Anxiety symptoms and disorder predict activity limitations in the elderly.

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Word count: 4738

Abstract

Background: In the elderly, little attention has been paid to anxiety both on a symptom dimension and as a disorder, as an independent risk factor for the incidence of activity limitations.

Methods: In a community-dwelling cohort of 1581 persons aged 65+, the association between trait anxiety symptoms (Spielberger Trait, third highest tertile) and baseline DSM-IV anxiety disorder, and 7-year incident activity limitations was determined using mixed logistic regression models. Repeated measures of activity limitations included, by increased severity level: social restriction (neighbourhood and house confined), mobility (Rosow and Breslau scale) and limitations in instrumental activities of daily living (IADL).

Results: Of the sample, 14.2% had an anxiety disorder at baseline. Adjusting for baseline socio-demographic and health variables, depression (past and current), antidepressant and anxiolytic drugs, baseline anxiety disorder was associated with an increased risk of incident IADL limitation (OR (95% CI): 1.84 (1.01-3.39), p=0.048) and trait anxiety with increased incidence of social restriction (OR (95% CI): 2.41 (1.42-4.09), p=0.001). Associations remained significant in participants free of depressive symptoms at baseline (OR (95% CI): 2.92 (1.41-6.05), p=0.004; OR (95% CI): 3.21 (1.31-7.89), p=0.011, respectively).

Limitations: activity limitations were self-reported and may have been over-reported in participants with anxiety.

Conclusion: Both trait anxiety symptomatology and anxiety disorder were independently associated with increased incidence of activity limitations with a gradient of severity: trait anxiety associated with incident social restriction and anxiety disorder with more severe IADL limitations, suggesting that anxiety is a predictor of activity limitations in the elderly independently of depression comorbidity.

Key words: anxiety, disability, aged, longitudinal studies.

INTRODUCTION

Anxiety is the most prevalent psychiatric disorder affecting one in four persons across their lifetime (Kessler et al., 2005; Ritchie et al., 2004). Prevalence estimates in later life range from 1.2% to 14.2% (Bryant et al., 2008; Wolitzky-Taylor et al., 2010) depending on sampling procedure, diagnosis tools used, age cut-offs for classification as elderly and exclusion or not of anxiety cases due to general medical conditions.

As in younger adults, anxiety and depression are frequently comorbid in older people. Cairney et al. (2008) found in a large community-based sample aged 55 and older, that 23% of those with anxiety disorders also met diagnosis criteria for major depressive disorder using the World Mental Health Composite International Diagnostic Interview (Cairney et al., 2008).

While depression has been consistently demonstrated to be an independent risk factor for functional loss in the elderly (Carriere et al., 2011; Carriere et al., 2009; Schillerstrom et al., 2008), little is currently known about the association between anxiety disorders and activity limitations: previous research being largely based on cross-sectional observations (Brenes et al., 2008; Cairney et al., 2008; de Beurs et al., 1999; Porensky et al., 2009; Sareen et al., 2006). To date only two prospective studies have been undertaken. In a sample of functionally limited women aged 65 and above, anxiety symptoms predicted activities of daily living (ADL) limitations and mild housework disability over a 3-year period (Brenes et al., 2005), and in a one-year prospective study of adults aged 72 and above, anxiety symptoms remained associated with incident ADL limitations after adjustment for physical functioning (Tinetti et al., 1995). Previous longitudinal research has been limited due to the absence of adequate anxiety disorder diagnosis, failure to take into account common co-occurence with depression, and the use of partial dependency measures incorporating different items from ADL or instrumental activities of daily living (IADL) scales over short follow-up periods.

Another point which has not always been considered in previous analyses concerns confounding by other mental health factors, especially depression and somatic comorbidity which are common in the elderly. Symptoms such as dizziness, chest pain, shortness of breath, tiredness, exhaustion, palpitations and nausea in anxiety disorders also occur in common pathologies such as heart disease, chronic obstructive pulmonary disease, postural hypotension, thyroid disease in conjunction with some medications taken and as part of the general frailty syndrome (Blazer, 1997). This may thus render difficult the diagnosis of anxiety especially when considering that the DSM-IV diagnosis of generalised anxiety disorder (GAD) cannot be established if it is the consequence of medical conditions. However, ruling out an organic disorder or a drug effect is often difficult in the elderly.

Anxiety pharmacotherapy also presents challenges. Benzodiazepines are the most frequently prescribed anxiolytic medication in older adults, of which approximately half are long half-life agents (Gray et al., 2006). However, they are associated with a number of adverse risks, especially those with a long half-life, including cognitive impairment, psychomotor impairment, excessive daytime sedation, instability of gait, falls, and hip fractures (Gray et al., 2002; Gray et al., 2006; Ried et al., 1998). The effect of anxiety on dependency may thus be confounded by benzodiazepine side-effects.

