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Review

Consent for the diagnosis of preclinical dementia states: A review

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ABSTRACT

It is now possible to detect the pathology of Alzheimer's disease (AD) many years before symptoms and signs otherwise become manifest. Biomarkers of disease include evidence of amyloid and tau in the cerebrospinal fluid and neuroimaging which (for instance) allows amyloid in the brain to be visualized. There is, thus, a preclinical state in which it is possible to identify Alzheimer's pathology long before there is clinical evidence of disease. Much research focuses on this preclinical state because it seems likely that treatments will be more effective before the disease is established. This means that researchers can discover Alzheimer's pathology some years before the person is at risk of developing the condition. In memory clinics, too, people may present with early (prodromal) symptoms which do not yet amount to a dementia syndrome (e.g. mild cognitive impairment), yet biomarker evidence that dementia is highly likely to develop. This is problematic because people will be required to consent to the disclosure of findings that indicate an uncertain risk of an alarming disease. We carried out a scoping review of the issues that arise in connection with a "diagnosis" of preclinical dementia. We identified four themes in the literature: stigma; ethical issues; psychological burden; and language. We shall discuss these themes and related issues that emerge to do with meaning, medicalization, virtues and values. More research is now required to understand these issues in detail, where the emphasis should be on the breadth of research, which must be biopsychosocial and ethical.

Contents

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1. Introduction

Within the last ten years, new concepts for understanding Alzheimer's disease (AD) have emerged [1,2]. Although these concepts differ in detail and are still evolving, there is general agreement that AD is a continuum from a preclinical state via a prodromal condition to full-blown Alzheimer's dementia.

Alzheimer's dementia is the well-recognized condition in which there is an acquired global impairment of cognitive function which is severe enough to affect activities of daily living, aspects of personality and behaviour, where the typical Alzheimer's pathology can be demonstrated post-mortem. Concepts such as mild cognitive impairment (MCI) emerged subsequently to describe the (prodromal) state, where limited cognitive impairment did not fulfil the criteria for full-blown dementia and did not affect activities of daily living. However, not all cases of MCI progress to dementia [3].

The new idea is that of a preclinical state, extending over many years, during which the person is asymptomatic but has detectable pathology. In fact, it has been known for some time that an albeit small group of people (less than 1.5% of those with Alzheimer's dementia) carry a dominant gene for AD and remain pre-symptomatic for many years. The new concept has emerged because it is now technically possible to detect Alzheimer's pathology preclinically. A variety of biomarkers allow much greater (albeit not perfect) accuracy in terms of predicting that a person will develop Alzheimer's dementia because of current asymptomatic pathology. Thus, amyloid (one of the hallmarks of Alzheimer's pathology) can be detected in the brain using both neuroimaging and analysis of the cerebrospinal fluid (CSF). Tau, another protein (like amyloid) found in the brains of people with Alzheimer's dementia, can also be detected in the CSF (and will soon be detectable by neuroimaging). There are other morphological changes in the brain that are more typical of Alzheimer's than of other dementias. These biomarkers, along with genetic markers for susceptibility such as the ApoE $\varepsilon 4$ allele, give meaning to the concept of "non-dementia AD".

Inasmuch as this is new, therefore, it raises new ethical challenges. For it is now perfectly possible that a researcher will learn that a person has significant Alzheimer's pathology in the absence of overt symptoms or signs of the disease. This possibility is stimulating ethical interest [4]. We decided to review the literature to consider issues around the identification of preclinical dementia.

2. Methods

2.1. Sources of information

We searched the databases PubMed, ScienceDirect and PsychSource separately.

2.2. Search terms and parameters

Our search used the terms "asymptomatic at risk for AD", "asymptomatic AD", "pre-dementia", "preclinical dementia", "presymptomatic AD", "prodromal AD", "mild cognitive impairment" and "MCI" each in combination with "consent" AND "diagnosis".

The search was limited to title and abstract, but any research methodology was accepted including meta-analyses, randomised controlled trials, observational studies, reviews and opinion pieces. The search was further limited to papers written in English, involving humans and published between 2006 and 2016. Age and type of potential dementia were not exclusion criteria. This was a scoping review in which we were concerned with broad topics and a variety of study designs without an intention to address a specific research question and without consideration of the quality of the studies identified [5].

2.3. Selection criteria

Papers included in this review were those specifically concerned with the consent for a diagnosis of pre-dementia states and the surrounding issues regarding disclosure of information and its implications. Papers concerning the consent for a diagnosis of clinical dementia were excluded; those concerned solely with capacity, screening measures and predictive prognosis were also not considered. We restricted our review specifically to preclinical states.

2.4. Synthesis

After the initial literature search, the papers were read in full by each member of the team. We then met to discuss emergent issues and themes in greater detail. Through our discussions numerous issues emerged; a narrative or descriptive account of the literature coalesced around four main themes.

3. Results [950]

The papers we identified mainly referred to AD, which was therefore the focus of our analysis. After the exclusion of duplicate papers, our search identified ten papers: seven were opinion pieces or non-systematic reviews [6–8,10,11,13,15]; three were based on empirical studies [9,12,14], one of which was a Delphi study [9]. The four themes to emerge were: stigma; ethical issues; psychological burden; and language. We shall discuss each theme in turn. However, the themes inevitably overlap.

3.1. Stigma

One significant concern is that preclinical identification of AD will lead to stigma [11,15]. Much of this concern reflects experience and research involving MCI and AD dementia. Stigma may show itself in a variety of forms, from discrimination in the work place to difficulty gaining insurance [8–10,15]. There may also be interpersonal stigma [9], public or social stigma [11], involving social isolation and distancing [10,15]. Johnson and Karlawish cite research that shows it is not AD itself that elicits stigma, but 'the label's association with expectations of certain future decline' [10]. They also identify civic rights and privileges, such as driving and voting, as further areas where there might be discrimination [10]. The negative perception of the AD label can become internalised causing self-stigma [7,11]. Stigma can also be directed at those who care for people living with dementia [11]. Worries about stigma have led some to suggest the need for new legislation around pri-