1 Alzheimer's Dementia

Background

Alzheimer's disease is named after the Bavarian psychiatrist and neuropathologist Alois Alzheimer (1864–1915). In November 1906, Professor Alzheimer gave a talk 'On a peculiar, severe disease process of the cerebral cortex' to the 37th Assembly of the Southwest German Psychiatrists in Tübingen. The case at the centre of Alzheimer's talk was that of a woman called Auguste Deter (1850–1906), who had been admitted to the Frankfurt asylum where Alzheimer worked on 25 November 1901. Deter passed away on 9 April 1906. For further discussion of the life of Alois Alzheimer and this index case of Alzheimer's dementia, readers are referred to Toodayan (2016).

Epidemiology

Alzheimer's disease is the most common cause of **dementia**, accounting for an estimated 60% to 80% of cases. An estimated 5.5 million Americans of all ages had Alzheimer's dementia in 2017 (Alzheimer's Association, 2017). Fiest *et al.* (2016) conducted a systematic review and meta-analysis of the **incidence** and **prevalence** of dementia due to Alzheimer's disease in a community setting. These authors reported an overall point prevalence of Alzheimer's disease in individuals 60+ to be 40.2 per 1,000 persons and a pooled annual period prevalence of 30.4 per 1,000 persons. The overall pooled annual incidence was 34.1 per 1,000 persons and the incidence rate was 15.8 per 1,000 person-years. Takizawa *et al.* (2015) conducted a systematic literature review of epidemiological studies of Alzheimer's disease in France, Germany, Italy, The Netherlands, Spain, the UK and the USA. The prevalence of Alzheimer's disease in these countries ranged between 3% and 7%.

Aetiology

Older age and genetic susceptibility are aetiological factors for Alzheimer's disease. A small number of cases (less than 2%) have an early-onset before the

age of 65 years. These individuals inherit the disease in **autosomal dominant** fashion. This familial form of the disease is related to mutations in one of three genes: amyloid precursor protein gene on chromosome 21, presenilin 1 gene on chromosome 14 and presenilin 2 gene on chromosome 1. For the vast majority of cases of Alzheimer's disease, the disorder is sporadic and late-onset (after 65 years). The apolipoprotein E gene is the most well-established genetic risk factor for this late-onset form of the disease (Gallagher *et al.*, 2016). Risk factors for Alzheimer's disease include vascular disease, and conditions and behaviours which are linked to the development of vascular disease (e.g. cigarette smoking, midlife high blood pressure and obesity, diabetes, and cerebrovascular lesions) (Qiu *et al.*, 2009). Females are at greater risk of developing Alzheimer's disease than males (Podcasy and Epperson, 2016).

Pathophysiology

Pathological changes associated with Alzheimer's disease are by now well documented. On a macroscopic level, the brain exhibits **cortical atrophy**, with widening of the **cerebral sulci** and compensatory enlargement of the **ventricles** (Gallagher *et al.*, 2016). On a microscopic level, there are extracellular plaque deposits of the beta-amyloid peptide and flame-shaped neurofibrillary tangles of the microtubule binding protein tau (Murphy and LeVine, 2010). Loss of neurones leads to deficits in cholinergic, noradrenergic and serotonergic transmitters.

Clinical Features

Adults with Alzheimer's disease present with insidious, progressive impairment of **episodic memory**, with the emergence of **aphasia**, **apraxia** and executive deficits as disease progresses (Gallagher *et al.*, 2016). Neurodegeneration is estimated to occur 20–30 years before the onset of symptoms. During this time, the burden of pathology increases to the point at which clinical expression of disease occurs. The pre-clinical phase of Alzheimer's disease is known as **mild cognitive impairment**. Adults with mild cognitive impairment have cognitive deficits in excess of those associated with normal aging, although they do not have significant functional impairments (Gallagher *et al.*, 2016). The mean annual conversion rate of mild cognitive impairment to dementia is estimated to be 4.2% (Mitchell and Shiri-Feshki, 2008). Adults with Alzheimer's dementia can also experience **hearing loss**, visual impairment and olfactory dysfunction (Kirby *et al.*, 2010; Lin *et al.*, 2011; Zou *et al.*, 2016).

Neuropsychiatric symptoms develop at some stage in almost all people diagnosed with Alzheimer's disease (Lyketsos *et al.*, 2011). Depression and

apathy are the most frequently observed neuropsychiatric symptoms in people with early Alzheimer's disease. Verbal and physical agitation is also common in early-stage disease. With disease progression, **delusions**, **hallucinations** and aggression can also become more common. Apathy can be present at all stages of the disease. There are also atypical presentations of Alzheimer's disease in which episodic memory loss is not the first and most salient domain of impairment. These non-amnestic **phenotypes** include a language presentation, a visuospatial presentation and **executive dysfunction**.

