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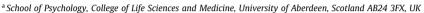
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Gaze detection and gaze cuing in Alzheimer's disease

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ABSTRACT

People with Alzheimer's disease (AD) show problems with social processing in tasks which require the understanding of others' mental states. However traditional social processing tasks are cognitively complex, which may influence the effects of AD. Less is known about how AD influences more basic aspects of social perception, such as the ability to decode eye gaze direction or follow the gaze of another. The current research assessed whether those with AD showed difficulty in both explicitly decoding subtle manipulations of gaze direction (Study 1), and reflexively following another's eye gaze (Study 2). Those with AD were more impaired than a matched control group when making explicit discrimination distinctions between direct and averted gaze. In contrast people with Alzheimer's disease performed comparably to a control group when following gaze. This pattern indicates that more automatic aspects of social perception such as gaze following are unaffected by AD. In contrast, more controlled processes such as deciding whether someone is looking towards you are impaired in AD. This has implications for socially engaging with other people and interpreting their focus of interest.

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1. Introduction

While Alzheimer's disease (AD) has traditionally been conceptualised in terms of declines in cognitive skills such as memory and attention, there is increasing evidence that AD can also impair social skills important in interpersonal interactions. Specifically, people with AD have more problems in social cue processing: the ability to decode information about mental states such as emotions, interest, intentions and beliefs from behaviour and demeanour. Considerable research indicates that people with AD have difficulty in understanding others' emotions (Klein-Koerkamp, Beaudoin, Baciu, & Hot, 2012) and beliefs (Sandoz, Démonet, & Fossard, 2014). These failures to read the social cues given by other people predict behavioural problems (Shimokawa et al., 2001) and poorer quality of life (Phillips, Scott, Henry, Mowat, & Bell, 2010) in people with AD, independent of assessments of basic cognitive functioning. However most of the studies to date have looked at the effects of AD in social cue tasks which are cognitive complex, and the main aim of our study is to explore whether AD also impairs performance on much simpler tasks of basic social cue perception: detecting and following others' gaze direction.

Most of the literature on dementia and social cue processing uses relatively complex tasks. For example many studies have explored the effects of AD on mental state understanding using 'theory of mind' tasks assessing the understanding of belief reasoning and particularly the ability to take others' perspectives and discern when they have a false belief about the state of the world (e.g. Fernandez-Duque, Baird, & Black, 2009). These tasks are cognitively complex, and so it is difficult to determine whether the effects of AD are primarily problems with the tricky reasoning and decision-making required in these tasks. Recent studies and reviews (Kemp, Despres, Sellal, & Dufour, 2012; Poletti, Enrici, & Adenzato, 2012; Sandoz et al., 2014; Shany-Ur et al., 2011) have concluded that AD causes poor performance on a range of tasks assessing different aspects of mental state understanding, and that the effects of AD are greatest when the task is most cognitively complex. For example false belief tasks, which require participants to inhibit their own viewpoint on the world to take another person's mistaken perspective, are performed poorly by people with AD (Fernandez-Duque et al., 2009). The reviews conclude that the effects of AD on these complex social reasoning tasks are likely secondary consequences of problems with executive function, attention and reasoning (e.g. Sandoz et al., 2014).

It is therefore important to explore further whether aspects of social understanding which are less cognitively complex are also affected by AD. According to Baron-Cohen (2005) the ability to process and interpret eye-gaze cues is an important precursor to

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higher level social processing. Processing of gaze cues involves the superior temporal sulcus (Engell & Haxby, 2007), and other key cortical regions (such as the temporo-parietal junction and ventromedial prefrontal cortex) which may underlie the effects of AD on social understanding (Poletti et al., 2012). There are multiple different components of gaze processing, with differing developmental trajectories and neural substrates (Shepherd, 2010). One key aspect of gaze processing is determining gaze direction. Deciding whether someone is looking towards or away from you, and in which direction they are looking, is a very important step in social communication (see Kleinke, 1986 for a review). A second key aspect is following the gaze of another person (also known as joint attention), where directional cues inform us where others are attending in the environment (Driver et al., 1999). These two aspects of gaze processing have different cognitive and neural components (Shepherd, 2010). While gaze following develops relatively early in childhood (<1 year) and is largely automatic, explicit discrimination develops much later (>3 years) and requires controlled cognition (Doherty, 2006; Doherty, Anderson, & Howieson, 2009).

However, little is known about how AD impacts on these basic gaze processing tasks. Given that gaze following is largely reflexive, we predict that there will be little effect of AD on this task. In contrast, the more controlled nature of explicit gaze direction decisions will result in AD-related deficits.