The purpose of this study, using data from a large cohort of community-living elderly persons allowing adjustment for a number of confounders (*e.g.* sociodemographic characteristics, physical and mental health, medications), is firstly to evaluate the 7-year longitudinal association between anxiety measured both with a standardized psychiatric interview and a self-reported symptom scale and activity limitations, and secondly to evaluate if the association persists independently of depressive symptoms.

METHOD

Study sample

The design of the ESPRIT study and participant recruitment have been published in detail elsewhere (Ritchie et al., 2004). Participants were recruited over a 2-year period from 1999 to 2001, by random selection from the electoral rolls in Montpellier, France. Eligible persons, who were at least 65 years of age and non-institutionalised, were invited to participate and provided written informed consent. Participants were administered a number of standardised questionnaires by trained staff and underwent clinical examinations at baseline, 2 years, 4 years and 7 years in a dedicated centre or at home. Ethics approval for the ESPRIT study was granted by the Ethics Committee of the University Hospital of Kremlin-Bicêtre (France).

Of the 2189 dementia-free participants included in the study, 141 were missing all follow-up evaluations for activity limitations (of whom 71 died) and 467 had missing data for at least one baseline adjustment variable. The present analysis was thus conducted on 1581 subjects.

Compared to the analysed sample, those not included in this analysis were more likely to be older ($p<0.0001$), have a lower level of education ($p<0.006$), have a lower level of income ($p=0.002$), be depressed ($p<0.0001$), have activity limitations ($p<0.0001$), and have visual ($p=0.0008$), hearing ($p<0.0001$) and cognitive impairment ($p<0.0001$). There was no significant difference regarding chronic disease status, intensity of anxiety symptoms or frequency of diagnosed anxiety.

Disability measures

As outcomes, we chose three disability measures widely used in elderly populations, in order to reflect varying forms of disability.

Social restriction was measured on a four-point scale ranging, by decreasing level of

severity, from confinement to bed, to home, to the neighbourhood, to no restriction. According to the World Health Organisation International Classification of Functioning, Disability, and Health (ICF, 2001), this can be considered as participation restriction resulting from personal functional and activity limitations and environmental factors. Subjects were classified as socially restricted if they reported any type of confinement.

With regard to activity limitations, mobility was assessed using the Rosow and Breslau scale (Rosow & Breslau, 1966) which assesses ability to perform physical tasks requiring mobility and strength such as doing heavy housework, walking half a mile, and climbing stairs, with binary yes/no responses for each item. The Lawton–Brody IADL scale was used to evaluate skills necessary to live independently such as the ability to use the telephone, to manage medication and money, to use public or private transport, to shop, and for women only, to prepare meals and do housework and laundry, with limitation severity response scales varying from three to five points (Lawton & Brody, 1969). Compared to the Rosow and Breslau scale, this scale investigates daily activities which implicate both physical and cognitive abilities. For both types of activity limitations, participants indicating inability to perform one or more activities without help were considered as having mobility or IADL limitations.

Anxiety disorders

At baseline, a standardized psychiatric examination the Mini International Neuropsychiatry Interview (MINI), was used to investigate lifetime and current psychiatric disorder (Sheehan et al., 1998). This interview has been previously validated in France and widely used in many clinical and research settings (Lecrubier et al., 1997). The interview was administered by nurses and psychologists trained using video recordings of interviews by the clinicians responsible for the development of the French version of the tool. The MINI

provides an extensive symptomatological examination, with diagnostic algorithms applied to assess 'caseness'. With regard to anxiety disorders, it provides diagnoses of both current and past GAD, social phobia, agoraphobia, obsessive compulsive disorder (OCD), panic and post-traumatic disorder(PTSD), according to DSM-IV criteria. Cases detected by the MINI were reviewed by a panel of psychiatrists to validate the initial diagnosis (Ritchie et al., 2004).

Spielberger's State-Trait Anxiety Inventory (STAI), a well-established and validated self-report measure of anxiety, was used to measure trait anxiety (Spielberger, 1983). The scale is composed of 20 items, each rated on a four-point intensity scale. Overall scores range from 20 to 80. Different cut-offs are available in the literature for the elderly but none of them have been validated (Devier et al., 2009; Himmelfarb & Murrell, 1984; Tinetti et al., 1995). Himmelfarb (1983) established a cut-off score of 44+ as best discriminating between a hospitalised clinical sample and a non-hospitalised community sample of older persons (Himmelfarb & Murrell, 1984). Devier at al. (2009) used a previously reported threshold of 30+ in studying conversion in patients from MCI to Alzheimer's disease (Devier et al., 2009) and Tinetti et al. (1995) used Spielberger's (1983) normative mean score value of 32 in 50-69 year old adults to dichotomise the score (Tinetti et al., 1995). In the absence of a validated cut-off score, we decided to group STAI trait scores into tertiles and to compare the highest tertile to the lowest two.

