REVIEW ARTICLE

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Semantic memory and language dysfunction in early Alzheimer's disease: a review

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Background: Language impairment in Alzheimer's disease occurs early, and language function deteriorates with progression of the illness to cause significant disability. This review focuses on language dysfunction in Alzheimer's disease and the contribution of semantic memory impairment.

Methods: Electronic publication databases were searched for literature relevant to the review. Additionally, individual references were examined to elicit further studies not found by online search.

Results: Language impairment in Alzheimer's disease initially affects verbal fluency and naming before breakdown in other facets. Naming and fluency require integrity of semantic concepts, and dysfunction may be a marker of primary semantic memory impairment rather than overall cognitive decline. Research suggests the presence of semantic loss several years prior to diagnosis. Imaging studies indicate an altered connectivity state with respect to language networks, and this is associated with potential semantic failure. This state may also be present in individuals with established risk factors for Alzheimer's disease. Compensatory recruitment of alternative cortical areas to supplement language function appears to occur and may be a target for future intervention.

Conclusions: Identifying and classifying the nature and degree of language impairment more closely could aid in developing targeted therapies. Treatments already established in other aphasic states, such as post-stroke, may be especially relevant. The nature of these and the protective nature of cognitive reserve are potential therapeutic avenues.

Key words: Alzheimer's disease; language; semantic memory; naming; category fluency
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Introduction

Loss of certain facets of language occurs in a significant proportion of Alzheimer's disease (AD) patients (Henry *et al.*, 2004; Taler and Phillips, 2008; Minati *et al.*, 2009; Clark *et al.*, 2009), in particular with verbal fluency and naming (Henry *et al.*, 2004; Apostolova *et al.*, 2008; Taler and Phillips, 2008). There is increasing evidence that language dysfunction begins several years prediagnostically (Auriacombe *et al.*, 2006), suggesting this could be a possible prognostic marker and target for early therapeutic intervention. This piece aims to review relevant literature and clarify whether dysfunction is a primary phenomenon or characteristic of overall cognitive deterioration in AD. In highlighting the nature of this dysfunction, an additional aim is considering potentially transferable therapies for the deficit.

Normal language function

Historically, language models have focused on Broca's and Wernicke's areas in the left perisylvian cortex (Saffran, 2000). However, the importance of other areas has been highlighted by neuroimaging (Dronkers, 1996; Wise *et al.*, 1999). Speech activated centres are noted in bilateral auditory cortices (Calvert *et al.*, 1997; Belin *et al.*, 2000), implying that function is not restricted to dominant hemispheres. Studies utilising selective disruption of function, by electrical stimulation, have suggested that there is high variability in language

localisation to classical areas (Ojemann *et al.*, 1989). The extent of regional activation depends on discourse, for example differential patterns exist between single word and sentence processing (Vigneau *et al.*, 2006). Finally, subregions within identified areas appear variably important in processing (Hickok and Poeppel, 2007; Shalom and Poeppel, 2008). The model has evolved to one describing a complex and intimate organisation of multiple specialised areas (Gitelman *et al.*, 2005; Vigneau *et al.*, 2006).

The wider nature of this network provides evidence for support of language function following injury to conventional regions. Research with children has supplemented arguments for cortical plasticity supporting linguistic function in nondominant hemispheres. Bates (1999) reported that for a population of under-five-year olds with unilateral damage to either hemisphere, there could be retained capacity for language development. Similarly, Vannest *et al.* (2009) used functional magnetic resonance imaging (fMRI) in children to show potential identification of reorganisation of classical language networks following cortical injury. Even in adult aphasics, individuals with left hemisphere lesions can show neuroplasticity (Thompson, 2000), and studies have shown right hemisphere recruitment when necessary (Karbe *et al.*, 1998; Ansaldo *et al.*, 2002).

The language network is more diffuse than originally postulated, and although select cortical foci may be vital, there may similarly be plasticity in response to injury. Highlighting this complexity is fundamental when considering whether clinical aspects of dysfunction result from isolated areas of cortical disturbance or an overall breakdown of the entire system, in correlation with cognitive decline in AD. Additionally, re-evaluating this model allows consideration of compensatory cortical plasticity in response to AD neuropathology.

