functional or encyclopaedic) and found that SD patients were more likely to omit the perceptual features of objects than their functional or encyclopaedic attributes. In addition, when patients are asked to draw common objects, their drawings lack many of the visual features produced by controls (Bozeat *et al.* , 2003). These findings have led some to conclude that knowledge deficits in SD are due primarily to damage to areas of the ventral, posterior temporal lobes specialised for coding the visual properties of objects (Antonucci and Alt, 2011, Bonner *et al.* , 2010, Gainotti, 2011, Yi *et al.* , 2007). This view is consistent with the observation that occasional, individual SD patients show better comprehension of abstract relative to concrete words (Bonner *et al.* , 2009, Breedin *et al.* , 1994, Macoir, 2009, Papagno *et al.* , 2009, Warrington, 1975, Yi *et al.* , 2007), although the reverse pattern is more common in case-series of SD patients (Hoffman and Lambon Ralph, 2011, Hoffman *et al.* , in press, Jefferies *et al.* , 2009).

The pan-modal and visual-deficit perspectives on SD are not mutually exclusive. Indeed, in terms of the hub-and-spoke model, it is possible that a combination of damage to the pan-modal hub region *and* the modality-specific visual spoke region gives rise to the pattern of deficits observed in SD (Bonner *et al.* , 2009, Pulvermuller *et al.* , 2010). To test

this hypothesis, we investigated the degree to which the function of the hub and spoke regions are impaired in SD, by analysing the patients' performance in object naming. Object naming is a sensitive and reliable indicator of conceptual knowledge impairment in SD and naming problems are evident even in the early stages of the disorder (Lambon Ralph *et al.* , 2001, Woollams *et al.* , 2008). We investigated the factors underpinning naming success in a large corpus of picture naming data collected by our research group over the past 10 years (43 observations from 16 SD patients). We assumed that the functional status of hub and spoke regions could be inferred from the patients' success in naming objects with particular properties. The hub-and-spoke model states that all concepts rely on the transmodal hub but, in addition, concepts rely on the individual modality-specific spokes to varying extents, depending on which modalities critically contribute to the concept (Pobric *et al.* , 2010a). For example, in addition to the transmodal hub, the action spoke is thought to be heavily involved in naming *scissors*, because a key element of our knowledge of scissors is the way in which we manipulate them. In contrast, the action spoke is not expected to be important for naming an *elephant*; however, the visual spoke makes a critical contribution because an elephant's most salient feature is its distinctive appearance. Thus, we assessed the status of the various spokes by contrasting sets of items with high vs. low dependence on particular spoke regions (while controlling for other relevant factors). Greater impairment for items that rely heavily on a particular spoke region would indicate that the underlying representations in that spoke were compromised. To quantify the dependence of particular concepts on different spokes, we used data from a recent study in which participants rated the extent to which they associated objects with experience in eight sensory-motor modalities (colour, visual form, motion, sound, taste, smell, tactile and action; Hoffman and Lambon Ralph, submitted). This allowed us to determine (a) whether objects that rely heavily on visual information are

particularly impaired in the disorder, as predicted by the visual deficit hypothesis and (b) whether information in other sensory-motor modalities was similarly affected.

We also assessed the impact of three pan-modal object properties that are not tied to any particular sensory modality: familiarity, typicality and sensory richness. If the loss of concepts in SD is due primarily to degradation of visual feature knowledge, these factors would not be especially influential because none is based directly on information from this modality. In contrast, the pan-modal hub theory of SD holds that these factors have a strong influence on success across a range of semantic tasks, including naming (Funnell, 1995, Jefferies *et al.* , 2009, Mayberry *et al.* , 2011, Patterson *et al.* , 2007, Woollams *et al.* , 2008). Highly familiar and typical items are thought to be represented more strongly in the hub, making them more robust to damage (Rogers *et al.* , 2004a). As a new additional measure of the transmodal hub contribution to semantic representation, we assessed whether knowledge in SD was influenced by the total amount of sensory-motor information associated with the concept over *all* modalities, which we termed its *sensory richness*.

Method

Participants

This study features data from 16 patients with SD, collected between 2001 and 2010. The patients were referred from the RICE memory clinic in Bath or from other specialist clinics in the north-west of England. Each had received a clinical diagnosis of SD based on caregiver interview, neuropsychological assessment and evidence of temporal lobe atrophy in structural brain imaging. All patients fulfilled current diagnostic criteria for SD (Gorno-Tempini *et al.* , 2011). Most have appeared in one or more previous studies by our research group (e.g., Hoffman and Lambon Ralph, 2011, Jefferies *et al.* , 2004, Lambon Ralph *et al.* , 2010, Patterson *et al.* , 2006).

Our analyses were conducted on data from the 64-item picture naming test that forms part of the Cambridge Semantic Battery (Bozeat *et al.* , 2000), which we use routinely to assess integrity of conceptual knowledge. As patients were studied longitudinally, many completed this test on multiple occasions. Due to the progressive nature of SD, and in keeping with previous studies (Lambon Ralph *et al.* , 2001, Woollams *et al.* , 2007, Woollams *et al.* , 2008), we treated each test administration as an independent observation. The delay between successive administrations of the naming test was typically between 6 and 12 months and was never less than 3 months. The 16 patients yielded a total of 43 observations. These were divided into three groups by classifying the 14 highest naming scores as “mild”, the 14 lowest scores as “severe” and the remaining 15 scores as “moderate”.