Medication

Use of antidepressant and anxiolytic medication in the previous month, validated by presentation of the prescription or medication, was recorded at baseline and type of medication was noted according to the World Health Organization's Anatomical Therapeutic Chemical (ATC) classification (for antidepressant medication: N06A; anxiolytics: N05B, of which short half-life benzodiazepines: N05BA04, N05BA06, N05BA12, N05BA21, and long

(≥20h) half-life benzodiazepines; N05BA01, N05BA05, N05BA08, N05BA09, N05BA11, N05BA16, N05BA18).

Depressive symptomatology

The MINI was also used for the diagnosis of current and past major depressive episodes (MDE), according to DSM–IV criteria. Severity of depressive symptoms was assessed using the 20-item Center for Epidemiologic Studies–Depression scale (CES–D) (Radloff, 1977). For this analysis, participants were classified into one of three groups (Ryan et al., 2008). 'Severe depressive symptomatology' included participants with a current MDE or a CES–D score of 23 or over (allowing for the fact that some participants with severe symptoms did not reach DSM classification criteria, principally because of the duration of symptoms). 'Mild depressive symptomatology' was defined as a CES–D score between 16 and 22 and ‘No depressive symptomatology' included participants with a CES–D score lower than 16.

Socio-demographic and clinical variables

The standardized interview included questions on demographic characteristics, level of education (≤5 versus 6+ years of education), marital status, mode of living (alone or not) and income as well as an inventory of all drugs (including anxiolytic and antidepressant drugs) used over the preceding month. Information was obtained on type and quantity of alcohol consumption (number of units of alcohol per day: 0-36 versus >36 g/day) and tobacco use (classified as past, present or never users). Detailed medical questionnaires included history of stroke, angina pectoris, myocardial infarction, and cardio-vascular surgery established according to standardized questions, history of cancer and fracture with hospitalisation during the last two years, asthma (attacks during the last year), chronic bronchitis, dyspnoea,

hypertension (>160/95 mm Hg or treated), diabetes (fasting glycemia > 7mmol/l or treated) and thyroid disease. Blood pressure was measured during the interview using a digital electronic tensiometer OMRON M4. The number of chronic diseases was calculated including: hypertension, diabetes, cardiovascular diseases, respiratory diseases, dyspnoea, thyroid disease, and cancer.

Cognitive impairment was defined as a Mini Mental State Examination (MMSE) (Folstein et al., 1975) score lower than 24. Visual impairment was defined as having a corrected near visual acuity (Parinaud scale) of more than 4 or difficulties recognizing a familiar face at 4 meters. Hearing impairment was defined as deafness or only being able to hear a conversation when a single person speaks loudly.

Statistical analyses

The Chi² test was used to compare subjects in the study sample to those excluded. For each indicator of activity limitations longitudinal associations with anxiety disorders were established from subjects free of that activity limitation at baseline. Thus the sample size was 955 for mobility, 1470 for IADL and 1456 for social restriction.

In longitudinal studies, the within-subject responses (repeated evaluations of activity limitations) are correlated. This correlation was accounted for by using a mixed logistic model (Carriere & Bouyer, 2002). Briefly, this model has four basic characteristics: (i) the individual time evolutions of activity limitations are entirely taken into account including possible reversion to normal state (ii) subjects with incomplete responses across time are included in the analysis; (iii) subjects do not have to be evaluated at the same time points; (iv) the model allows within-subjects dependency to vary from one subject to another, via the random part of the covariable linear combination. The SAS procedure NLMIXED was used to estimate the parameters (version 9.2).

We used univariate and multivariate models to determine if baseline anxiety was associated with odds of activity limitations or social restriction during follow up. Odds ratios were adjusted for sex, age, time and interaction time*age (**Model 0**). Multivariate adjusted logistic regression included covariates that were associated with the follow-up responses ($p<0.15$ in univariate model). **Model 1** was adjusted for age, time, time*age, income, educational level and living alone. **Model 2** was further adjusted for alcohol, body mass index (BMI), smoking, chronic disease status (three or more chronic diseases versus two or less), cognitive, and visual impairment and hearing impairment. **Model 3** was further adjusted for depression (none, mild, severe) and **Model 4** for past MDE, antidepressant and anxiolytic medication consumption. Interactions between anxiety and sex, and anxiety and depression were tested for all anxiety-activity limitation combinations. A stratified analysis was also carried out, testing the association between anxiety and activity limitations among subjects with and without depressive symptoms. Finally, concerning specific anxiety diagnoses, models were run for phobic disorders only as the frequency of the other disorders was too low.