Prognosis

Life expectancy in Alzheimer's disease can vary between three and ten years (Zanetti *et al.*, 2009). Survival time after diagnosis varies with age of diagnosis. Brookmeyer *et al.* (2002) reported that median survival times ranged from 8.3 years for persons diagnosed at 65 years of age to 3.4 years for persons diagnosed at 90 years of age. There was no difference in survival time for men and women in this study. Race/ethnicity and comorbid diabetes and hypertension are known to influence survival (Helzner *et al.*, 2008). Adults with familial Alzheimer's disease become dependent in self-care and die earlier than adults with sporadic Alzheimer's disease (Swearer *et al.*, 1996).

The course of Alzheimer's disease is generally characterized in three stages. In Stage I, the patient exhibits **anomia** and empty speech. Memory is defective and there is impairment of visuospatial skills and calculation. The motor system is normal at this stage. Brain scans reveal medial temporal atrophy. In Stage II, patients display fluent aphasia, and memory and visuospatial skills are severely impaired. Patients exhibit restlessness (motor system) and scans reveal temporal-parietal atrophy. In Stage III, patients exhibit severely impaired intellectual function and are incontinent. All meaningful communication is lost and there may be **palilalia**, **echolalia** or **mutism**. Brain scans reveal diffuse atrophy.

Cognitive Profile

Cognitive impairment is present in all individuals with mild cognitive impairment and Alzheimer's disease. Baudic *et al.* (2006) reported that patients with very mild Alzheimer's disease had deficits of visuospatial short-term memory, episodic memory, flexibility and self-monitoring abilities, concept formation and reasoning relative to normal controls. It was concluded that deficits of episodic memory and **executive functions** occurred early in the course of disease and preceded impairment of **constructional praxis**, language and sustained attention. Cognitive and affective **theory of mind** (ToM) is also impaired in clients with Alzheimer's disease. This impairment cannot be fully

explained by executive function deficits (Laisney *et al.*, 2013). ToM impairments are associated with pragmatic language difficulties in clients with Alzheimer's disease (Cuerva *et al.*, 2001; Maki *et al.*, 2013). See *Pragmatics and Discourse* for further discussion.

The course and rate of cognitive decline have been found to vary in patients with Alzheimer's disease. Wilkosz *et al.* (2010) found that the trajectory of cognitive decline varies with age and Mini-Mental State Examination (MMSE) scores at initial assessment. Older subjects followed a trajectory of slower cognitive decline. Subjects with higher initial MMSE scores followed trajectories of slower decline, while those with lower initial scores declined more rapidly. The presence of **psychosis** predicted a more rapid cognitive decline in all patients with Alzheimer's disease.

Language and Communication Profile

Adults with Alzheimer's dementia have a complex and changing language and communication profile. They can exhibit aphasic and non-aphasic language impairments, **motor speech disorders** such as **dysarthria** and **apraxia of speech**, and **orofacial apraxia**. These features have been shown to be related to dementia severity. Cera *et al.* (2013) found that the severity of dementia in adults with Alzheimer's disease was significantly associated with severity of orofacial apraxia and speech apraxia. Although it is not an aspect of communication, the swallowing disorder **dysphagia** must also be assessed and treated by **speech-language pathologists** who work with clients with Alzheimer's dementia.

Language subsystems deteriorate at different stages in the progression of Alzheimer's disease. Semantic and pragmatic aspects of language are first to be disrupted, while structural aspects of language (e.g. phonology, syntax) are impaired in more advanced stages of the disease. In a review of studies of language impairment in Alzheimer's disease, Emery (2000) reported a negative relation between sequence in **language development** and language decline. Specifically, language forms which are learned last in the sequence of language development and are most complex are the first to deteriorate in Alzheimer's disease.

Phonology

The standard view is that **phonology** remains intact in adults with Alzheimer's dementia until an advanced stage of disease (Emery, 2000). This view receives support from an examination of Cookie Theft picture descriptions which were conducted as part of the Alzheimer and Related Dementias Study of the School of Medicine at the University of Pittsburgh (Becker *et al.*, 1994). The study

included 208 adults with probable or possible Alzheimer's dementia. An examination of 32 picture descriptions revealed only one phonological error. This error was produced by a 77-year-old man with possible Alzheimer's dementia:

> The tair [chair] uh the chair is uh tilting and he's gonna fall off.

