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Evidence of semantic processing impairments in behavioural variant frontotemporal dementia and Parkinson's disease

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Abstract

Purpose of review—Category-specific impairments caused by brain damage can provide important insights into how semantic concepts are organized in the brain. Recent research has demonstrated that disease to sensory and motor cortices can impair perceptual feature knowledge important to the representation of semantic concepts. This evidence supports the grounded cognition theory of semantics, the view that lexical knowledge is partially grounded in perceptual experience and that sensory and motor regions support semantic representations. Less well understood, however, is how heteromodal semantic hubs work to integrate and process semantic information.

Recent findings—Although the majority of semantic research to date has focused on how sensory cortical areas are important for the representation of semantic features, new research explores how semantic memory is affected by neurodegeneration in regions important for semantic processing. Here, we review studies that demonstrate impairments to abstract noun knowledge in behavioural variant frontotemporal degeneration (bvFTD) and to action verb knowledge in Parkinson's disease, and discuss how these deficits relate to disease of the semantic selection network.

Summary—Findings demonstrate that semantic selection processes are supported by the left inferior frontal gyrus (LIFG) and basal ganglia, and that disease to these regions in bvFTD and Parkinson's disease can lead to categorical impairments for abstract nouns and action verbs, respectively.

Keywords

basal ganglia; behavioural variant frontotemporal dementia; inferior frontal gyrus; Parkinson's disease; semantic selection; semantics

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Conflicts of interest

The authors have no conflicts of interest to report.

INTRODUCTION

Semantic memory is a long-term memory system that stores lexical, concept and object knowledge, and is fundamental to the ability to generalize information. Here, we review research that reveals how semantic processing is affected by neurodegenerative disease and degradation of the semantic selection network.

The consequences of degraded semantic memory are apparent with temporal lobe degeneration, resulting in the devastating loss of object and word recognition or production, seen most notably in semantic variant primary progressive aphasia (svPPA), but also in logopenic variant primary progressive aphasia (lvPPA) and Alzheimer's disease [1–4]. A primary goal within the field of neurolinguistics is to understand how the semantic system is organized, and how different regions in the semantic network work in combination to support lexical representations. The theory that semantic cognition is grounded in sensory and motor experience has gained much popularity in recent years, and has dominated the semantic debate for the past decade [5–7]. With the rise of grounded cognition, research has been dedicated to detailing the feature content of lexical representations and how lexical knowledge is composed of different sensory, perceptual and motor features. In support, functional imaging studies have shown that words with high action content activate motor processing regions [8,9], and similar findings have been observed with respect to olfactory content [10], auditory content [11] and colour content [12]. Critiques of grounded views of semantics have pointed out that activation of sensory and motor cortices during semantic processing may be auxiliary and not necessary for the representation of lexical concepts per se [13,14]. Patient studies thus provide an important line of evidence, showing that focal damage to sensory or motor cortices can cause specific deficits for different semantic categories. Accordingly, impaired action concept processing in amyotrophic lateral sclerosis (ALS) has been linked to disease in the primary motor and premotor cortex [15,16], impaired auditory concept processing in lvPPA has been related to disease in auditory association cortex [17], and impaired visual concept processing in late stages of svPPA has been related to disease in visual ventral stream [18]. Thus, semantic category effects in patients have demonstrated how modality-specific regions functionally contribute to lexical representations.

Many semantic models theorize that, beyond the contributions of sensory and motor networks, heteromodal convergence zones, or hubs, also play an important role in high-level processing, including abstraction and the integration of lexical information [19,20]. Several processing hubs have been proposed, including the inferior frontal cortex, inferior parietal cortex, superior temporal cortex, middle/inferior temporal cortex, anterior temporal cortex and temporal pole [5,21]. Although there is general agreement that hubs of semantic processing exist, their specific contributions to the integration and representation of lexical information is still vague. By examining disorders that affect heteromodal convergence and processing regions, we can better understand how words are represented. In this review, we focus on one processing hub, the left inferior frontal gyrus (LIFG), which is thought to support the semantic selection of an appropriate meaning from a set of competing alternatives [22,23]. In addition, we discuss the contribution of the basal ganglia, which have been recognized as playing an important supervisory role during semantic selection and

other language operations [24,25]. It may be that semantic selection and control functions of the LIFG and basal ganglia are especially important in the representation of complex words, including abstract nouns and action verbs, whose various interpretations place high demands on the semantic processing system. To better understand the function of the LIFG and basal ganglia in semantic processing, we review both historical and recent evidence of semantic category deficits in two patient groups who are traditionally considered nonaphasic: behavioural variant fronto-temporal degeneration (bvFTD) and Parkinson's disease. The semantic category deficits in these patients can provide important insights into how semantic information is processed, and the role of selection and control in semantic retrieval.