Background neuropsychological testing

Data from standard neuropsychological tests are presented in Table 1, which shows mean scores for the mild, moderate and severe naming groups. In addition, data from each individual patient, taken from the first occasion on which they completed the full assessment battery, is provided in the Supplementary Materials. In Table 1, figures in italics indicate the number of observations contributing to each mean. In the most recent incarnation of our assessment regime, patients complete a full assessment battery once a year but additionally complete core semantic knowledge tests (i.e., picture naming and word-picture matching) every six months. For this reason, there are some occasions on which a naming score was available but other tests were not completed. Mean values are shown in bold if they are outside the normal range (i.e., below published cut-off for the test, or greater than two standard deviations below the mean for healthy subjects). All three groups performed outside the normal range on a series of tests that probe semantic/conceptual knowledge. These consisted of picture naming, matching spoken words to pictures, the Camel and Cactus test (a

semantic association test similar to the Pyramids and Palm Trees; see Bozeat *et al.* , 2000) and generation of examples belonging to six semantic categories (category fluency). Naming was considerably impaired even in the mild group (the cut-off for normal performance is 59/64 on this relatively easy test) and declined steadily. On the other tests, performance declined in parallel with naming, indicating that the naming deficit in these patients was symptomatic of a more general deterioration in conceptual knowledge.

In contrast, other cognitive functions were relatively spared, in keeping with the usual clinical picture in SD. General cognitive status was assessed with the MMSE (Folstein *et al.* , 1975). Attention and executive function were tested using forward and backward digit span (Wechsler, 1987), letter fluency (FAS) and Raven's coloured progressive matrices (Raven, 1962). Finally, visuospatial function was assessed with copying of the Rey complex figure (Lezak, 1976) and four subtests from the VOSP (Visual Object and Space Perception Battery; Warrington and James, 1991). The mild group displayed no impairments on any of these tests. There was evidence for some slight decline in the moderate and severe groups, most notably on the MMSE and the object decision component of the VOSP. These can be attributed to deterioration in language comprehension/production, which is an integral part of the MMSE, and in object recognition, which declines as patients lose their knowledge of previously familiar objects (Rogers *et al.* , 2004b). A mild impairment in letter fluency was evident in the most severe group, reflecting their impoverished vocabulary.

Stimuli and Test Administration

The Cambridge picture naming test consists of 64 black-and-white line drawings from the Snodgrass and Vanderwart (1980) set. Half represent living and half non-living objects. During the test, each picture was presented individually to the patient and they were asked to

give its name. The item was scored as correct if they provided its name, or any of the acceptable alternatives listed by Woollams et al. (2008), as part of their response.

Stimulus factors and data analysis

We focused on six factors of potential importance to object knowledge in SD. With the exception of typicality, all factors were based on ratings collected by Hoffman and Lambon Ralph (submitted) from 100 British undergraduate students. Participants in this study were presented with a series of object names (animals, fruits and vegetables and manmade objects) and were asked to rate, on a 7-point scale, (a) how familiar they were with the object and (b) how strongly they associated the object with experience in each of eight sensory-motor modalities (colour, visual form, observed motion, sound, taste, smell, tactile and performed actions). We also used ratings of semantic typicality collected by Garrard et al. (2001). In this study, participants were presented with object names and asked to rate, on a 4-point scale, whether the object was a typical example of items from its superordinate category (e.g., a dog is a highly typical animal and a seahorse atypical).

From this pool of data, we derived six factors. The first two factors, *familiarity* and *typicality*, were pan-modal in the sense that raters were not asked to take any particular modalities into account when making their judgements. We assumed, therefore, that raters made use of all types of information available for the concept when making these ratings. The third factor, *sensory richness*, was a composite measure of the total amount of sensory-motor experience associated with each object. It was calculated by taking the average of each item's experience ratings across all eight modalities. The remaining three factors indexed how strongly each item was associated with experiences in particular sensory-motor domains. We created three composite measures by combining ratings from closely-related modalities. The decision to group modalities in this way was guided by a previous study in which we

performed a principal components analysis on the ratings for 156 objects (Hoffman and Lambon Ralph, submitted). This analysis indicated that the eight modalities collapsed into four distinct factors, with two modalities loading heavily on each factor:

Factor 1: taste and smell

Factor 2: sound and motion

Factor 3: colour and visual form

Factor 4: tactile and action

These groupings capture a number of intuitive assumptions about modality correlations. For example, items with distinctive smells can often be eaten and objects that move (principally animals and vehicles) usually make sounds. For the present study, we discarded the taste and smell factor because these modalities are irrelevant for the majority of objects. The other modalities were used to construct the final three factors in the following manner:

1. *Colour/form* value of the object, calculated by averaging its ratings for colour experience and visual form experience.
2. *Sound/motion* value of the object, calculated by averaging its ratings for sound experience and experience of observed motion.
3. *Tactile/action* value of the object, calculated by averaging its ratings for tactile experience and action experience.

This approach for grouping modalities also aligns with the presumed neuroanatomical correlates of each modality. Colour and visual form information are both thought to be underpinned by posterior fusiform areas that form part of the ventral visual stream (Chao *et al.* , 1999, Martin *et al.* , 1995, Thompson-Schill *et al.* , 1999). Motion characteristics are associated with a different locus of activation in the posterior middle temporal gyrus (Beauchamp *et al.* , 2002), which is close to the superior temporal region activated during processing of the auditory properties of objects (Kiefer *et al.* , 2008, Lewis *et al.* , 2004).

Finally, tactile information and knowledge of the actions associated with objects are thought to be stored in more dorsal parietal and frontal sites (Buxbaum and Saffran, 2002, Goldberg *et al.*, 2006, Ishibashi *et al.*, 2011, Kellenbach *et al.*, 2003).