RESULTS

Within this sample, 14.2% of the subjects had a least one DSM-IV anxiety disorder at baseline, 10.8% any type of phobia, 4.1% GAD, and less than 1% PTSD, OCD or panic disorder; 25.9% had at least one past anxiety disorder **(Table 1)**. Mean score on the STAI Trait at baseline was 40.1 (SD: 9.1). Scores were dichotomised according to the upper tertile value, which corresponds to a cut-off score of 44. Among patients in the upper tertile defined as having a high level of trait anxiety, 24.1% reached criteria for a DSM-IV anxiety disorder compared to 9.8% in the lower tertiles.

Anxiolytic consumption was reported by 10.3% of the sample - the majority being benzodiazepine drugs (9.4%) of which half (5.1%) with a long (≥20h) half-life - and antidepressant consumption by 6.5%. The prevalence of mild depression was 15.5% and severe depression 13.1%. Of the 225 subjects with anxiety disorder at baseline, 17.8% also had mild depression and 27.6% severe depression. Of the 490 subjects with scores in the upper tertile for trait anxiety, 28.6% reached criteria for mild depression and 32.6% for severe depression.

Mobility limitation at baseline was reported by 36.8% of the subjects compared to 4.3% for social restriction and 3.2% for IADL limitations. Cross-sectional associations with baseline anxiety disorder and symptomatology are shown in **Table 2**.

The analysis of repeated activity limitations over time was undertaken for each scale on the subjects without limitation on the considered scale at baseline. **Table 3** shows rates and odds ratios for incident activity limitations over seven years according to the presence or absence of anxiety at baseline, in terms of both trait symptomatology and DSM-IV anxiety disorder. The odds ratios for having incident activity limitations are adjusted for sex, age, time and the interaction between time and age (Model 0). With regard to anxiety symptoms, the probability of developing any type of activity limitations increased significantly for subjects with a high trait symptom level at baseline. Anxiety disorder diagnosis was associated with a significantly increased probability of social restriction and IADL limitation but not mobility limitation.

All mixed logistic models showed a significant effect of age. Time showed a significant effect for IADL limitations only and age-time interaction for social restriction and IADL limitations, reflecting an increased effect of time with age. There was no interaction between anxiety and sex on activity limitations in any of the six mixed logistic regression models.

Table 4 shows the odds ratios for activity limitations according to anxiety at baseline with different levels of adjustment for possible confounders. All of the preceding associations persisted when adjusting for socio-demographic (Model 1) and physical health and lifestyle variables (Model 2). For social restriction, only trait anxiety symptoms remained significant when adding baseline depression (Model 3), baseline anxiolytic medication use and past MDE to the model (Model 4) (OR (95% CI): 2.41 (1.42-4.09)). The probability of incident limitations in mobility according to Trait anxiety symptoms at baseline became non significant when adjusting for further confounders in Models 3 and 4. With regard to IADL limitations, the probability increased significantly for anxiety disorder diagnosis at baseline only with an odds ratio (95% CI) of 1.84 (1.01-3.39) (Model 4).

None of the interaction terms between anxiety and baseline depressive symptomatology, further adjusted for covariates in Model 2, were significant. In a stratified analysis according to the presence or absence of mild and severe depressive symptoms, the association between anxiety disorder and incident IADL limitation remained significant in non-depressed subjects (CES-D <16) at baseline with a higher odds ratio (OR (95% CI) = 3.21 (1.31-7.89), p=0.011) than that obtained for the whole sample (OR (95% CI) = 1.84 (1.01-3.39), p=0.048). The association between baseline trait anxiety and social restriction also remained significant in the sub-sample of non-depressed subjects (OR (95% CI) = 2.92 (1.41-6.05), p=0.004).

None of the interactions between chronic disease status and anxiety (symptoms and disorder) on the 3 activity limitation variables were significant. With regard to specific anxiety disorders, phobia was associated with incident IADL limitations in Model 1(OR (95% CI) = 1.9 (1.06-3.39), p=0.03); however the association became borderline significant when further adjusted on physical health and lifestyle variables (Model 2) (OR (95% CI) = 1.78 (0.99-3.20), p=0.053).

DISCUSSION

This study is one of the first to examine anxiety, both on a trait symptom level and as a diagnosed disorder, as an independent predictor of 7-year incident activity limitations in a representative sample of community-dwelling elderly persons. Our findings suggest both trait anxiety symptoms and disorders meeting strict diagnostic criteria are associated with incident activity limitations. Interestingly, trait anxiety was associated with social restriction, whereas anxiety disorders were associated with more severe IADL limitations. Associations remained significant when adjusting for both past and current depressive symptoms at baseline and in non-depressed subjects only, suggesting that despite the high level of comorbidity between anxiety and depression, anxiety is an independent risk factor for activity limitations.