The language deficit in Alzheimer's disease

Published work over the last 30 years has established a language deficit in AD, suggesting this can be documented early. Appell *et al.* (1982) highlighted the paucity of AD studies describing language dysfunction at that time. The authors noted that AD patients showed a mixture of expressive and receptive deficits. Utilising standardised testing, they found early loss of naming and comprehension, although contrastingly retained articulation and syntax. Subsequently, it has been confirmed that there are deficits in verbal fluency and naming (Taler and Phillips, 2008), with little deterioration in syntax (Taler and Phillips, 2008). Focal elements appear to be impaired early, arguing for primary deterioration rather than simple overall decline.

Fluency and naming

A comprehensive meta-analysis by Henry *et al.* (2004) focused on verbal fluency. The tests scrutinised were semantic fluency (for example naming animals, also described as category fluency) and phonemic fluency (naming words beginning with 'f, a, and s'; frequently referred to as letter or, confusingly, verbal fluency). They established that significant deficits were consistently seen in semantic and phonemic fluency in AD. Both semantic fluency and Boston Naming Test (BNT) performance were worse than phonemic fluency, although this was less marked with BNT. The authors argue that the BNT results were less impaired because BNT provides more support in lexical searching.

Another meta-analysis focused on category naming (Laws *et al.*, 2007). The primary question was whether a naming deficit in AD is category specific, that is: does the disease affect concepts of living versus nonliving things differentially? This was based on previous work that argued distinctive features of living objects make these concepts more vulnerable to early damage (Chan *et al.*, 2001). Analyses showed large impairments in lexical semantics of AD patients but no significant differences between identifying living and nonliving items. Interestingly, there was no relationship between mini mental state examination (MMSE) and performance. A finding replicated in other studies and one suggesting language deficit is not accurately represented by MMSE. Lack of correlation supports ideas that language disturbance can be distinguished from overall cognitive decline.

Evolution of dysfunction

How then does language dysfunction progress? Taler and Phillips (2008) compared language function with AD and mild cognitive impairment (MCI), and highlight performance differences on standardised and nonstandardised language measures. They conclude language deficits occur preclinically in AD and arise in fields of semantic fluency and naming. It is suggested that these are semantic deficits rather than phonological, as in probable AD.

A longitudinal analysis of patients, with both preclinical and established AD (compared with normal ageing), showed steeper decline in category (semantic) relative to verbal (phonemic) fluency (Clark *et al.*, 2009). Patients were categorised within three groups:

preclinical AD, prevalent AD and normal ageing. Following baseline neuropsychological testing, patients were followed up over 2 years. Baseline testing showed significant differences in performance on verbal fluency tasks between prevalent AD and normal groups. Semantic fluency was more impaired than phonemic, as previously established. Preclinical AD patients had a similar pattern of deficits on semantic fluency tasks (although not phonemic) to AD patients. In the longitudinal element, semantic fluency declined at a greater rate than phonemic fluency among all groups. Rate of decline in the preclinical and prevalent AD groups was significantly greater than with normal ageing. Interestingly, there was greater decline in semantic fluency than phonemic with the unimpaired group, possibly representing heterogeneity from prediagnostic AD patients as part of the group or indicative of semantic decline as part of normal ageing?

In a separate longitudinal study (PAQUID), older subjects were tested on verbal fluency measures at baseline, 3 and 5-year intervals (Auriacombe *et al.*, 2006). From an initial cohort, 52 incident probable AD cases became apparent and were matched to controls. AD patients showed significantly poorer performance on verbal fluency tasks as early as 5 years prior to diagnosis. The most significant drop in performance occurred 2 years prediagnosis, although there remained slight decline between 5 and 3 years. There was a decline in verbal fluency with normal controls, although not to the same degree. Both results support selective impairment of key language processes prior to threshold for AD diagnosis, highlighting primary failure prior to significant cognitive decline.