To assess the effect of each of these factors on conceptual knowledge in SD, we constructed twelve subsets of sixteen items, all taken from the pool of 64 items in the naming test. The subsets were arranged in six pairs, with each pair manipulating one of the factors while being matched as closely as possible on the other five. The properties of each subset are shown in Table 3. Note that each pair differed significantly on exactly one of the six factors. In addition, none of the pairs differed in log word frequency (taken from the CELEX database; Baayen *et al.*, 1993) and each subset contained an equal number of living and non-living things. The items in each subset are listed in the Supplementary Materials.

Results

Data from each stimulus manipulation were analysed separately. Results from each manipulation were subjected to a 2×3 mixed ANOVA that included the manipulated variable as a within-subjects factor and severity as a between-subjects factor. As expected, the main effect of severity was highly significant in every analysis. Therefore, we report only main effects of the manipulated stimulus factors and their interactions with severity. Post-hoc t-tests were used to explore the significance of effects at each level of severity.

Familiarity: Naming performance for high and low familiarity items is shown in the left-hand panel of Figure 1. Highly familiar items were named much more successfully than less familiar items, which was confirmed by the significant main effect of familiarity in the 2×3 ANOVA ($F(1, 40) = 105, p < 0.001$). There was also a significant interaction between familiarity and severity ($F(2, 40) = 8.09, p = 0.001$). T-tests indicated that the familiarity effect was highly significant at every level of severity ($t > 4.42, p < 0.002$). However, it was

smallest in the severe group, presumably reflecting a slight floor effect in the most severe patients.

Typicality: Results for the high and low typicality sets are shown in the centre of Figure 1. Highly typical items were more likely to be named than less typical ones ($F(1, 40) = 31.5, p < 0.001$) and this effect did not interact with severity ($F(2, 40) < 1$). The effect was highly significant in every severity group ($t > 3.11, p < 0.009$).

Sensory richness: Results for the overall richness across all sensory modalities are presented in the right-hand panel of Figure 1. Patients were more accurate at naming objects with high sensory richness ($F(1, 40) = 31.5, p < 0.001$). This factor did not interact with severity ($F(2, 40) < 1$) and was highly significant at every stage of the disease ($t > 4.41, p < 0.002$).

Colour/form: Figure 2 shows the manipulations of representation in particular sensory modalities (colour/form in the left-hand panel). In contrast to the results for *overall* sensory richness, items that had strong colour and form characteristics were named more poorly than matched items with weaker colour/form ratings ($F(1, 40) = 16.8, p < 0.001$). However, this effect was qualified by a significant interaction ($F(2, 40) = 4.18, p = 0.022$). T-tests indicated that colour/form had no effect on naming in the mildest patients ($t = 0.18, p = 0.86$), a modest effect on the moderate patients ($t = 2.58, p = 0.022$) and the strongest effect on the most severe patients ($t = 4.60, p < 0.001$).

Sound/motion: The effect of the sound/motion manipulation (middle panel of Figure 2) mirrored that of overall sensory richness. Items that were high in sound/motion information were named more successfully ($F(1, 40) = 91.3, p < 0.001$). There was no interaction with severity ($F(2, 40) < 1$) and the effect was highly significant in all three groups ($t > 3.57, p < 0.004$).

Tactile/action: Finally, the manipulation of tactile/action qualities is shown in the right-hand panel of Figure 2. The effect of this manipulation was significant ($F(1, 40) = 18.7$, $p < 0.001$), indicating a naming advantage for items rated strongly for tactile/action knowledge. There was no interaction with severity ($F(2, 40) = 1.04$, $p = 0.36$); however, when the three groups were considered separately, the effect only reached significance in the moderate ($t = 2.28$, $p = 0.038$) and severe ($t = 5.00$, $p < 0.001$) groups.

Are high colour/form items more difficult to name?

Analysis of picture naming results indicated that highly familiar and typical items were more likely to be named correctly at all stages of the disorder and that high sensory richness also benefited naming. This richness advantage was also apparent for sound/motion and tactile/action modalities when these domains were studied separately. Conversely, no advantage was observed for items with rich colour/form characteristics; in fact, richness in this domain had a negative effect on performance in the more severe patients. This result supports the idea that representations of visual attributes are particularly affected later the disorder. However, another possibility is that high colour/form items were simply more difficult to name, perhaps because colour plays an important role in their identification and this information was absent from the black-and-white drawings used. To rule out this possibility, we turned to reaction time data collected from seventeen healthy subjects (mean age = 22) who named the same line drawings. Pictures were presented on a 15-inch computer monitor and participants were asked to name each picture as quickly as possible. No time limit was placed on responses. Reaction times were recorded using an electronic voice-key, with responses scored online and digitally recorded for later verification. If high colour/form items were more difficult to name, one would expect these items to be named more slowly by healthy participants. In fact, the opposite was observed. Reaction times for high colour/form

items ($M = 848\text{ms}$) were considerably faster than those for low colour/form items ($M = 991\text{ms}$) and this difference was highly significant ($t(16) = 6.73, p < 0.001$). Error rates were very low and did not differ between the two conditions. This result confirms that high colour/form items are intrinsically easier to name in the healthy population, making the significant disadvantage for these items in the severe SD cases all the more striking. Indeed, the reaction time advantage for high colour/form items in healthy subjects contrasts with the lack of any such advantage in the mild SD group, suggesting that some subtle impairment to visual attributes may be present even at an early stage.

