



# Anxiety in old age and dementia - implications for clinical and research practice

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## ABSTRACT

While extensive research has been performed in relation to anxiety in general, there is a marked paucity of investigation on older adulthood, especially in relation to those individuals living with mild cognitive impairment (MCI) and dementia, with the majority of such studies clinically based and focusing upon 'formal' anxiety disorders. It is however becoming increasingly evident that the detrimental effects of anxiety are not limited to clinical anxiety disorders but can instead occur in response to anxiety per se, i.e., sub-syndromal anxiety including various levels of trait and state anxiety. Furthermore, it is increasingly apparent that even non-clinical anxiety can influence many more components of information processing than previously recognized.

## Keywords

Anxiety, Ageing, Cognitive impairment, Dementia

## Introduction

In ageing and dementia-related research, it is now common practice to determine the functional integrity of a much wider range and level of brain function rather than focusing predominantly on memory and cognition in order to improve disease characterization and understanding. Nevertheless, in many studies individuals with clinical anxiety disorders are excluded whereas those with lower levels of state or trait anxiety may be included. In the first scenario the results are applicable only to the population without an anxiety disorder and resultant failure to gain information about the effects of anxiety upon the function measured. In the second scenario we fail to take into account the potential effects of non-clinical anxiety upon brain function and thus study outcome, interpretation and general applicability and relevance.

In this review we explore evidence indicative of the potential influence anxiety per se may have upon tests of some aspects of brain function in

order to raise awareness, promote discussion and to possibly lead to a change in methodological practice in which anxiety-related factors are more appropriately considered. Anxiety in relation to MCI and dementia is given particular emphasis: a pertinent strategy when one considers the importance of dissociating the effects of potentially treatable anxiety from those of neurodegenerative disease, and the influence anxiety may have upon the outcome of research in this area.

## Data bases searched

Medline, PubMed, Web of Science, PsycARTICLES, PsycINFO and searches of the References sections of published papers.

## Principle Search terms

Anxiety, anxiety and ageing, cognitive impairment, dementia, information processing,

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vision, attention, inhibition, sleep, health and depression

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### **Anxiety**

Although definitions of anxiety vary it is generally recognized as an aversive feeling of unease, worry, nervousness or fear about something that is happening or might happen. State anxiety refers to temporarily experienced anxiety, related to a specific situation, with Trait anxiety describing a longer lasting response or a general disposition to anxiety. Psychiatric or clinical disorders such as general anxiety disorder (GAD), panic disorders and specific phobias are commonly described with respect to a wide range of assessment instruments [1-6]. Nevertheless, over the lifespan, irrespective of classification, anxiety tends to result in, or be associated with, a wide range of physical, affective and cognitive responses including palpitations, sleep problems, muscle tension, apprehension, poor concentration, restlessness and reassurance seeking behavior [7-13].

Anxiety aetiology and risk factors across the lifespan appear multidimensional and complex, and include personality traits (e.g. neuroticism and low self-efficacy) and environmental factors (e.g. trauma and stress) [3,6,9,14-17] and it is often associated, or coexistent, with health issues such as osteoarthritis, stroke, obesity; intellectual disability, cancer, cardiovascular disease, diabetes, Alzheimer's disease, pain, sleep issues, chronic physical illness, medical illness and increasing frailty (although ageing per se does not appear to be a risk factor), vision and hearing impairment [1,2,18-33] and depression [34-36]. Underpinning these anxiety-related associations are a variety of models, mechanisms and pathways [2,5,7,8,14,26,34-42]. Nevertheless, of particular relevance to this review, is that irrespective of its cause and associations, anxiety appears to affect a wide range of brain functions.