Further, deterioration appears hierarchical. From a comprehensive review, Olga and Emery (2000) concluded a relation between complexity of language function and decline, hypothesising language forms learned last deteriorated first. The possibility of a relationship with integrity of episodic memory is postulated, with suggestions that naming ability is affected relative to frequency of item use and age of acquisition (Small and Sandhu, 2006, 2008). It may be that although early deficits are focal, later decline corresponds with global deterioration and involves separate cognitive processes.

Primary progressive aphasia and Alzheimer's disease

Comparative studies of primary progressive aphasia (PPA) and AD patients reveal similar impairments (Mendez *et al.*, 2006; Mesulam *et al.*, 2009). Mendez *et al.* (2006) investigated language function with several tests, including verbal fluency and BNT, in three groups: PPA, probable early AD and control participants. Results showed that both disease groups were impaired on naming, verbal fluency and information content. The PPA group had additional deficits, with literal paraphasias and neologisms. Although AD language deficits may not be present to the same extent as in PPA, they may still be clinically significant. Adlam, Bozeat, *et al.* (2006) discussed the relationship between fluent PPA and semantic dementia and concluded that both sets of deficits likely resulted from similar initial neuropathology. They proposed the varied clinical symptoms that simply represent differential destruction of key nodes in language networks. PPA is established as a primary language disorder, and AD appears to share the nature of core deficits and reinforces hypotheses that observed difficulties arise from a primary process in AD.

A semantic memory deficit

The language tasks identified as showing earliest impairment have a clear dependence on semantic memory and hence our interest in its nature and integrity. Semantic knowledge relates to entities around us, and semantic memory represents neural concepts of these. Through life, these concepts are learned and built upon with experience and interaction with the world.

The neuroanatomy of semantic memory

The nature of the neural semantic substrate has been debated widely (Cappa, 2008; Joubert *et al.*, 2010) from arguments that semantic memory is represented by a widely distributed cortical network to it, conversely being within modality specific regions (Lambon Ralph and Patterson, 2008; Cappa, 2008). Imaging studies postulate that the semantic system occupies an extended, predominantly left-sided network (Cappa, 2008). A comprehensive meta-analysis by Binder *et al.* (2009) identified a complex left-lateralized network, and one sharing many areas with the aforementioned language network (Gold and Buckner, 2002; Binder *et al.*, 2009). These areas are significant expansions from the nonhuman primate brain, perhaps reflecting the unique human cognitive function of language.

However, there remains disagreement as to whether diffuse areas share function, with some proposing the prioritisation of subregions. Lambon Ralph and Patterson (2008) argue that evidence exists for a localised subsystem of amodal representations within temporal lobes. This subsystem may allow the brain

to link attributes and concepts when presented with new knowledge. Such hypotheses arise from review of isolated destruction of these regions in semantic dementia. Perhaps a similar model is transferable to semantic loss in AD?

The nature of deficits

Naming and category fluency deficits in AD are essentially semantically based in nature (Hodges *et al.*, 1992; Hodges and Patterson, 1995; Hodges *et al.*, 1996; Grossman *et al.*, 2003; Minati *et al.*, 2009; Joubert *et al.*, 2010; Laisney *et al.*, 2011; Wierenga *et al.*, 2011). For several years, it has been unclear whether the semantic (category) fluency deficit results from primary semantic store degradation or impaired lexical (and so semantic) search (Salmon *et al.*, 1999; Hodges *et al.*, 1992). Chertkow and Bub (1990) examined semantic memory loss in AD, agreeing with earlier hypotheses that fluency deficits resulted from either impaired semantic search or a degraded semantic store. Investigating AD patients, they found poorer item naming performance in the presence of semantic distractors but retained ability in the absence of these. Clinical impairment seems to result from a primary semantic level dysfunction, and in particular, observed naming disturbances appear intertwined with semantic disruption.