Discussion

Though there is no doubt that SD patients present with selective conceptual knowledge deficits, the underlying cause of this impairment remains a subject of active debate. Some researchers hold that the deficit primarily reflects damage to a pan-modal hub, which develops representations that are independent of any particular sensory modality and license the formation of coherent concepts (Lambon Ralph *et al.* , 2010, Patterson *et al.* , 2007). Others propose that deficits in SD are primarily due to disruption to areas of the cortex that are specifically implicated in representing the visual characteristics of objects (Bonner *et al.* , 2009, Breedin *et al.* , 1994, Macoir, 2009). We investigated these two possibilities by exploring the impact of pan-modal and modality-specific stimulus factors on conceptual knowledge in SD. Naming was strongly influenced by pan-modal factors. Patients were more likely to name items that were highly familiar and highly typical of their class. We also found an advantage for concepts with high overall sensory richness, which was also observed in two specific modalities. Items were more likely to be named correctly if were rich in sound/motion or tactile/action characteristics. In contrast to all the other factors, a different pattern emerged for items rich in visual colour/form information. There was no advantage for

these concepts and, in the more severe patients, such items were instead disproportionately impaired.

How are these findings best reconciled with the theories of SD described above? We propose that the full pattern of results is best explained through a combination of continually increasing atrophy to pan-modal representations and later damage to visual-specific areas of cortex. Specifically, we suggest that the initial cause of knowledge impairment is damage to the pan-modal representations stored in the ventrolateral, anterior temporal lobes. This remains the primary cause of impairment throughout the progression of the disease, since atrophy remains centred on the same anterior region, explaining the large effects of pan-modal factors at all stages of severity. As the disease becomes more severe, however, additional impairments begin to emerge for concepts that rely heavily on visual characteristics. These are most likely to reflect the later spread of atrophy, which begins to envelop the posterior ventral temporal lobes (Bright *et al.* , 2008, Rohrer *et al.* , 2009), which are specialised for processing the visual features of objects (Chao *et al.* , 1999, Martin *et al.* , 1995, Thompson-Schill *et al.* , 1999).

We will consider the evidence for pan-modal degradation first. As discussed in the Introduction, conceptual knowledge in SD is lost for information presented in all sensory modalities and for all categories of object (Bozeat *et al.* , 2000, Patterson *et al.* , 2007). This pattern is unlikely to occur as a result of damage to a single, modality-specific system. Instead, the hub-and-spoke theory holds that the ventrolateral ATL-centred atrophy in SD affects all types of concepts because it damages central modality-invariant representations (Lambon Ralph *et al.* , 2010, Patterson *et al.* , 2007, Pobric *et al.* , 2010a). These representations are learned through the co-activation of information in different sensory-motor modalities but are themselves independent of any particular modality (Rogers *et al.* , 2004a). Damage to these representations consequently affects all concepts, regardless of

which particular modalities they are associated with. Neuroimaging evidence indicates that these representations are primarily underpinned by the ventrolateral anterior temporal lobes (centred on the anterior fusiform and inferior temporal gyri). This region is activated by a range of semantic processing tasks, including understanding of spoken words (Sharp *et al.* , 2004), comprehension of concrete and abstract written words (Binney *et al.* , 2010), classification of objects presented as words, pictures and environmental sounds (Visser and Lambon Ralph, 2011) and judgments of semantic association for word and picture stimuli (Visser *et al.* , 2012). In line with this evidence, a recent study of SD patients found that the degree of hypometabolism in the anterior fusiform correlated with their performance on tests of conceptual knowledge (Mion *et al.* , 2010). Hypometabolism in other regions was not related to semantic performance, even though the entire anterior temporal lobe, including the pole, was markedly hypometabolic. This study, taken with the converging evidence from functional neuroimaging in neurologically-intact participants, helps to pinpoint the anterior fusiform as the centre-point of the pan-modal “hub” cortex.

Consistent with the hub-and-spoke theory, in the present study we found that two pan-modal stimulus factors, familiarity and typicality, had strong effects on naming in SD, at all stages of disease severity. These effects have been reported previously in SD patients (Lambon Ralph *et al.* , 1998, Woollams *et al.* , 2008) and are consistent with breakdown in modality-invariant conceptual knowledge. The representations of highly familiar concepts are more strongly instantiated because the system has more opportunities to acquire their meanings. They also tend to be acquired earlier in life and to be encountered more often during the disease process, which may contribute to their relative preservation in the face of the progressive representational degradation (see Jefferies *et al.* , 2011, Lambon Ralph *et al.* , 1998). This phenomenon has been formally simulated in computational models that employ a layer of modality-independent processing units to capture conceptual structure. These

simulations indicate that more familiar concepts come to occupy a larger portion of the semantic space formed by the modality-independent layer, providing them with a greater robustness to damage (Simulation 5.4; Rogers and McClelland, 2004). Highly typical items may be preserved for similar reasons – typical exemplars, by definition, are similar in meaning and share many attributes in common. This means that, during development, learning about one typical exemplar will also boost the representations of other overlapping concepts within that semantic cohort. In comparison, atypical concepts do not overlap with as many other items and thus do not benefit from this same type of collateral boost.

We found that overall sensory richness, based on an item's average ratings of association with all sensory-motor modalities, was positively related to the level of remaining item knowledge in the SD cases. Concepts that were associated with a rich set of sensory-motor information were more likely to be named correctly, even though they were matched to less rich concepts in terms of familiarity and typicality. This positive effect supports the idea that rich sources of information about a concept lead to a strong representation that is relatively robust to damage (Plaut and Shallice, 1993). Words associated with richer semantic representations are also processed more efficiently by healthy subjects in a range of tasks (Pexman *et al.* , 2008). Similarly, we found that, within the domain of concrete objects, weaker sensory-motor information was associated with poorer object knowledge at all stages of SD. Extrapolating from this trend, one would expect abstract concepts, associated with more impoverished sensory-motor information, to be even more susceptible to damage. Case-series investigations suggest that this is indeed the case for the majority of SD patients (Hoffman and Lambon Ralph, 2011, Jefferies *et al.* , 2009). In a small number of cases, the reverse pattern has been observed (e.g., Breedin *et al.* , 1994, Macoir, 2009, Warrington, 1975) though these effects may be due to individual differences in the location of cortical

atrophy or in premorbid experience (Hoffman and Lambon Ralph, 2011, Jefferies *et al.* , 2011).