#### **■ The potential impact of anxiety**

The prevalence of anxiety disorders in older adults is high [12], with estimates up to 15.3% [10,11] with prevalence rates for anxiety sometimes equal to, or even exceeding, those for depressive disorders [2, 10,13,38,43-46]. Rather surprisingly, given the relative lack of research in this area [43,47], sub-syndromal anxiety symptoms appear more widespread than anxiety disorders [12], with prevalence ranging from 15% to 52.3% [10]. Furthermore, irrespective

of aetiology, type and theoretical approach, in practical, real life terms, a substantial body of research indicates that anxiety in older adults can be associated with considerable disease burden, poor outcome, detrimental impact upon daily living and quality of life, poor functional status and physical activity, poorer self-perceptions with regards to health, decreased life satisfaction, increased loneliness and service use, depression, urinary incontinence, sleep disturbance, unhealthy behaviors such as smoking, physical inactivity, poor diet and alcohol misuse [12,48,49], diabetes, stroke, cardiovascular disease, tachycardia, increased arousal and muscle tension, altered interoceptive prediction signals, enhanced sensitivity to new stimuli, impeded decision making skills, language and cognitive function, cognitive decline and dementia [2,9,24,26,38,41,42,45,47,50-62]. Less well known are the effects of anxiety upon some of the more fundamental levels of information processing, as described in the following sections. Despite such evidence, anxiety can reportedly be largely undetected and untreated in older adults, especially in medical settings [63-65]; a possible consequence of diagnostic difficulty in older adults with multiple psychiatric, medical conditions [2], the attribution of symptoms to other factors [12], issues related to clinical practice [43], limitations to classification systems and the definition of anxiety in diseases such as dementia and the properties of assessment instruments [65]. Arguably therefore, improvement in health and wellbeing in older adulthood may be attained by raising awareness of the potential detrimental effects of anxiety in this age group and of the benefits of diagnosis and treatment [66,67]. Lack of appreciation of the potential influence of anxiety is especially pertinent in relation to the clinical assessment, characterization, diagnosis and follow-up of mild cognitive impairment and dementia in older adults [2,45,68-72], especially when one considers that anxiety can be amenable to treatment [12] and that the physiological response to anxiety may also detrimentally influence cognitive function over time [42,51,73,74].

#### **■ Anxiety, older adulthood, mild cognitive impairment and dementia**

Anxiety in general is associated with decreased cognitive functioning in older adulthood and increased risk of cognitive decline [35,36,51,62,72-76]. Although there is some evidence of decreased performance in some components of cognition, including processing

speed, attention shifting and inhibition in sub-syndromal anxiety [72] in older adults, the majority of studies, especially those related to memory and executive function, have tended to include clinical samples, i.e., individuals meeting full diagnostic criteria for anxiety disorders or with comorbid anxiety and depressive disorders [12]. Arguably, this approach is at odds with the known high prevalence of sub-syndromal anxiety [12,76].

Anxiety is also increasingly recognized (independently from depression) as a common symptom in older adults individuals living with various aetiologies of dementia, including Alzheimer's disease, vascular dementia, fronto-temporal dementia, Lewy body disease, posterior cortical atrophy, dementia associated with Parkinson's disease, and in subjective and mild cognitive impairment, tending to result in poorer quality of life, problematic behaviours, limitations in activities of daily living, nighttime awakening and poorer neuropsychological performance [43,65,69,77-85]. The relationship between anxiety and dementia is however both complex and controversial with overlap between the symptoms of anxiety and dementia and other behavioral and psychological problems such as agitation and depression [10,12,43,62,65,71,73,77,82,86-88]. Although anxiety may increase the rate of conversion of MCI to Alzheimer's disease, be related to neuropathological status, associated with an increased risk of developing AD, and to influence cognitive impairment in MCI [19,47,62,68,73,74,87,89], directionality is complex [47,71,74,90]. For example, in some individuals, perceived change in cognition or a diagnosis of MCI or SCI, can promote anxiety, whereas others are more susceptible to both anxiety and cognitive impairment [12,65,68,70,79,82]. Nevertheless, one can argue that treating anxiety in cognitive impairment or dementia may both remove a potential detrimental contributor to cognitive function and also improve the health and wellbeing of the individual living with these conditions.

#### ■ Anxiety and Clinical and Research Test Performance

While there is clearly a body of research examining the relationship between anxiety, cognitive decline and dementia, the potential for anxiety to influence the performance of tests used in the clinical assessment of cognitive function in older adults, especially in SCI, MCI and dementia, is

less well investigated, this is particularly the case with subclinical anxiety [91-93].