Semantic memory deterioration

It is important to evaluate whether semantic memory dysfunction is itself allied with overall cognitive failure. Hodges and Patterson (1995) investigated whether impairments in semantic memory were correlated with disease progression based on MMSE. They recruited 52 AD patients, and separated groups on the basis of illness severity (guided by MMSE score). Subjects were examined on a range of semantic memory tasks, including tasks requiring both verbal and nonverbal responses; even the minimal impairment group (defined as an MMSE > 23) had deficits on category fluency and naming tasks. Additionally, participants were tested on visuospatial ability and object-matching tasks, and corresponding deficits were found. Previous research had indicated that patients consistently perform poorly across different semantic tasks identifying the same item, again arguing for overall semantic degradation. Wierenga *et al.* (2011) focused on neural correlates of semantic memory in mild AD. Under an event-related fMRI paradigm, a range of group differences in language-related areas were shown, and also highlighted was an increased response in the right homologue of Broca's area and rostral cingulate cortex. Hence, semantic failure appears in part to result from degradation in specific areas and is not necessarily a consequence of global decline. Additionally, there seems to be a compensatory response early in disease.

Further, semantic impairment can be detected in MCI (Backman *et al.*, 2005; Auriacombe *et al.*, 2006; Adlam, Bozeat, *et al.*, 2006, Adlam, Patterson, *et al.*, 2006; Brandt and Manning, 2009; Lonie *et al.*, 2009). Adlam, Patterson, *et al.* (2006) investigated patients with mild AD and MCI. Both groups showed deficiencies on traditional semantic memory tests, with wider impairments in AD, suggesting early semantic breakdown. Lonie *et al.* (2009) completed similar work to show that early AD and MCI patients had similar deficits relative to healthy and depressed controls.

Joubert *et al.* (2010) focused on groups with early AD, amnestic MCI and older controls, and demonstrated that naming of famous faces was impaired in the first two. Additionally, they investigated semantic disruption, finding object and famous person knowledge impaired in both groups. They noted that knowledge of famous people was disproportionately affected, hypothesising this to result from there being less intra-category attributes shared in this type of information than in abstract object naming. The principle is of early loss of peripheral concepts and greater preservation of central ones (a similar model to hierarchical language loss previously discussed). Semantic loss was studied by analysing performance across modalities, demonstrating a similar deficit. Using voxel-based morphometry, the authors reported the degree of grey matter volume loss, particularly in left anterior temporal lobes, correlated with test performance. These regions have been noted as key in semantic loss in semantic dementia (Joubert *et al.*, 2010). It may be that anatomical foci can be targeted in primary deficits, although further consideration is needed.

Cognitive mapping

Recent analyses of semantic memory in AD have relied on complex multidimensional scaling models, which provide an aid in dissecting the hierarchical nature of deterioration. In one example, responses are taken and analysed for strength of association. Responses with close semantic proximity are plotted closer on a 'cognitive map.' Maps demonstrate clustering of target responses, with clusters occupying characteristic dimensions, for example size for animals. Salmon *et al.* (1999) showed that cognitive maps for verbal fluency tasks in AD patients are markedly more

disordered than in both matched controls and Huntington's disease (HD). The HD group are a useful comparison as they share fluency difficulties but are known to have a semantic retrieval deficit rather than storage disorder.

Chan *et al.* (1998), using similar methodology, took sets of three target words and asked respondents to choose two. Strength of association between words was estimated, and multidimensional mapping was applied. AD patients showed greater focus on concrete rather than abstract information, which was not the case for normal or HD subjects. This is evidence that impairment arises principally from semantic store degradation. When AD patients make errors, these tend to be superordinate replacements, rather than intrusions and repetitions as in other neurological language disorders (Auriacombe *et al.*, 2006). There appears to be early loss of peripheral, subordinate features and, with disease progression, gradual erosion of higher superordinate levels (Rogers and Friedman, 2008; Salmon *et al.*, 1999). These results support hypotheses of hierarchical semantic structure breakdown, with loosening of category associations. Conclusions that AD presents a stepwise degradation of semantic memory in later life may indeed be correct (Henderson, 1996).