Croot *et al.* (2000) take a different view of phonology in Alzheimer's disease. These authors state that 'a growing number of pathologically confirmed and clinically diagnosed cases in the literature dispute the claim that phonological processing and articulation are generally spared in dementia of the Alzheimer's type until the final stages' (279). These investigators examined phonology in six patients with pathologically confirmed Alzheimer's disease and four patients with clinically diagnosed dementia of the Alzheimer's type across three speech contexts: conversational speech; single-word production; and series speech (e.g. counting). In conversation, the percentage of phonological retrieval errors ranged from 19.1% to 73%. Similarly high rates of phonological errors were also observed in the other speech tasks. For example, during single-word production one patient with Alzheimer's dementia named only 35.4% of pictures correctly. Some 25% of this patient's errors were phonologically related. The authors explain the discrepancy between these high rates of phonological error and previous findings of limited phonological impairment in Alzheimer's dementia in terms of the types of subjects that have been recruited to studies – a priori assumptions about phonological processing in Alzheimer's dementia may have precluded Alzheimer's patients with phonological impairments from investigation. However, it is also possible that Croot *et al.* have been investigating patients with an atypical presentation of Alzheimer's disease. Around 19% of cases of **primary progressive aphasia** are caused by Alzheimer's disease pathology (Spinelli *et al.*, 2017). Given the dominant language impairment in patients with primary progressive aphasia, it is to be expected that phonological errors will be common.

Morphology and Syntax

Like phonology, it has been widely held that **morphology** and **syntax** are relatively unimpaired in Alzheimer's dementia at least until an advanced stage of disease (see Kempler *et al.* (1987, 1993) for the preservation of syntax). Kavé and Levy (2003) examined morphology and syntax in the picture descriptions of 14 Hebrew speakers with Alzheimer's disease. It was found that these speakers produced the same syntactic structures and morphological forms as control participants. Adults with probable and possible Alzheimer's dementia in the Pittsburgh Study also exhibited few morphological and

syntactic difficulties. These adults used the full range of derivational and inflectional morphological forms, as the following examples illustrate:

Derivational morphology:
66-year-old woman: Making a mess out of the place by no neatness (morpheme *–ness*)
74-year-old woman: He has a handful of cookies in one hand (morpheme *–ful*)

Inflectional morphology:
55-year-old woman: The water's running out of the sink (Progressive *–ing*)
60-year-old woman: He's handing some cookies down to the little girl (Plural *–s*)
71-year-old woman: She was climbing and the stool tipped over (Past tense *–ed*)
74-year-old woman: The mother is washing dishes absent-mindedly (Adverb *–ly*)

These adults also used a range of syntactic structures including complex phrases and clauses. The grammatical knowledge needed to produce these structures was clearly intact for the most part. The following examples illustrate some of the phrases and clauses that were used by adults with Alzheimer's dementia in the Pittsburgh study:

Phrases:
68-year-old woman: There's a little girl with him (Noun phrase)
87-year-old woman: A boy is putting something in the closet (Verb phrase)

77-year-old man: The cookies must be pretty good they're eating (Adjective phrase)

78-year-old man: The lady here's standing right in the water (Adverb phrase)
83-year-old man: All the water is coming over the sink (Prepositional phrase)

Clauses:
60-year-old woman: The stool he's standing on tilts over (Relative clause)
66-year-old woman: The little boy is standing on a chair which is crooked (Relative clause)
68-year-old woman: I guess this is breakfast (Subordinate clause)
70-year-old woman: I think that he'll lose his cookies (Subordinate clause)
68-year-old woman: The little boy is trying to get cookies (*To*-infinitive clause)

Some investigations have reported morphological and syntactic deficits in adults with Alzheimer's dementia. Walenski *et al.* (2009) examined the production of regular and irregular past participle and past tense forms by Italian-speaking patients with probable Alzheimer's disease. Relative to control participants, patients were impaired at inflecting past participle and past tense forms for irregular verbs but not for regular verbs. Bates *et al.* (1995) found that grammatical production was impaired in patients with Alzheimer's disease when grammar was assessed under highly constrained conditions in a film description task. Clearly, further research is needed to establish the extent to

which grammar is impaired at different stages in the progression of Alzheimer's disease.