Semantic selection mechanisms in the processing of abstract nouns in behavioural variant frontotemporal degeneration

Since the 'concreteness effect' – the phenomenon that concrete words tend to be recognized more quickly than abstract words [26,27] – was first observed in healthy adults, researchers have tried to understand what systems might underlie differences in the semantic features that comprise concrete and abstract words. That is, concrete nouns tend to refer to concepts that have physical or temporal existence and are strongly associated with visual features, whereas abstract nouns do not. Thus, the dual-coding theory hypothesizes that, while both abstract and concrete representations have a symbolic/verbal form, only concrete representations are additionally supported by sensory/visual features. Because of their high feature content, concrete concepts are thought to be more semantically rich than abstract. This perspective also predicts that because concrete nouns are highly imageable, their representation includes bilateral visual and auditory cortical regions, whereas the representation of abstract nouns will be limited to the auditory regions centred in the left superior temporal lobe. The dual-coding theory is related to more contemporary theories of grounded cognition; both perspectives emphasize that the feature content of a concept shapes its representation, and both agree that perceptual features are especially important for the representation of concrete objects. Unlike the dual-coding theory, however, grounded cognition views propose that abstract nouns are also embodied, but through metaphorical invocations or through emotional experience [28,29].

In addition to differences in perceptual features, studies of semantic memory in bvFTD point to important processing differences between concrete and abstract nouns. Patients with bvFTD are typified by extensive atrophy to the frontal lobes, and can experience profound cognitive alterations, including behavioural changes and executive functioning impairments [30,31]. Compared with temporal variants of frontotemporal dementia (e.g. svPPA and lvPPA), however, language capabilities in bvFTD remain relatively preserved [32]. Still, a few studies have noted subtle deficits to discourse [33] and syntax [34] in bvFTD due in part to executive dysfunction. Most recently, studies have shown that bvFTD patients are impaired for both the comprehension [35▪] and production [36▪] of abstract nouns. In both studies, impaired performance for abstract nouns in bvFTD related to atrophy of the frontal lobes including the LIFG, as well as the bilateral caudate for abstract noun production.

Why might disease to the LIFG in bvFTD lead to impairment for abstract noun knowledge, more so than concrete? A possible explanation is that the processing demands for abstract

nouns are higher than for concrete nouns. While concrete concepts are strongly associated with perceptual experience, abstract concepts are less tangible and tend to be encountered more through the mind or language [37]. In addition, abstract concepts are more polysemous and appear in a more diverse set of contexts than their concrete counterparts [38]. This increased semantic diversity means that abstract nouns are more ambiguous, with more competing interpretations than concrete nouns, and may thus rely more on the surrounding linguistic context to facilitate meaning selection and efficient processing [39]. Because of high processing demands, abstract concept knowledge is thought to be supported in part by the LIFG [40▪]; the LIFG has been shown to facilitate semantic selection amongst competing alternatives [22,41,42], as well as in the unification of a lexical item with its surrounding context [43,44]. The role of the LIFG in abstract noun processing is further supported by functional imaging studies, which show increased activation of the LIFG when healthy individuals are presented with abstract nouns, compared with concrete [23,45]. Taken together, these findings indicate that impaired abstract noun knowledge in bvFTD may be due to atrophy of the LIFG and semantic selection network.

Executive functioning and control in the processing of verbs in Parkinson's disease

Although object nouns are thought to rely on sensory and visual features, grounded cognition predicts that the representations of action verbs are associated with motor experience. In support, functional imaging shows that the presentation and production of action verbs elicits activation in the premotor and supplementary motor regions [46,47]. To test whether motor dysfunction leads to impaired action verb knowledge, multiple studies have examined action verb deficits in patients with Parkinson's disease with and without overt cognitive impairment. Compared with relatively preserved noun knowledge, studies have consistently shown that patients with Parkinson's disease are impaired for action verbs during lexical decision [48], comprehension [49], generation [50,51] and naming tasks [52▪, 53,54]. The role of the motor system during action verb processing is further supported by an experiment demonstrating that levodopa treatment – which is commonly administered as therapy for basal ganglia dysfunction – is associated with increased activation of motor and premotor cortex during the generation of action verbs [55]. Although action verb impairment in Parkinson's disease is a consistent finding, few studies have specifically examined the effect of motor content. In two studies that controlled for part of speech by comparing nouns to nouns and verbs to verbs, patients with Parkinson's disease demonstrated no effect of high and low motor content; while patients with Parkinson's disease were impaired for verbs compared with nouns, there was no significant difference in performance between manipulable and nonmanipulable object-nouns, or between verbs with motor and nonmotor content ([56,57]; but see also [52▪]). These findings suggest that the verb impairment in Parkinson's disease may be due to more than impoverished motor representations.

There is evidence that verbs place increased demands on the semantic processing system [58–60], contributing to their dissociation from nouns. Verbs do not only differ from nouns in their perceptual feature content, but they also have more morphological forms than nouns, and contain grammatical and syntactic information that assume thematic roles [61]. For example, the verb 'drink' assumes an agent that is doing the drinking and a recipient that is being drunk. The complexity of semantic, thematic and syntactic information associated

with verbs means that their processing likely requires additional support from semantic selection and integration mechanisms of the LIFG and basal ganglia [62].