Priming studies

Finally, AD studies have suggested a remarkable phenomenon called hyper-priming (Laisney *et al.*, 2011), which adds to the idea of reduced conceptual boundaries. Here, the patient is provided with a priming word prior to the task word; if the word is semantically related, there should be greater accuracy and a faster reaction time in task response. Studies have suggested that some early AD patients demonstrate a hyper-priming response, where elicited reaction times are faster than normal controls. An explanatory hypothesis is breakdown of peripheral boundaries between related subordinate concepts (e.g. 'tiger' and 'lion'), resulting in the concept being accessed quicker (Laisney *et al.*, 2011). Impaired inhibitory frameworks in Alzheimer' disease may be relevant here (Amieva *et al.*, 2004). However, as a cautionary note, work with AD patients has shown differential priming responses, with impaired, normal and hyper-priming observed (Giffard *et al.*, 2005; Rogers and Friedman, 2008; Laisney *et al.*, 2011). This priming model provides weight to principles of gradual breakdown in semantic concepts contributing to the clinical presentation with progression in dysfunction.

Neuroimaging studies in Alzheimer's disease language research

Functional imaging

In AD, functional imaging studies have suggested links between reduced neural metabolism and impaired language or semantic memory performance (Grossman *et al.*, 2003; Zahn *et al.*, 2006). In one study, in an event-related word repetition paradigm, while controls showed a response in left hemisphere areas with new words (relative to older), there was relative loss of this response in the left medial temporal lobe in early AD patients (Olichney *et al.*, 2010). Additionally, there were decreased word repetition effects in widespread left cortex, supplementing arguments for isolated language areas as points of early dysfunction. Other work has suggested correlation between cortical hypometabolism and poor performance (Zahn *et al.*, 2006), with focus on the left temporoparietal and left prefrontal cortex (Teipel *et al.*, 2006; Morris and Balota, 2001). These are similar areas to those identified in established studies of semantic networks (Binder *et al.* 2009).

In a combined fMRI and positron emission topography (PET) study, estimated amyloid load was correlated with performance during semantic, visuoperceptual and BNT tasks in early AD patients (Nelissen *et al.*, 2007). The authors hypothesised that increasing injury from amyloid load influences functional language network reorganisation. The fMRI paradigm analysed associative-semantic against visuoperceptual task performance and showed relatively (to controls) reduced activity in the left-sided superior temporal gyrus and increase on the right temporal gyrus in early AD in the former task. The left-sided responses inversely correlated with PET measures of amyloid. It is argued that amyloid angiopathy accounted for diminished left-sided response, and increased right-side activation was indicative of compensatory recruitment, highlighting the capacity for functional reorganisation as a potential therapeutic target (Nelissen *et al.*, 2007).

Wang *et al.* (2007) commented on effects of altered connectivity by examining low-frequency fluctuations of blood oxygen level–dependent signals in AD patients. They found fewer positive correlations between prefrontal and parietal regions, suggesting that these arise from an anterior-posterior disconnection. Whether this is a compensatory response to disease or part of the process itself is unclear. Similarly, it has been proposed that altered connectivity may also be responsible for the deficit noted in PPA (Adlam, Bozeat, *et al.*, 2006; Sonty *et al.*, 2007). Perhaps AD shares this mechanism for the postulated primary semantic, and so language, deficit seen?

Structural imaging

There are few structural MRI studies that have targeted language directly (Richardson and Price, 2009). Attempting to identify associations in probable AD and amnestic MCI patients, Apostolova *et al.* (2008) found correlation between poor BNT and fluency performance, and atrophy in language areas within left temporal and parietal lobes, both frontal lobes and the right temporal pole (estimated by a novel 3D surface-based computational analysis of brain MRIs).

Preclinical imaging correlates

A systematic review of neuropsychological and neuroimaging studies demonstrated similar findings of physiological changes prior to AD diagnosis (Twamley *et al.*, 2006). Bookheimer *et al.* (2000) have shown increased activation for ApoE4 carriers (not demented) relative to controls with verbal memory tasks. Similarly, Seidenberg *et al.* (2009) have demonstrated increased activation patterns in ApoE4 carriers and those with a family history of AD in bilateral prefrontal cortex and temporoparietal areas in semantic memory activation tasks from event-related fMRI. Increased activation may arise from compensatory mechanisms, present physiologically to account for regional deficits. These observations could be early compensation to a primary semantic deficit.