Vocabulary and Semantics

Lexical-semantic deficits are one of the most marked linguistic impairments in Alzheimer's dementia. These deficits are consistently reported in clinical studies. Smith *et al.* (1989) investigated **confrontation naming** in 18 patients with Alzheimer's disease. These patients produced a greater number of naming errors than a group of institutionalized, non-neurologically impaired control participants who were matched for age, sex and education level. The errors of these patients suggested that they were able to recognize objects that they could not name. Patients were able to identify the semantic class to which target words belonged but were not able to provide the lexeme for the individual class member (e.g. *animal* instead of *dog*). Glosser *et al.* (1998) examined priming of certain semantic relationships in patients with probable Alzheimer's disease. Like healthy elderly controls, patients with Alzheimer's disease displayed preserved priming of the superordinate category label, e.g. use of *daughter* as a prime for *relative*. However, unlike control subjects, there was no evidence of priming between words designating coordinate exemplars within a semantic category (e.g. *cousin-nephew*). Glosser *et al.* concluded that the semantic deficit in Alzheimer's disease affects relationships among basic-level concepts rather than the relationship between these concepts and their superordinate category of membership. More recently, Caputi *et al.* (2016) have demonstrated deterioration of four semantic associative relationships (part/whole, function, superordinate and contiguity) in patients with amnestic mild cognitive impairment as well as in clients with mild and moderate Alzheimer's disease. Deterioration was more marked in the verbal than the visuoperceptual **semantic network**.

Lexical-semantic problems were commonplace in the Cookie Theft picture descriptions of adults with Alzheimer's dementia in the Pittsburgh Study. One of the most frequent errors to occur was the use of general **superordinate terms** in place of more specific lexical items. This was evident in the use of *lady* and *woman* for 'mother', *food* for 'cookie', *kid* for 'boy', and *place* for 'kitchen'. Another common error was the use of words from the same semantic category as the target word. Participants in the study frequently used *chair* for 'stool'. Less often, the following semantically related substitutions were made:

Bench for 'stool' (68-year-old woman)
Closet for 'cupboard' (87-year-old woman)
Cake for 'cookie' (76-year-old woman)

Sometimes, substitutions were based on the function of objects denoted by words or on similarities of shape. For example, a ladder and a stool can both be

used to climb up onto something, while a dishwasher and a sink can both be used to wash dishes. A ball has the same circular shape as a cookie:

Ladder for 'stool' (72-year-old man)
Dishwasher for 'sink' (76-year-old woman)
Ball for 'cookie' (76-year-old woman)

These clients also displayed lexical-semantic difficulties in the use of verbs. Like nouns, these difficulties were in the direction of use of general verbs over specific verbs. For example, a 70-year-old woman said the boy was *getting the food* rather than pinching or stealing cookies. The same woman described the mother in the scene as *working* rather than washing or drying dishes. A 69-year-old woman described the water as *falling* rather overflowing from the sink. The use of general nouns and verbs in place of specific nouns and verbs, respectively, suggests a deterioration of lower category members in **semantic memory** in Alzheimer's dementia.

Apart from these various lexical substitutions, there was other evidence that clients with Alzheimer's dementia in the Pittsburgh Study had lexical-semantic deficits. Indefinite pronouns were used when more specific lexemes were not available to speakers. This is illustrated by the following examples from the study:

Busy at something (69-year-old woman)
Someone down out there or something (74-year-old man)

Fillers like 'uh' and 'um' were used extensively leading up to the production of nouns, as in the following utterance of a 78-year-old woman:

And he the uh uh yeah that there uh uh stool I'd call it

Also, speakers often explicitly stated that they were having difficulty producing a target word. For example, the woman who produced the above utterance said later in her picture description 'I don't know what you call them'. Other speakers with Alzheimer's dementia said 'What do you call it?'.

These lexical-semantic difficulties had the effect of reducing the informational content of speakers' picture descriptions. But there were other semantic problems which also served to reduce the information that speakers conveyed in their descriptions. **Semantic roles** (also known as participant or thematic roles) were frequently omitted. This occurs in the first example below where the AGENT role is omitted. In other cases, speakers assigned incorrect semantic roles to verbs. This can be seen in the second example below where *food* fulfils the semantic role of PATIENT. But this semantic role cannot occur in preverbal position with the verb 'dropped' (compare this example to *The vase shattered* where the verb 'shattered' can have a PATIENT in preverbal position). Sometimes, noun phrases occupied the wrong semantic roles in a

sentence. This occurs in the third example below where the noun phrase *the water* should occupy the AGENT role:

> Snitching cookies (69-year-old woman)
> Food dropped (70-year-old woman)
> The sink's running over the water (81-year-old woman)

The semantic role difficulties of these clients are consistent with the findings of studies of this aspect of **semantics** in clients with Alzheimer's dementia (e.g. Grossman *et al.*, 2007; Manouilidou *et al.*, 2009).