Anxiety in the elderly

While the association between depression and onset of disability in the elderly has been extensively explored (Carriere et al., 2009; Schillerstrom et al., 2008) with depression being confirmed as an independent risk factor even when multiple confounding effects are taken into account (Carriere et al., 2011), less is known about the association between anxiety and disability even though the prevalence of anxiety disorder in the elderly appears to be as high and maybe even higher than that of depression. In the present sample, 2.3% of subjects aged 65 and above had a baseline major depressive episode and 13.2% were classified as having severe depressive symptoms, whereas 14.2% had at least one baseline anxiety disorder; there was a three-fold increase in the prevalence of MDE (6.7%) among subjects with at least one anxiety disorder. In the elderly, medical comorbidity is also very frequent and several physical conditions such as cardiac, respiratory and vestibular problems may both be a source of anxiety and be exacerbated by anxiety (Wolitzky-Taylor et al., 2010). Cognitive impairment may affect presentation of symptoms, experience of symptoms and the

ability to communicate them, rendering difficult the recognition of anxiety. At last it is still unclear whether older anxious persons experience other symptoms (not taken into account in existing assessment tools) than younger persons. Anxiety among older adults has been suggested to take a more somatic form with complaints such as dizziness and shakiness (Flint, 2005).

Anxiety as a risk factor for disability

Most studies of the association between anxiety and disability have been cross-sectional, precluding inference about direction of causation. Only two studies have analysed the prospective association between anxiety symptoms (but not anxiety disorder) and disability or its progression in the elderly. In a sample of 1002 functionally limited women aged 65 and over, past week anxiety symptoms identified using the Hopkins Symptom Checklist predicted 3-year ADL and mild housework limitations, but not mobility and lifting disability (Brenes et al., 2005). Models were adjusted for potential confounders (eg. number of chronic diseases and depressive symptoms) and mediators (eg. benzodiazepine and psychotropic medication use). In a one-year follow-up of adults aged 72 and over, Tinetti et al. (1995) examined anxiety symptomatology measured by Spielberger's Trait Inventory applying the normative average score of 32 among 764 working adults aged 50-69 years as the cut-off (Spielberger, 1983). Anxiety remained a significant predictor of functional dependence after adjusting for other predisposing factors (lower extremity and upper extremity impairment and sensory impairment), incontinence and falling (Tinetti et al., 1995). However, neither of these studies excluded from the analysis subjects with functional dependence or activity limitations at baseline precluding the distinction between a cross-sectional and longitudinal effect. In the current study we not only examined incident disability over a longer time-period (7-years) than previous studies, but for each type of limitation

investigated we excluded subjects with the condition at baseline thus giving accurate estimates of predictive risks.

Anxiety symptoms versus disorder

Our findings suggest that both anxiety symptoms and disorder are risk factors for disability, with anxiety symptoms associated with a less severe form of disability: a high level of trait anxiety was associated with incident social restriction, whereas anxiety disorder was associated with onset of IADL limitations. A tendency was also found for an association between trait anxiety symptoms and mobility limitations. Contrary to De Beurs' cross-sectional study where current sub-syndromal and DSM-IV anxiety disorder were considered as two mutually-exclusive categories based on strict diagnostic criteria (de Beurs et al., 1999), we used two different approaches to measure anxiety which are likely to capture different forms of anxiety. In fact, only 52.4% of patients with anxiety disorder had a high level of trait anxiety (defined as the overall top tertile) indicating only partial overlap. There are many possible explanations for this. Firstly, trait anxiety measures long-lasting persistent symptoms referring to how the subject usually feels, with responses given on a four-point severity scale and no specific time-frame whereas anxiety disorders refer to symptoms experienced over the past month (or six months for GAD), with binary responses and filter questions. Secondly, Spielberger's STAI is a self-report instrument whereas the MINI is administered by a trained-lay interviewer, each approach introducing different types of bias. It can tentatively be argued that these different forms of anxiety will trigger different types of disability. Subjects with underlying anxiety symptoms may be more likely to become social restricted as a result of actual physical limitations or through fear of falling and going out. On the other hand, anxiety disorder would lead to dependency for specific daily living skills through a combination of reduced physical and cognitive abilities.

Our findings stress the importance of considering underlying trait anxiety in the elderly, anxiety symptoms not necessarily fulfilling diagnostic criteria also causing distress and activity restriction.

With regard to specific anxiety disorders, the association between phobia and incident IADL limitations became non significant when adjusting for physical and mental health disorders. Given that two-thirds of persons with anxiety disorder at baseline had phobic disorder, the lack of association probably results from a loss of statistical power.