The potential for therapeutic intervention

There appears to be a primary AD language deficit, likely semantic in nature, detected by neuropsychology and neuroimaging and developing years before disease onset (Wierenga *et al.*, 2010). Potential treatment avenues may be conceived from evaluating language dysfunction treatment following stroke. (Price *et al.*, 2010; Berthier and Pulvermüller, 2011). Aphasia following stroke is considered one of the most common cognitive disorders, with estimates that 10–20% of patients develop a chronic language deficit (Winhuisen *et al.* 2005, Berthier and Pulvermüller 2011). The extent of loss is widely variable and dependent on ischaemic damage, although anomia is noted frequently. It may be that therapies in this field are translatable to models in AD.

Post-stroke therapies

For many years, there was little clarity on the true effectiveness of speech and language therapy in post-stroke aphasia. An early randomised controlled trial (Lincoln *et al.*, 1984) suggested no benefit. In more recent work, Crinion and Leff (2007) summarise work in post-stroke rehabilitation and highlight two approaches: functional imaging monitoring recovery and research focusing on neural plasticity responses to treatment. Post-stroke aphasia patients share language deficits with AD, including frequently anomia. Recovery of naming seems dependent on areas of BA37, BA44/45 and BA22. Additionally, there appears significant integration between motor and language networks, such that therapies in each may influence each other (Berthier and Pulvermüller, 2011).

Research has identified the nondominant hemisphere as important in language recovery, with studies showing activation in right homologues of established language areas. Saur *et al.* (2006) note key activity in the right inferior frontal gyrus acutely following stroke. Winhuisen *et al.* (2005), utilising disruption of areas with repetitive transcranial magnetic stimulation, have suggested that right homologues show a supportive rather than replacement function. In studying treatment effects, there is evidence of activity change in both left-lesioned areas and right homologues (Crinion and Leff 2007). Functional improvements may arise from adaptive neurophysiological or neurometabolic changes in both regions (Berthier and Pulvermüller, 2011).

A key therapy now suggested in post-stroke aphasia is intensive language action therapy, in particular, a subtype-constraint-induced language therapy (Crinion and Leff 2007). This involves patients practising language tasks in the context of 'games,' which require combination with actions. Randomised controlled trials have shown a positive effect, including chronic deficits post-stroke, a state potentially more translatable to AD. A recent Cochrane review (Kelly *et al.*, 2010) also states the effectiveness of intensive therapy.

Pharmacological therapies

A small trial with donepezil in post-stroke aphasia has suggested potential improvement in speech, word repetition and naming (Berthier and Pulvermüller 2011). Berthier *et al.* (2006) report improvements in severity of aphasia with donepezil in chronic post-stroke aphasia patients. Language benefits seem to decrease after therapy cessation, although function remains above baseline (Berthier *et al.*, 2006; Berthier and Pulvermüller, 2011).

A randomised controlled trial where memantine was administered in conjunction with speech and language therapy showed improvement in aphasia

severity relative to placebo (Berthier *et al.*, 2009). Other agents considered in post-stroke aphasia have included dexamphetamine, levodopa and bromocriptine. There is minimal comment from this research regarding concurrent cognitive deficits in the population (such as dementia). There will be natural overlap between both groups, given the demographic, although eligibility criteria restricting recruitment to younger patients with stroke in the mentioned studies should limit this.

The same drugs have been considered in PPA, although there are no identifiable randomised controlled trials demonstrating effectiveness. Reed *et al.* (2004) report a small trial of patients with PPA given bromocriptine. They assessed language function and found no significant effect with bromocriptine. Johnson *et al.* (2010) similarly showed no significant difference in a slightly larger trial, although reported a smaller degree of decline (nonsignificant). Boxer *et al.* (2009), investigating memantine in frontotemporal dementias, argue for larger trials focusing on cognitive outcomes.