In contrast to the positive overall effect of rich sensory-motor information, there was no advantage associated with strong visual colour/form characteristics. Instead, items with strong colour/form ratings were named more poorly than matched items for which such visual information was less prominent. This effect was not present in the mildest cases but was apparent, with increasing magnitude, in the moderate and severe cases. This finding fits with previous investigations which found that, within the context of generally impoverished feature knowledge, SD patients were especially poor at reporting visual attributes (Breedin *et al.* , 1994, Lambon Ralph *et al.* , 1999, Lambon Ralph *et al.* , 2003, Tyler and Moss, 1998). Before turning to our preferred interpretation of these findings, there are a couple of alternative possibilities to address. The representations of living things are often thought to be more strongly dependent on visual information than those of manmade objects (Farah and McClelland, 1991, Warrington and Shallice, 1984), raising the possibility of a semantic category effect underpinning the observed reversed effect of visual-colour richness. However, the present results cannot be interpreted as a category effect because our high and low colour/form sets contained equal numbers of living and non-living items. Indeed, dissociations between living and non-living items are rare in SD (Lambon Ralph *et al.* , 2007). Nor was it the case that high colour/form items were intrinsically more difficult to name, because healthy subjects showed a processing advantage for these items. Instead, these results suggest that objects that are strongly associated with visual information are disproportionately impaired in the more severe stages of SD, in line with damage to visual association cortex.

This view is also consistent with the known progression of cerebral atrophy in SD. Representations of colour and visual form are associated with the posterior, ventral temporal

lobe, particularly the posterior fusiform gyrus (Chao *et al.* , 1999, Martin, 2007). Importantly, this region appears to be involved in conceptual knowledge of visual object properties, and not merely processing of visual input, because it is activated when visual property knowledge is probed verbally (Kellenbach *et al.* , 2001, Thompson-Schill *et al.* , 1999). The ventral, posterior temporal lobe is typically spared in the early stages of SD, in which the damage principally affects the temporal poles and the ventrolateral surface of the anterior temporal lobes (evident in terms of atrophy, hypometabolism and reduced connectivity; Acosta-Cabronero *et al.* , 2011, Galantucci *et al.* , 2011, Galton *et al.* , 2001, Nestor *et al.* , 2006) As the disease progresses, atrophy in these regions increases. In addition, cortical thickness measures and voxel-based morphometry indicate that the increasing atrophy begins to envelop posterior ventral temporal regions (Bright *et al.* , 2008, Rohrer *et al.* , 2009). This posterior spread of atrophy could be expected to disproportionately affect concepts that rely heavily on the visual attribute information assumed to be coded by the region. In contrast, the posterior middle and superior temporal gyri, associated with sound and motion characteristics, are less severely affected as atrophy spreads, as are the parietal and frontal sites associated with tactile information and knowledge of object manipulation.

In the present study, we probed conceptual knowledge through picture naming, because this task is reliably impaired at all stages of the disorder and because it is clear that anomia in SD is the consequence of core conceptual deterioration and not a visually-specific deficit. The use of pictures raises an important question, however: is the visual spoke region solely a representational area, concerned with representing object properties that are usually experienced through vision, or is it directly involved in the perceptual identification of visually-presented objects? This distinction has sometimes caused confusion in discussion of modality-specific semantic systems (Coltheart *et al.* , 1998). In our view, however, these two positions are difficult to disentangle. Identification of objects from vision relies very heavily

on having intact semantic knowledge of how objects usually appear. Similarly, identifying an object from its sound depends critically on an intact representation of the object's auditory properties. So if we assume that the visual spoke region codes the typical visual characteristics of *giraffes*, for example, then it follows that this region (in concert with the hub) will make a critical contribution when someone is asked to identify a picture of a giraffe. The important point from our perspective is that spoke regions contribute to conceptual knowledge even when the modality of input does *not* match the modality of the probed knowledge. Posterior, ventral fusiform activation has been demonstrated, for example, when visual object properties are probed verbally (Kellenbach *et al.* , 2001, Thompson-Schill *et al.* , 1999); inferior parietal regions associated with action knowledge are activated when object manipulation judgements are made in response to static pictures (Van Dam *et al.* , in press); and superior temporal regions linked to auditory knowledge are activated when the names of sound-making objects are presented as written words (Kiefer *et al.* , 2008). It seems likely, therefore, each spoke region contributes to semantic processing whenever attributes in its modality are relevant to the task in hand, irrespective of the modality of the sensory input.

To summarise, our investigation of the factors underpinning impairment of object knowledge in SD supports a multi-component model, which is consistent with the known progression of cortical atrophy in the disorder. Based on the hub-and-spoke theory of conceptual knowledge, we propose that atrophy to the ventrolateral anterior temporal lobes, present from the earliest stages of neurodegeneration, affects transmodal 'hub' representations that are independent of any particular sensory-motor modality. This results in a pan-modal, pan-categorical knowledge deficit which remains the principal feature throughout the disorder as the severity of atrophy in this region increases. . Later in the disorder, the boundary of atrophy extends into the posterior ventral temporal lobes, affecting a modality-specific "spoke" region that codes the visual attributes of objects. This later

damage begins to disproportionately affect concepts that rely heavily on this source of information. By positing a multi-component explanation, this approach has the potential to reconcile the differing viewpoints on the functional basis of conceptual impairment in SD.