Pragmatics and Discourse

There are marked pragmatic and discourse deficits in clients with Alzheimer's dementia. The comprehension of non-literal and **figurative language** is disrupted early in the course of Alzheimer's dementia. Maki *et al.* (2013) investigated **sarcasm** and **metaphor** comprehension in aged normal controls, patients with amnestic mild cognitive impairment and patients with mild Alzheimer's disease. These investigators found that sarcasm comprehension started to deteriorate in aged normal controls, while metaphor comprehension started to deteriorate in patients with amnestic mild cognitive impairment. Sarcasm comprehension requires more complex (second-order) ToM skills than metaphor comprehension (first-order ToM skills), possibly explaining the earlier deterioration of sarcasm in aged normal controls. The comprehension of **proverbs** (e.g. *A stitch in time saves nine*) and **idioms** (e.g. *Bill hit the sack*) is also compromised in Alzheimer's dementia. Studies have found a tendency towards literal interpretation in patients with Alzheimer's dementia, and a relationship between comprehension and executive functions (Kempler *et al.*, 1988; Papagno *et al.*, 2003; Rassiga *et al.*, 2009).

Conversational, narrative, expository and procedural discourse can be difficult to follow in adults with Alzheimer's disease. This difficulty arises because patients are poor at tailoring their utterances to address the informational needs of hearers. Adults with Alzheimer's disease make inadequate use of **cohesive devices** like **anaphoric reference** to link their utterances across extended discourse (e.g. *Mary bought the blue dress. It was very expensive*) (Ripich *et al.*, 2000a). They also use **deictic expressions** such as *next week*, *there*, and *this book* without providing hearers with **referents** of these terms (Carlomagno *et al.*, 2005; Feyereisen *et al.*, 2007). It was discourse anomalies of this type which particularly compromised the Cookie Theft picture descriptions of adults with Alzheimer's dementia in the Pittsburgh Study. Consider the following description of a 74-year-old male participant (PAR) with probable Alzheimer's dementia ('INV' is the investigator):

1 INV: Tell me what you see going on in the picture.
2 PAR: Well she's washin(g) dishes.

3 PAR: He's climbin(g) up to get cookies.
4 PAR: He's gonna fall.
5 PAR: And she's laughin(g).
6 INV: Okay.
7 PAR: And she's spill runnin(g) the water over.
8 INV: Anything else?
9 PAR: That looks like someone down out there or somethin(g).
10 PAR: I don't know what that is.
11 INV: Okay.

This speaker makes pronominal reference to the characters in the picture from the outset of the description. This occurs in lines 2 and 3 where the speaker says *she's washing dishes* (referring to the mother) and *he's climbing up to get cookies* (referring to the boy). In the absence of visual information provided by the picture, the hearer is unable to establish the referents of these pronouns. Preceding these first uses of pronouns should be the noun phrases *the mother* and *the boy*, with pronouns used subsequently to achieve anaphoric reference to the individuals denoted by these phrases. This is particularly important in the case of the pronoun *she* as there are two female characters in the picture – the mother and the girl – who are potential referents of this pronoun. This is not the only referential anomaly in this short picture description. In line 2, the referent of the pronoun *she* is the mother. However, in line 5 the referent of the same pronoun is the girl. In line 7, the referent of the pronoun *she* returns once again to the mother. The speaker fails to signal for his hearer that a shift in pronominal reference occurs between lines 2, 5 and 7. A further referential anomaly occurs in line 10 with the use of the demonstrative pronoun *that*. In the absence of the speaker directly pointing to a feature in the picture, the hearer is unable to establish the referent of this deictic term.

Several other discourse impairments have been documented in adults with Alzheimer's dementia. It is common for these adults to repeat and omit information, and include irrelevant and incorrect information in discourse (Drummond *et al.*, 2015; Fraser *et al.*, 2016). All of these discourse anomalies were evident in the picture descriptions of adults with Alzheimer's dementia in the Pittsburgh Study. The following extract is taken from the picture description of a 70-year-old woman with probable Alzheimer's dementia. In line 8, she repeats her earlier utterance in line 2 that *they're grabbing the cookie jar*. Also, the speaker produces an irrelevant utterance in line 9 when she states *wonder what my husband is doing*:

1 INV: Tell me what you see going on in the picture.
2 PAR: Well (.) they're grabbing the cookie jar.
3 PAR: Right?
4 PAR: (.) and mother is working.
5 INV: (..) tell me if you see anything else going on here.