In addition to the traditional aspects of cognitive function explored in older adulthood, SCI, MCI and dementia, particularly in relation to diagnosis and progression, research has revealed that many other components and levels of information processing, particularly those related to attention [94-97], can also be abnormal in these conditions. However, the potential impact of anxiety upon such function remains a relative unknown and in the following section we highlight evidence related to the possibility that anxiety may directly or indirectly influence the results of both clinical and research tests of attention-related function.

#### ■ Anxiety and Attention-related processing

The brain's functionally and structurally independent yet cooperative attention network [98], is a fundamental component of our ability to selectively direct the brain's limited processing resources to the information of most relevance within the environment, which in turn influences many other aspects and levels of processing including cognition and perception. Research evidence indicates that some aspects of attention-related function can be influenced and modulated by anxiety [12,47,99-101]. These include attentional narrowing [100], selective attention, attentional control [7,102], inhibition, alerting, orienting and attentional resource allocation [7,15,102-117], pre-attentive change detection, sensory processing, contrast sensitivity involved in low level visual processing, processing speed, increased processing of task-irrelevant information [106,118-123] and selective attention bias in relation to threat-relevant information [108-110,120,122,123], and which in some cases, is related to state or trait anxiety [114]. Furthermore, average pupil diameter can be greater in the presence of moderate to severe anxiety compared to mild or no anxiety symptoms [124] and thus may influence the pupillary light reflex [125-127] and possibly some aspects of attention-related function [128]. As pupillary function and the pupillary light reflex have been found to be significantly abnormal in AD [129] concomitant anxiety in AD may further exacerbate the effects of the disease and confound research results. Anxiety has also been reported to slow processing speeds in older adults with severe state anxiety [101,130,131].

As some of these functions or component processes have been found to be abnormal in AD and/or MCI [94-97], generally in studies in

which participants with anxiety disorders have been excluded, the detrimental effect may be exacerbated further in individuals with various forms of anxiety. It is possible that everyday environmental interpretation and response, highly dependent upon vision and attention-related function, may be significantly poorer in MCI and dementia compared to cognitively healthy ageing, as a result, at least in part, of concomitant anxiety in these disorders. Closely associated with attention-related processing is balance. The finding that state and trait anxiety can affect sensory inputs involved in balance [103,132-134] may have implications in relation to the already high risk of falls in MCI and dementia which may be further exacerbated by anxiety. Furthermore, expectations and beliefs may also modulate activity in the anxiety network [134], thus one must also consider the potential for 'testing' per se to induce anxiety which can adversely affect test performance in general [8,41,131,135,136], again potentially confounding study results.

### Summary

In view of the research evidence highlighted above, one might argue that as anxiety is a potentially treatable condition [69,136-139], intervention may prove an important factor in the management of individuals living with cognitive impairment and dementia [2,62,75], with dissemination of information regarding late-life anxiety disorder vital as evidence-based treatments, pharmacological and psychotherapy, are available [43,131-141]. There are however important caveats to consider. For example,

the majority of anxiety-related research has been performed in younger adults and in the context of exploring theoretical approaches; there is a paucity of evidence relating to the potential effects of anxiety upon cognitive and other aspects of information processing in both cognitively healthy ageing and in cognitive impairment and dementia. Also apparent from this review process is the diversity in the types of anxiety investigated in previous studies and the instruments used to define and diagnose these events in both clinical and research domains. Many manuscripts failed to provide a definition or formal criteria for identifying the type of anxiety investigated, with many simply stating only the scale used in its measurement, rather than inclusion and exclusion criteria. Further study is also required in order to determine whether treatment of anxiety corresponds to improved functionality and changes in test scores in SCI, MCI and dementia [51].

### Conclusion

We therefore call for debate of, and consensus in such matters as formally examining the anxiety status per se of both patients and controls taking part in dementia and cognitive impairment-related research studies, and determining and expressly stating the type of anxiety present (e.g., state, trait, general anxiety disorder, sub-syndromal anxiety) with respect to inclusion and exclusion criteria. Further improvement in this area could be made by explicitly stating the test(s) used to diagnose or exclude the presence of anxiety and by including anxiety as a factor in statistical analysis.

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