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Table 1: Mean test scores for each group

Test/factor	Max	Mild		Moderate		Severe		Healthy Controls
		Mean	<i>N</i>	Mean	<i>N</i>	Mean	<i>N</i>	Mean (cut-off)
Age	--	62	<i>14</i>	64	<i>15</i>	68	<i>14</i>	
Education (leaving age)	--	15.8	<i>14</i>	15.5	<i>15</i>	16.3	<i>14</i>	
Picture Naming	64	43	<i>14</i>	22	<i>14</i>	9	<i>14</i>	62.3 (59)
Category fluency (6 categories)	--	48	<i>7</i>	26	<i>11</i>	17	<i>9</i>	95.7 (62)
Word-Picture Matching	64	55	<i>12</i>	41	<i>13</i>	31	<i>13</i>	63.8 (62)
Camel and Cactus test (pictures)	64	45	<i>8</i>	31	<i>10</i>	32	<i>9</i>	59.1 (51)
Letter fluency (FAS)	--	19	<i>7</i>	21	<i>11</i>	17	<i>9</i>	41.1 (17)
MMSE	30	27	<i>7</i>	25	<i>9</i>	21	<i>8</i>	28.8 (24)
Digit span forwards	--	6.5	<i>8</i>	6.3	<i>12</i>	5.3	<i>10</i>	6.8 (4)
Digit span backwards	--	4.8	<i>8</i>	4.3	<i>12</i>	4.4	<i>9</i>	4.8 (3)
Raven's progressive matrices	36	33	<i>7</i>	28	<i>11</i>	30	<i>10</i>	
Rey figure copy	36	35	<i>8</i>	29	<i>12</i>	33	<i>10</i>	34.0 (31)
VOSP: incomplete letters	20	19.3	<i>7</i>	16.9	<i>11</i>	15.0	<i>10</i>	18.8 (16)
VOSP: object decision	20	17.0	<i>7</i>	13.6	<i>11</i>	13.9	<i>10</i>	17.7 (14)
VOSP: number location	10	9.7	<i>7</i>	9.5	<i>11</i>	9.5	<i>10</i>	9.4 (7)
VOSP: cube analysis	10	9.6	<i>7</i>	9.3	<i>11</i>	8.5	<i>10</i>	9.2 (6)

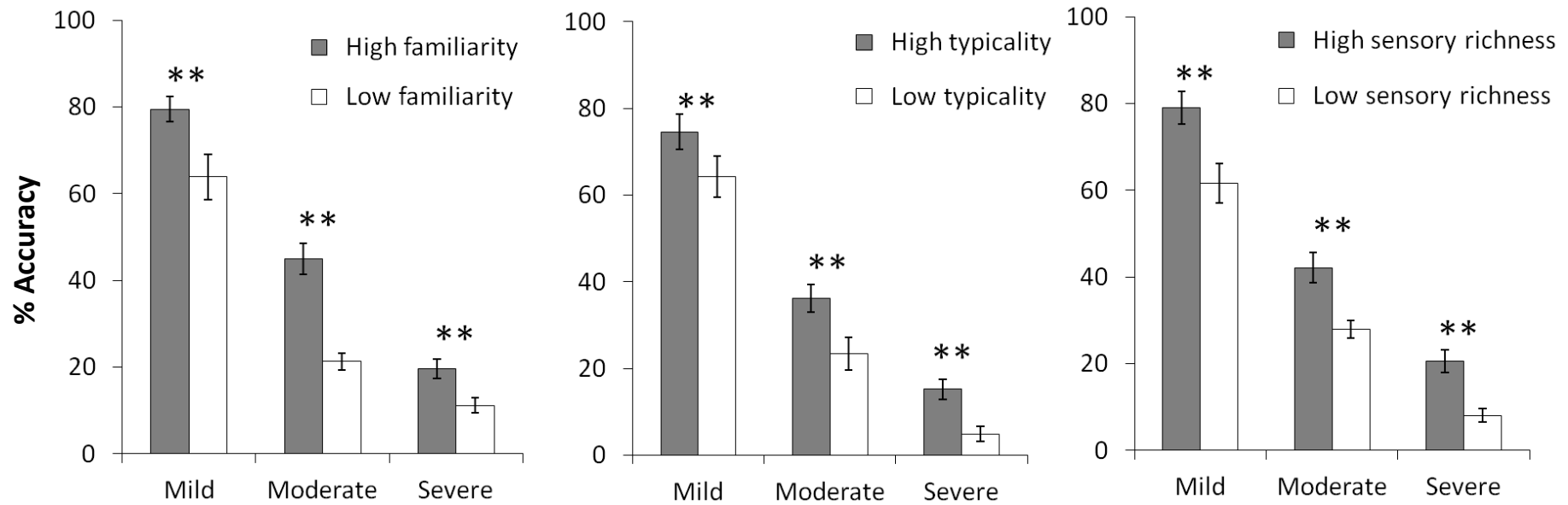
Impaired scores are shown in **bold** (below published cut-offs or greater than two standard deviations below the mean in healthy subjects). Numbers in italics indicate the number of observations contributing to each mean.