Finally, Ferris *et al.* (2009) report improvements in language testing for patients with memantine in moderate and severe AD. This is a post-hoc analysis of clinical trials, with criticisms of it utilising a novel language tool (the Severe Impairment Battery-Language Scale) of unclear clinical correlation. It is clear from pharmacological data that there are difficulties with small trials and paucity of samples. Overall, greater emphasis on pharmacological research into language rehabilitation is needed.

Transcranial electrical stimulation

Away from pharmaceuticals, Berthier and Pulvermüller (2011) discuss the potential impact of transcranial electrical stimulation, a technique that Cotelli *et al.* (2008, 2010) have reported success with in AD. Research here is in relative infancy, with studies reporting both inhibitory and excitatory effects. Cotelli *et al.* (2008) investigated repetitive transcranial magnetic stimulation (rTMS) and picture naming. They reported that stimulation improved naming performance, with increased correct responses, in early and advanced AD. In a further trial, Cotelli *et al.* (2010) investigated long-term effects of cognitive performance with rTMS applied to the left dorsolateral prefrontal cortex. AD patients received 25 min of rTMS once daily for a week. Cognitive performance was measured at intervals post-therapy and showed resulting improvement in sentence comprehension. Mechanisms for success here are unclear; perhaps transcranial stimulation has an effect on impaired inhibition as well as aiding normal function?

Future directions in Alzheimer's disease

What are future avenues for improvement of AD language function? There may be correlation between pre-existing ability and cognitive training, and targeting preserved yet inefficiently used functions is a potential mechanism for optimising functioning (Lustig and Flegal, 2008).

There has been increasing interest in cognitive stimulation programmes (Grandmaison and Simard, 2003; Buschert and Bokde, 2010), which could be transferable to impaired language. Cognitive reserve may be useful in long-term resilience against language dysfunction. Buckner (2004) notes the capacity for recruitment of alternative cortical areas, suggesting that compensatory processes occur in normal ageing as well as neurodegenerative illnesses.

Craik *et al.* (2010) studied bilingualism as a protective element. They found that AD diagnosis occurred approximately 4 years later in bilingual patients, with reported symptom onset 5 years later. They suggest bilingualism as a form of cognitive reserve against neurodegenerative illness. A well-reported study with a group of nuns considered impact of early linguistic ability on later life AD incidence (Snowdon *et al.*, 1996). As part of joining the convent, the nuns would handwrite autobiographies. These were analysed by investigators for idea density, as a measure of early life linguistic function. They showed that all those with confirmed AD had low idea density from earlier autobiographies. These results support relationships between early cognitive capacity and later AD development.

Conclusions

Language function is not restricted to classical left perisylvian areas, but instead occupies a widespread network with the capacity for reorganisation following cortical injury. The language deficit in early AD is principally a primary semantic one, affecting naming and fluency, and appears prediagnostically. Semantic deterioration early in AD is not simply a consequence of global cognitive decline. Progression of the dysfunction appears hierarchical, such that in later disease, central core concepts become disturbed. Early language disturbance results from isolated semantic deficits, whereas contrastingly widespread language failure in the later stages of illness seems to result from a combination of a severely degraded semantic store and impairment of other cortical processes.

Direct language function imaging in AD research suggests altered metabolism and connectivity states.

There may be compensatory recruitment of cortical areas many years before disease, as suggested in ApoE4 carriers. This physiological mechanism may be a valuable target for future therapies. Post-stroke research that has utilised speech and language therapy in specific contexts could be readily transferable in ameliorating the sequelae of neuropathology. Additionally, maximising an individual's cognitive potential may serve as a beneficial avenue in optimising daily functioning and tackling the primary semantic deficit.

Key points

- Language impairment is an early feature in Alzheimer's disease, with predominant deficits in naming and fluency.
- Early language manifestations in Alzheimer's disease arise as a consequence of deficits in semantic memory rather than global cognitive decline.
- There may be physiological compensation to an altered connectivity state early in Alzheimer's disease and even prediagnosis.
- Supporting language function by utilising cognitive reserve may offer a potential therapy.

Conflict of interest

None declared.

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