Depressive symptoms as a potential confounder

The complex relationship between anxiety and depression, with shared symptoms and high levels of comorbidity especially at low symptom levels, warrants a study of the independent association of both anxiety symptoms and disorder with disability. In the two prospective studies of anxiety symptoms, Brenes et al (2005) adjusted their analysis on depression at baseline only, whereas Tinetti et al (1995) selected anxiety symptoms over depressive symptoms as a predisposing risk factor for three outcomes: falls, incontinence and functional dependence (Brenes et al., 2005; Tinetti et al., 1995). In the latter study, the selection which aimed to reduce the number of covariates actually eliminated depressive symptoms in the final model based on a slightly higher risk for anxiety symptoms. Our findings remain significant when adjusting for both current and past depression at baseline and when restricting the analysis to subjects free of mild and severe depression at baseline, suggesting that anxiety is an independent predictor of disability.

Other confounding and mediating effects

Anxiolytic use, particularly benzodiazepines, is a known risk factor for disability and was entered as an adjustment variable in the final models. It remained a significant and

independent predictor of mobility and IADL limitations, but not of social restriction. Associations between benzodiazepines use and onset of mobility and ADL limitations have previously been found (Gray et al., 2006) and benzodiazepine use in the past year has been shown to be associated with both ADL and IADL limitations (Ried et al., 1998). Although many possible confounding variables such as antidepressant use have been taken into account, the observed associations for mobility and IADL limitations are likely to be more strongly related to underlying symptoms associated with anxiolytic use rather than with use itself: an independent effect of anxiolytic use on activity limitations cannot be ruled out but the mechanisms involved are likely to be complex, especially over a 7-year follow-up period. Taking into account both antidepressant and anxiolytic use in the final model, the relationships between trait anxiety and social restriction, and anxiety disorder and IADL limitations remain significant, suggesting medication use would only partially explain the associations.

Analyses were also adjusted for all other baseline covariables significantly associated with incident activity limitations. The associations of trait anxiety symptoms with social restriction and anxiety disorders with IADL remained significant after multiple adjustments indicating their robustness. In particular we adjusted for the main chronic diseases and health behaviours such as smoking and alcohol, which did not substantially change the estimation of the anxiety effect. We also adjusted for sensory impairments which have been demonstrated to be predictors of both functional disability and anxiety (Crews & Campbell, 2004; Mehta et al., 2003).

Potential mechanisms for the relationship between anxiety and incident activity limitations

The mechanisms by which anxiety may lead to activity limitations are likely to be complex involving physical and psychiatric comorbidity, cognitive and sensory impairments, health behaviours and biological factors. Mechanisms have previously been reported for the association between depression and incident activity limitations (Carriere et al., 2011) but it is unclear to what extent they also apply to anxiety symptoms and disorder. Anxiety and depression have been shown to have different relationships to mortality (Mykletun et al., 2009) which suggests the mechanisms may differ. Early signs of cognitive impairment are likely to induce anxiety. Yet the relationships between anxiety and activity limitations found in our study remained significant after adjusting for cognitive impairment at baseline with no significant interaction between cognitive impairment and anxiety. It is possible that the threshold for cognitive impairment was set too high (MMSE score <24) which identified as impaired only 3.3% of the sample and not those with early signs of impairment.

Brenes et al examined physical activity, benzodiazepine and psychotropic medication use and lack of emotional support, as possible mediators for the effect of anxiety on disability (Brenes et al., 2005). Their findings failed to prove support for these three variables. Although we did not examine the effect of mediating factors, our results suggest anxiolytic use in the month preceding baseline plays a limited role in explaining this relationship. Another possible mechanism could be through the somatic symptoms of anxiety such as dizziness and shaking which affect functional capacity and thus the ability to carry out everyday functions (Blazer, 1997; Flint, 2005). This may hold for anxiety disorders but is unlikely to explain the relationship between underlying long-term trait anxiety and social restriction.

Comorbidity with physical diseases is a likely candidate for explaining the association between anxiety and incident activity limitations. For example, anxiety is often comorbid with hypertension (Mehta et al., 2003) and heart disease (Wolitzky-Taylor et al., 2010), both of

which could result in increased activity limitations. This explanation is unlikely though, as we controlled for the main chronic diseases at baseline in our study. However, anxiety may precede these physical diseases which in turn cause disability. Finally, behavioural mechanisms could explain the association between anxiety and incident activity limitation with, for example, anxiety symptoms shaping the perception of risk and inducing fear which in turn would curtail activity levels especially social participation.

Strengths and Limitations

Our study is based on a large community sample of elderly subjects (Ritchie et al., 2004) with three follow-up examinations over 7 years, permitting a dynamic evaluation of activity limitation. We used validated scales to measure social restriction and activity limitations, corresponding to distinct levels of disability severity. We examined disability in relation to baseline anxiety, both on a symptom scale and as a diagnostic category. Our study is the first to include these complementary measures of anxiety, the former taking into account the severity of underlying and persisting symptoms and the latter, disorders meeting strict DSM-IV diagnostic criteria. Whereas symptom severity was self-reported, we used a structured diagnostic interview for anxiety disorders, thus minimizing misclassification. However, we were not able to fully rule out medical conditions or medication use as a cause of anxiety symptoms in the diagnosis of GAD. Nonetheless we controlled for a large number of potentially confounding factors particularly measures of physical and mental comorbidity and baseline use of antidepressant and anxiolytic medication. We used a statistical model particularly adapted to longitudinal analyses of reversible states; furthermore it did not require fixed time points at follow-up and included subjects with incomplete follow-up thus maximising sample size.