Table 2: Mean (standard deviation) properties of each stimulus set

Manipulation	Item set	Familiarity	Typicality	Sensory richness	Colour and form	Sound and motion	Tactile and action	Log word frequency
Familiarity	High	6.52 (.33)	3.10 (.57)	4.08 (.58)	5.73 (.78)	3.95 (1.49)	4.07 (.66)	1.34 (.38)
	Low	5.27 (.45)	2.96 (.76)	3.85 (.38)	5.48 (.55)	4.79 (1.19)	3.80 (.83)	1.14 (.43)
Typicality	High	6.04 (.75)	3.55 (.23)	4.00 (.48)	5.54 (.74)	4.49 (1.38)	3.88 (.81)	1.07 (.41)
	Low	5.96 (.56)	2.13 (.67)	3.95 (.53)	5.84 (.75)	3.76 (1.35)	3.92 (.84)	1.00 (.41)
Sensory richness	High	6.11 (.58)	2.97 (.88)	4.33 (.39)	5.80 (.76)	4.62 (1.59)	4.13 (.67)	1.34 (.46)
	Low	5.89 (.78)	2.91 (.84)	3.62 (.31)	5.65 (.67)	3.90 (1.01)	3.68 (.89)	1.21 (.33)
Colour/form	High	5.94 (.77)	3.06 (.73)	4.03 (.51)	5.94 (.59)	4.40 (1.04)	3.84 (.80)	1.16 (.51)
	Low	5.84 (.80)	3.06 (.73)	3.77 (.44)	5.25 (.53)	4.53 (1.26)	3.79 (.81)	1.18 (.47)
Sound/motion	High	5.90 (.74)	2.88 (1.0)	4.04 (.41)	5.51 (.71)	5.32 (.70)	3.75 (.89)	1.15 (.43)
	Low	6.03 (.77)	2.83 (.87)	3.78 (.68)	5.70 (.72)	3.07 (.64)	3.96 (.84)	1.11 (.44)
Tactile/action	High	6.15 (.75)	3.03 (.78)	4.12 (.36)	5.57 (.65)	4.40 (1.23)	4.55 (.63)	1.29 (.59)
	Low	6.02 (.59)	2.89 (.81)	3.91 (.61)	5.63 (.79)	4.38 (1.32)	3.53 (.65)	1.09 (.40)

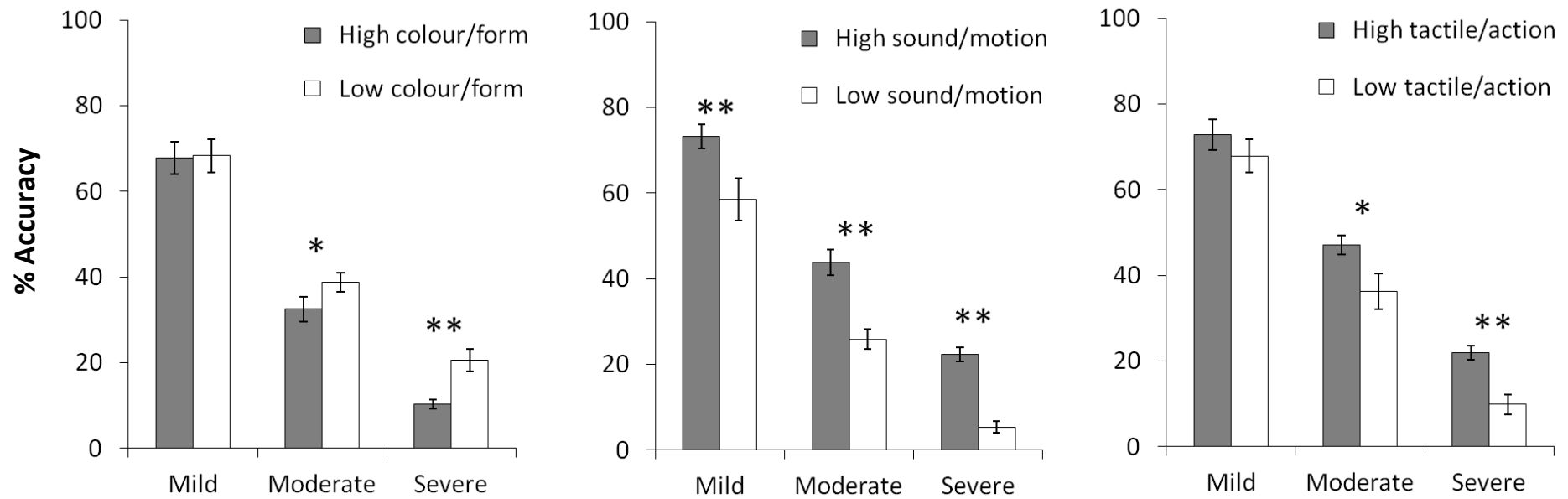
High and low values shown in bold differed significantly from each other ($p < 0.005$). No other pairs differed significantly ($p > 0.09$).

Figure 1: Manipulations of familiarity, typicality and sensory richness



** indicates high and low conditions differ at $p < 0.01$. Bars indicate one standard error of mean.

Figure 2: Manipulations of richness in particular sensory modalities



* indicates high and low conditions differ at $p < 0.05$. ** indicates $p < 0.01$.