Differences in processing demands between parts of speech may explain why action verbs are impaired in Parkinson's disease, while object noun knowledge is relatively preserved. Although Parkinson's disease is classically thought of as a movement disorder, cognitive impairments have recently been recognized as commonly occurring [63]. Although many studies have linked the verb deficit in Parkinson's disease to degraded motor representations [53–55], there is also evidence that poor executive functioning due to fronto-striatal disease contributes to the verb deficit in Parkinson's disease [64,65]. Although the basal ganglia are not thought play a language-specific role in verb processing, their function in supervisory operations – inhibition of irrelevant information and enhancement of relevant information – may be important for efficient semantic selection processes [66,67]. Indeed, poor verb processing in Parkinson's disease has been linked to basal ganglia dysfunction and the role of the basal ganglia in inhibition and semantic selection processes during verb processing [25]. Moreover, when semantic selection demands are increased, patients with Parkinson's disease significantly delayed word generation, regardless of part of speech [68▪▪].

Semantic selection, control and the role of the left inferior frontal gyrus and basal ganglia

Findings demonstrate that disease to the LIFG in bvFTD or basal ganglia in Parkinson's disease may lead to impaired processing for complex, semantically diverse words, including abstract nouns or action verbs. Importantly, there is some overlap in the regions affected by degeneration between bvFTD and patients with Parkinson's disease; disease in Parkinson's disease can include frontal regions and striatal connections, especially in later stages [69], and atrophy in bvFTD can extend to the basal ganglia in some cases [31]. It may be that semantic deficits observed in both patient groups are due to the degeneration of multiple regions within the semantic selection and control network. In the case of abstract noun production in bvFTD, decreased production of abstract nouns related to atrophy of the LIFG as well as the bilateral caudate nucleus [36▪]. Thus, both the LIFG and basal ganglia may be components of the semantic selection system and play an important role in the processing of abstract nouns and action verbs. Indeed, a functional imaging study by Canini *et al.* [70▪▪] implicates both the LIFG and basal ganglia in semantic control processes, showing increased activity of the LIFG and left caudate nucleus with cumulative semantic interference, the phenomenon of increasing naming latency after the presentation of categorically related/competitive items. This contribution of both the LIFG and basal ganglia in semantic selection processes is supported by diffusion tensor imaging studies, which demonstrate white matter connections between the two regions [71,72]. These connections are functional, and deep brain stimulation of the subthalamic nucleus in patients with Parkinson's disease is associated with decreased cerebral blood flow of the LIFG [73], and impaired ability to select from competing alternatives ([57]; but see also improved selection from competing alternatives, [74]). Together, studies indicate that disease to the semantic selection processes can result in category-specific deficits for patient groups not typically associated with aphasia.

It should be noted that we have focused on research that examines how neurodegeneration impairs retrieval of single words. Importantly, however, lexical representations are likely dynamic: processing demands and the role of perceptual features can change across different semantic tasks [8,75]. Surrounding linguistic and nonlinguistic information provides context that can alter the salience of sensory features and thereby affect how words are processed. Concepts are acquired over repeated and varied experiences, which can be physical, emotional, social or linguistic in nature [37]. Likewise, the understanding or expression of concepts in the real world is within unique situations that carry varying frames of reference. Thus, a word is not strictly defined through subordinate sensory features, but always encountered within a context that modifies its processing. As Binder [20] points out, concepts have semantic and thematic associates that are flexible and context-dependent. This flexibility means that the significance of sensory and motor features can change depending upon taskdemands or patient group, and semantic selection and control processes are only a part of a larger semantic network that contribute to lexical representations. It is therefore important to reiterate that both perceptual feature and processing differences between abstract and concrete nouns and between nouns and verbs likely contribute to their dissociation.

CONCLUSION

Research examining dissociations between word categories – abstract versus concrete, or nouns versus verbs – in patient groups has largely focused on differences in feature content. However, there is evidence that differences in processing demands may also contribute to categorical disassociations. We highlight studies which demonstrate that bvFTD patients are selectively impaired for abstract nouns compared with concrete nouns, while patients with Parkinson's disease are selectively impaired for action verbs compared with object nouns. These deficits are associated in part with disease to the semantic selection and control network, including the LIFG and BG. Importantly, perceptual feature and semantic processing perspectives are compatible, and understanding how each contributes to concept representations is an important focus for future research.

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KEY POINTS

- Semantic selection mechanisms are thought to be important to the processing of words with high semantic diversity, such as abstract nouns or action verbs.
- Degradation of the LIFG in bvFTD has been linked to a deficit for abstract nouns, compared with concrete nouns.
- Patients with Parkinson's disease are impaired for action verbs compared with object nouns, due in part to degradation of the basal ganglia.
- These impairments implicate the LIFG and the basal ganglia in semantic selection mechanisms important for abstract noun and action verb processing.