Concerning the limitations of our study, activity limitations were self-reported and may have been over-reported in subjects with anxiety. Although subjects with activity limitations at baseline were excluded, self-reported anxiety symptoms may have been over-reported in subjects with early signs of social restriction and activity limitation. Bias could also be introduced by the non-random exclusion of subjects with missing data at baseline or lost to follow-up, who were more likely to have depressive symptoms, as well as activity limitations. However there was no difference regarding anxiety symptoms or disorders at baseline. Whereas the association between depression and incident disability was previously found to be gender-dependent (Carriere et al., 2011), this appears not to be the case for trait anxiety symptoms or anxiety disorder. However this could be due to smaller sample size, the interaction term failing to reach significance. In spite of extensive adjustments for a large number of potential confounding factors, the possibility remains with observational data that unmeasured confounders such as individual behaviour or social environment may partly explain the associations. Lastly, despite the large overall sample size, we were not able to analyse ADL limitation due to too low incidence rate (0.7% to 2.0%).

Conclusion

In conclusion, our findings highlight the importance of considering anxiety both on a dimensional symptom scale and as a disorder reaching diagnostic criteria. Firstly, both measures of anxiety are associated with incident disability with different levels of severity. These associations are independent of comorbid depressive symptomatology and persist in non-depressed elders. In addition, focusing on trait anxiety symptoms would allow the identification of a wide range of subjects who are missed if applying diagnostic criteria only but whose symptoms are likely to lead to dependency. Our study underlines the necessity to

increase the recognition of anxiety in the elderly which to date remains largely under-diagnosed and undertreated.

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Table 1. Sample description at baseline

	Total (N=1581) %	Subjects with Trait anxiety (N=490) %	Subjects with DSM IV anxiety disorder (N=225) %
Sex (male)	42.0	29.18	24.89
Age			
65-69	32.19	35.31	31.56
70-74	36.06	36.12	44.0
75-80	21.38	20.0	16.0
80+	10.37	8.57	8.44
Education (≤ 5 years)	22.52	24.49	28.0
Living alone	26.12	29.18	32.0
Income (> 1500 €/month)	75.08	70.41	72.44
Alcohol consumption			
0	16.26	22.45	22.67
1-36 g/day	73.75	69.59	71.11
> 36g/day	9.99	7.96	6.22
Smoking			
Never	56.86	61.22	65.33
Former	36.75	33.88	29.33
Current	6.39	4.90	5.34
BMI			
Normal (<25)	55.09	55.71	60.0
Overweight (25-29)	36.88	35.71	32.44
Obese (≥30)	8.03	8.58	7.56
Number of chronic pathologies*			
None	37.70	36.53	35.56
1-2	56.35	57.35	56.44
3-5	5.95	6.12	8.0
Cognitive impairment (MMSE score <24)	3.29	4.90	6.22
Visual impairment	5.88	7.76	5.78
Hearing impairment	3.67	4.08	3.56
Social restriction: home or neighbourhood confined	4.30	5.51	7.11
Activity limitations: Mobility	36.81	46.94	48.0
Activity limitations: IADL	3.23	3.67	4.44
Trait Anxiety (mean (SD))	40.13 (9.1)	50.95 (5.60)	45.03 (10.43)
At least one baseline anxiety disorder (DSM-IV)	14.23	24.08	-
At least one past anxiety disorder (DSM-IV)	25.95	33.74	72.32
Anxiolytic consumption	10.31	17.55	17.78
Antidepressant consumption	6.45	12.65	11.11

Depressive symptomatology at baseline	71.34	38.78	54.67
No	15.50	28.57	17.77
Mild	13.16	32.65	27.56
Severe			
History of major depressive episode	24.79	37.14	37.78

*chronic pathologies include: hypertension, diabetes, cardiovascular diseases, respiratory diseases, dyspnoea, thyroid disease, and cancer.