Supplementary Table: Neuropsychological test scores for individual patients

Test/item	Max	DF	MT	JW	MB	SJ	BS	NH	PL	EK	KI	GE	GT	PW	TM	JT	PD
<i>Naming observations</i>		5	4	2	4	3	3	5	3	3	1	2	2	3	1	1	1
Sex		M	F	F	F	F	M	F	F	F	M	M	M	M	M	M	F
Age		62	60	62	60	59	68	64	72	59	65	50	70	73	66	66	72
Education (leaving age)		16	16	16	15	16	16	16	15	15	14	16	14	17	24	16	14
Picture Naming	64	55	46	43	36	30	29	26	22	19	15	13	11	8	7	6	4
Word-Picture Matching	64	60	57	61	47	59	40	37	44	45	36	32	32	35	50	34	17
Camel and Cactus test (pictures)	64	53	45	49	41	51	37	41	30	33	20	32	27	34	51	31	17
Category fluency (6 categories)		57	65	53	45	31	45	30	26	31	27	22	24	22	NT	9	7
Letter fluency (FAS)		13	30	19	20	23	33	14	24	29	17	19	24	13	NT	17	22
MMSE	30	26	29	29	27	23	25	NT	23	27	23	NT	26	23	NT	25	13
Digit span forwards		7	7	6	6	5	8	5	8	6	8	7	6	5	3	8	7
Digit span backwards		4	5	6	6	3	4	4	5	7	5	4	7	4	NT	4	5
Raven's progressive matrices	36	34	35	32	32	34	30	20	31	33	21	33	35	34	29	36	25
Rey figure copy	36	36	36	34	33	33	33	26	31	34	34	35	34	34	31	31	36
VOSP: incomplete letters	20	19	20	19	20	20	19	18	19	20	8	18	18	16	18	18	3
VOSP: object decision	20	20	20	12	18	16	18	15	15	12	15	13	12	18	19	15	6
VOSP: number location	10	10	10	8	10	10	10	10	7	10	10	9	10	10	8	9	9
VOSP: cube analysis	10	10	10	10	9	10	10	9	9	10	10	10	10	10	8	10	5

NT = Not tested. **Bold** indicates impaired scores.

Items in each stimulus set

High familiarity		Low familiarity	
Item	Value	Item	Value
bicycle	6.7	basket	5.9
brush	6.9	camel	5.1
candle	6.6	eagle	4.9
cat	6.9	frog	5.1
chicken	6.4	hammer	5.6
comb	6.5	helicopter	5.3
duck	6.1	horse	6.0
dustbin	6.5	lorry	5.4
elephant	5.9	monkey	5.0
key	6.9	mouse	5.1
pineapple	6.3	owl	4.7
plane	6.6	piano	6.3
plug	6.8	pliers	4.7
rabbit	6.6	saw	5.4
swan	6.0	spanner	5.1
tomato	6.8	tiger	5.1

High typicality		Low typicality	
Item	Value	Item	Value
brush	3.5	candle	2.3
bus	3.9	cherry	3.2
comb	3.3	elephant	3.1
duck	3.5	frog	1.7
eagle	3.4	paintbrush	2.5
hammer	3.8	penguin	1.2
lorry	3.7	piano	1.6
motorbike	3.3	pineapple	2.2
owl	3.6	plane	2.6
pear	3.8	sledge	1.2
rabbit	3.5	squirrel	3.1
screwdriver	3.8	stool	2.7
strawberry	3.8	suitcase	1.9
swan	3.4	tomato	1.8
tiger	3.2	tortoise	1.4
toaster	3.4	watering can	1.6

High sensory richness		Low sensory richness	
Item	Value	Item	Value
bus	4.3	barrel	2.9
candle	4.0	bicycle	3.8
cherry	4.7	brush	3.5
chicken	5.2	camel	4.0
duck	4.4	comb	3.4
elephant	4.3	eagle	3.4
frog	4.1	key	3.8
glass	3.9	mouse	4.0
hammer	4.0	penguin	3.7
helicopter	3.9	plug	3.4
horse	4.7	rabbit	3.9
lorry	3.8	screwdriver	3.5
motorbike	4.3	squirrel	3.5
piano	4.3	suitcase	3.4
pineapple	4.9	swan	3.8
tomato	4.6	tiger	4.0

High colour/form		Low colour/form	
Item	Value	Item	Value
bus	5.7	bicycle	4.7
camel	6.5	brush	4.9
candle	5.4	cat	5.4
chicken	6.2	comb	5.0
cow	6.3	duck	6.0
elephant	6.7	eagle	5.3
hammer	5.2	lorry	4.7
key	5.7	motorbike	4.4
peacock	6.4	mouse	6.0
penguin	6.5	ostrich	5.6
scissors	5.5	pliers	5.0
spanner	5.5	rabbit	5.3
stool	5.2	squirrel	6.0
swan	6.8	suitcase	4.8
tiger	6.4	tortoise	6.0
toaster	5.3	train	5.1

High sound/motion		Low sound/motion	
Item	Value	Item	Value
bicycle	4.8	apple	2.9
bus	5.8	basket	2.0
cat	6.2	cherry	2.1
cow	5.5	dustbin	2.3
duck	5.8	envelope	2.8
eagle	4.9	glass	3.3
frog	5.5	orange	2.8
helicopter	6.0	ostrich	3.3
lorry	5.6	peacock	3.7
motorbike	6.4	rabbit	4.1
owl	5.7	screwdriver	3.2
penguin	4.8	squirrel	4.2
piano	5.5	stool	2.5
scissors	4.4	suitcase	3.3
sledge	4.0	tortoise	3.5
swan	4.5	watering can	3.2

High tactile/action		Low tactile/action	
Item	Value	Item	Value
bicycle	4.7	brush	4.1
camel	3.5	chicken	3.9
cat	4.9	cow	3.8
cherry	4.1	duck	3.0
dog	5.0	dustbin	3.4
envelope	4.7	elephant	3.3
frog	3.5	helicopter	3.4
glass	5.3	motorbike	4.1
horse	5.0	penguin	2.4
mouse	3.4	plug	4.3
paintbrush	5.4	squirrel	2.6
piano	5.1	stool	4.2
rabbit	4.4	suitcase	4.1
saw	4.5	swan	2.9
scissors	4.9	toaster	4.3
spanner	4.7	tortoise	2.9