2. Study 1: Eye gaze detection in Alzheimer's disease

Gaze detection tasks require people to make decisions about whether someone else is looking towards or away from them, and to decide whether any averted gaze is to the right or left. Different neural systems are involved in processing information about direct and averted gaze (Shepherd, 2010), with detection of potentially threatening direct gaze more automatic compared to decisions about direction of averted gaze. Deciding where someone else's gaze is directed is important in social interaction and in understanding others' intentions. Normal adult aging can influence gaze processing. Healthy older adults are less accurate than young at decoding gaze direction (Slessor, Phillips, & Bull, 2008), and less likely to use information about gaze direction to influence their social decisions (Slessor, Phillips, & Bull, 2010). There is relatively little literature on the effects of AD on gaze detection. A couple of studies have investigated whether people with AD used information about which object a person was looking at to attribute object preferences (Castelli et al., 2011; Laisney et al., 2013). For example, from a picture showing someone was looking at an icecream rather than a chocolate it can be concluded that they preferred the ice cream. People with AD were less likely to make preference attributions in accordance with gaze direction. However, Laisney et al. (2013) concluded that these differences were not due to any problems in *detecting* gaze direction, but instead might relate to the preference-attribution aspect of the task. Also Castelli et al. (2011) reported that AD-related errors in the gaze preference task were mostly due to a failure to understand the rather complex task instructions.

Bediou et al. (2009) more directly investigated the effects of AD on the ability to categorize subtle variants in gaze. The stimuli were photographs of faces with gaze averted varying degrees to the left or right. They found no effect of AD on the ability to detect gaze direction. However, there are a number of reasons to question whether this is a definitive demonstration that AD does not impact on gaze detection. Firstly only 10 participants with AD were assessed, and the analysis was as part of a larger study including people with mild cognitive impairment and frontotemporal dementia. This may mean that effects of AD were not clear in the

larger sample. Also, the task presented relatively gross differences in gaze which may have resulted in ceiling effects. In addition, they did not include a 'direct gaze' condition, and this is important as distinguishing between direct and averted gaze involves different cognitive and neural components compared to making left/right decisions (Shepherd, 2010). Errors of judgment in a social context which involve misinterpreting whether someone is looking at you or not may have particularly important consequences for social interaction. Including more subtle variants of gaze, and direct gaze stimuli, allows for more sensitive testing of any impact of AD in gaze detection.

The current study aims to investigate how AD impacts on the ability to discriminate between direct and averted gaze. Given that the cognitive load of this task is relatively low, and the previous results of Bediou et al. (2009) indicating no effect of AD on gaze processing it could be predicted that there should be no differences between people with AD and age-matched healthy controls on this task. However, previous arguments that gaze detection requires controlled social processing (Baron-Cohen, 2005; Doherty, 2006; Shepherd, 2010) leads to the opposite prediction, that participants in the AD group will be significantly less accurate than the controls in determining eye gaze direction.

2.1. Method

2.1.1. Participants

Two groups of participants were recruited. 24 older adult controls (10 male) ranging in age from 65 to 87 years (M = 74.00 years, SD = 5.43 years) recruited from the participant panel at the University of Aberdeen and reimbursed for their travel expenses. All control participants were tested at the University of Aberdeen. The clinical group were 24 people with AD (10 male) ranging in age from 65 to 89 years (M = 74.56, SD = 5.70). Those with AD were recruited from three sources: (1) the Department of Old Age Psychiatry at Royal Cornhill Hospital, Aberdeen (2) local Alzheimer Scotland groups and (3) registered volunteers from the Scottish Dementia Clinical Research Network, Regardless of source of recruitment, all participants with AD included in this research received their diagnosis from an old age psychiatrist based at Royal Cornhill Hospital, Aberdeen. All patients met the diagnostic criteria for "probable" AD as established by the National Institute of Aging working group (McKhann et al., 2011) and had Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) scores between 17 and 30, falling in the mild to moderately demented range. Some of the participants with AD were medicated, with the majority being prescribed more than one medicine. Prescriptions for medications included cholinesterase inhibitors and antidepressants in addition to treatment for physical illnesses such as hypertension. All those with AD were tested in their own home. Exclusion criteria for all participants included comorbidity of dementia subtypes (other than probable AD for the AD group), other neurological disorders, and history of alcohol or drug abuse.

A contrast sensitivity function (CSF) chart (Pelli, Robson, & Wilkins, 1988) was used to assess visual contrast sensitivity in both groups. CSF is a measure of how well the visual system can discriminate objects from their background. This aspect of visual perception could be important in making the fine-grained judgments necessary for discriminating gaze direction. The MMSE was used to determine the cognitive status of both groups. All members of the control group achieved a score higher than 24, which is the recommended cut off (Chayer, 2002). The age, education, CSF and Mini-Mental State Examination (MMSE; Folstein et al., 1975) scores for both groups were analysed (see Table 1). The groups were generally well matched: there were no significant group differences for age, education or CSF. Participants with AD scored significantly lower in terms of their MMSE scores than the

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