Table 2. Cross-sectional association between anxiety (baseline anxiety disorder and trait anxiety) and activity limitation (N=1581)

	Activity limitation			
	N	(%)	OR (95% CI) [#]	p-value
Social restriction: : home or neighbourhood confined				
Baseline Anxiety Disorder				
No	1356	3.83		
Yes	225	7.11	1.95 (1.05-3.63)	0.034
Baseline Trait Anxiety				
Low-Moderate	1091	3.756		
High*	490	5.51	1.51 (0.89-2.55)	0.12
Activity limitations: Mobility				
Baseline Anxiety Disorder				
No	1356	34.96		
Yes	225	48.0	1.61 (1.18-2.0)	0.003
Baseline Trait Anxiety				
Low-Moderate	1091	32.26		
High*	490	46.94	1.83 (1.43-2.33)	<0.0001
Activity limitations: IADL				
Baseline Anxiety Disorder				
No	1356	3.02		
Yes	225	4.44	1.56 (0.76-3.24)	0.23
Baseline Trait Anxiety				
Low-Moderate	1091	3.02		
High*	490	3.67	1.26 (0.69-2.31)	0.44

*high=top third tertile

[#] adjusted for age and sex

Table 3. Incident cases of activity limitation at each follow-up by baseline anxiety: any DSM IV anxiety disorder and Spielberger Trait anxiety.

	Follow-up				
	2 years %	4 years %	7 years %	OR (95%CI) #	p-value
Social restriction: home or neighbourhood confined					
	N=1421	N=1278	N=1024	N=1456	
Baseline Anxiety Disorder					
No	3.09	3.86	9.36	1	
Yes	5.26	5.49	13.87	2.01 (1.10-3.66)	0.02
Baseline Trait Anxiety					
Low-Moderate	2.13	3.46	8.15	1	
High*	6.24	5.51	14.10	2.82(1.75-4.54)	<.0001
Activity limitations: Mobility					
	N=895	N=839	N=676	N=955	
Baseline Anxiety Disorder					
No	37.19	39.41	34.66	1	
Yes	44.44	41.94	49.32	1.33 (0.86-2.05)	0.20
Baseline Trait Anxiety					
Low-Moderate	35.93	39.20	35.12	1	
High*	44.05	41.12	39.53	1.41 (1.03-1.94)	0.04
Activity limitations: IADL					
	N=1425	N=1293	N=1015	N=1470	
Baseline Anxiety Disorder					
No	4.07	7.66	12.71	1	
Yes	6.15	12.94	18.66	2.04 (1.23-3.38)	0.006
Baseline Trait Anxiety					
Low-Moderate	4.43	7.81	11.87	1	
High*	7.20	11.83	19.79	1.89 (1.19-2.99)	0.007

Models 0 adjusted for sex, age, time, age*time

*high=top third tertile

Table 4. Incident cases of activity limitation by baseline anxiety: any DSM IV anxiety disorder and Spielberger Trait anxiety. Adjusted models

	Model 1		Model 2		Model 3		Model 4	
	OR (95%CI)	p-value	OR (95%CI)	p-value	OR (95%CI)	p-value	OR (95%CI)	p-value
Social restriction: home or neighbourhood confined N=1456								
Baseline Anxiety Disorder								
No	1		1		1		1	
Yes	2.05 (1.12-3.74)	0.02	1.91 (1.04-3.52)	0.04	1.75 (0.93-3.16)	0.08	1.65 (0.89-3.04)	0.11
Baseline Trait Anxiety								
No	1		1		1		1	
Yes	2.71 (1.69-4.36)	<.0001	2.60 (1.63-4.15)	<.0001	2.50 (1.47-4.24)	0.0007	2.38 (1.40-4.03)	0.001
Activity limitations: Mobility N=955								
Baseline Trait Anxiety								
No	1		1		1		1	
Yes	1.42 (1.03-1.96)	0.03	1.41 (1.02-1.93)	0.04	1.38 (0.97-1.95)	0.07	1.35 (0.95-1.92)	0.09
Activity limitations: IADL N=1470								
Baseline Anxiety Disorder								
No	1		1		1		1	
Yes	2.24 (1.22-4.10)	0.009	2.14 (1.17-3.90)	0.01	1.93 (1.05-3.55)	0.03	1.84 (1.00-3.37)	0.049
Baseline Trait Anxiety								
No	1		1		1		1	
Yes	1.88 (1.17-3.03)	0.009	1.76 (1.10-2.82)	0.02	1.41 (0.83-2.40)	0.20	1.30 (0.77-2.19)	0.32
Adjustment variables:								
Socio-demographic	Sex, Age, Time, Time*Age Income, Living alone, Education		Sex, Age, Time, Time*Age Income, Living alone, Education		Sex, Age, Time, Time*Age Income, Living alone, Education		Sex, Age, Time, Time*Age Income, Living alone, Education	
Physical health and lifestyle			BMI, Alcohol consumption, Smoking, Chronic disease Visual, Hearing, and Cognitive impairment		BMI, Alcohol consumption, Smoking, Chronic disease Visual, Hearing, and Cognitive impairment		BMI, Alcohol consumption, Smoking, Chronic disease Visual, Hearing, and Cognitive impairment	
Mental Health					Current depression		Current depression Current antidepressant use Current anxiolytic use Past MDE	