

**Temporal Associations between Sexual Function and Cognitive Function in
Community-dwelling Older Men: The Concord Health and Ageing in Men Project**

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ABSTRACT

Background: Previous cross-sectional studies have reported bi-directional associations between sexual activity and cognitive function among older people. However, the temporal associations have not been studied.

Methods: Community-dwelling men aged 70+ years from the Concord Health and Ageing in Men Project were assessed. This study was based on 986 men at baseline, 829 men at 2-year and 595 men at 5-year follow-up. Sexual function using a standardized questionnaire (erectile function, sexual activity, sexual satisfaction, sexual desire) was analyzed by Generalized Estimating Equations to examine associations between changes in sexual function and changes in mini-mental state examination (MMSE) across three time-points over 5-years. Age, BMI, comorbidity, self-rated health, smoking, no of medications, country of birth, education, marital status, depression and reproductive hormones were also measured at all time-points.

Results: In unadjusted models, declines in erectile function ($\beta=-0.317$) and sexual activity ($\beta=-0.575$) over time were statistically significantly associated with a decline in MMSE over time. The associations observed in the unadjusted models remained after adjusting for a range of covariables. Declines in sexual satisfaction and sexual desire over time were not associated with changes in MMSE.

Conclusions: Our findings provide evidence of a longitudinal temporal relationship between sexual activity and cognitive function. Further studies are warranted to

examine whether maintaining a healthy sexual life has a positive effect on cognitive function in older men.

INTRODUCTION

Sexual health and the expression of sexual identity are central to life and well-being.[1, 2] The intensity, quality, and frequency of sexual functioning are affected by age and there is often an assumption that older people are not capable of, or lack interest in sex.[3, 4] However, current research demonstrates that sexuality and sexual behaviour and function remain important among older people. [5, 6] The importance of sexuality for older people, and particular for those living with cognitive impairment, is often overlooked or underestimated.

Very little research has focused specifically on possible associations between sexual activity and cognitive function in older people. Previous cross-sectional studies have shown that older men who are sexually active also have increased levels of general cognitive function.[7-10] A recent review reported that older people experiencing cognitive decline and dementia engaged in fewer sexual activities than their cognitively intact, non-demented counterparts.[11] Nevertheless, the cross-sectional nature of these previous analyses limits their validity; longitudinal studies are needed to explore the temporal relationship between sexual function and cognitive function in older men over time.

The aims of this study were to investigate temporal associations between changes in sexual function and changes in mini-mental state examination (MMSE) scores across three time-points over 5-years in community-dwelling older men.

METHODS

Study Population

The Concord Health and Ageing in Men Project (CHAMP) is an epidemiological population-based cohort study of a wide range of health issues in 1705 community-dwelling Australian men aged 70 years and over.[12] Baseline data were collected between 2005-2007, 2-year follow-up between 2007-2009 and 5-year follow-up between 2012-2013.

Measurements

Sexual Function

Men were invited to complete a self-reported sexual health questionnaire during the study visit which included questions about sexual function (erectile function, sexual activity, sexual desire and sexual satisfaction). Detailed description for each of the sexual function measurements have been described in previous studies.[13, 14]

Cognitive function

At baseline, participants were screened for cognitive status and undergone detailed clinical assessments, which categorized them into having dementia, mild cognitive impairment (MCI) or normal cognition.[15] The MMSE was assessed at baseline, 2-year and 5-year follow-up.[16]

Statistical analyses

A total of 986 men at baseline, 829 men at 2-year and 595 men at 5-year follow-up were included in the final analyses. We excluded men with missing sexual function data (n=486) and/or men with a non-English speaking background (n=605) because of language difficulties affecting the validity of the MMSE. Men who had dementia at baseline were also excluded (n=93).

Generalized estimating equations (GEE) was used to study the temporal associations between changes in individual sexual function measures (erectile function, sexual activity, sexual desire, sexual satisfaction) and changes in cognitive function (MMSE) across baseline, 2-year and 5-year follow-up. GEE method takes into account the time-varying nature of the exposure and provides estimated population average models by using all longitudinal data, which is robust when treating missing data.[17]

The model building for all analyses included covariates of significance and relevance from all three time-points: age, self-rated health, number of comorbidities, BMI, smoking status, number of medications, education, country of birth, marital status, depressive symptoms and reproductive. Models were fit using SPSS software version 20 (IBM Corp., Armonk, NY, USA) and SAS software 9.3 (SAS Institute Inc., Cary, NC, USA).

Ethics approval and informed consent

All participants gave written informed consent. The study was approved by the Sydney South West Area Health Service Human Research Ethics Committee, Concord Repatriation General Hospital, Sydney, Australia.

RESULTS

Participants had a mean age of 77.5 (SD: 5.7) years with a large proportion of men had self-reported erectile dysfunction (65%), sexual inactivity (60%), low sexual satisfaction (46%) and/or low sexual desire (70%) (see Table 1). The participants that were excluded from analysis had a mean age of 75.9 (SD: 4.9), BMI of 28.5 (SD:3.9) kg/m², and comorbidity of 2.41 (SD: 1.7) conditions (data not shown).

In unadjusted models, decline in erectile function ($\beta=-0.317$, $p<0.001$) and sexual activity ($\beta=-0.575$, $p<0.001$) over time were statistically significantly associated with decline in MMSE over time (see Table 2). Decline in erectile function ($\beta=-0.209$, $p=0.009$) and sexual activity ($\beta=-0.360$, $p<0.001$) remained associated with decline in MMSE over time in the multivariable-adjusted model. The declines in sexual satisfaction and sexual desire over time were not associated with changes in MMSE in neither unadjusted nor multivariable-adjusted models.

Similarly, erectile dysfunction ($\beta=-0.267$, $p=0.02$) and sexual inactivity ($\beta=-0.286$, $p=0.01$) were cross-sectionally associated with MMSE at baseline (data not shown). Erectile dysfunction ($\beta=-0.278$, $p=0.004$) and sexual inactivity ($\beta=-0.424$, $p<0.001$) at

baseline, but not low sexual satisfaction or sexual desire, was also shown to be associated with decline in MMSE over time (data not shown).

DISCUSSION

This is a novel study exploring the temporal relationship between sexual and cognitive function in older men. The declines in erectile function and sexual activity frequency over time were associated with decline in cognitive function. Likewise, men with erectile dysfunction and sexual inactivity at baseline were at a greater risk of declining cognitive function over time. The inclusion of several potential confounders did not change the strong relationships observed between erectile dysfunction and sexual inactivity and cognitive impairment.

The English Longitudinal Study of Ageing (ELSA) is to date the only population-based study to have explored this relationship in older age.[9, 10] In cross-sectional analysis, older men in ELSA who were sexually active showed increased levels of general cognitive function and ability to perform specific cognitive tasks such as number sequencing, recall, fluency and visuospatial ability. Another cross-sectional study of 352 older Italian men recruited from primary care clinics has suggested that cognitive functioning may play a significant role in the maintenance of sexual interest in older age.[18] However, the cross-sectional study design in these studies are unable to determine the direction of the association between sexual and cognitive function in older adults.

In CHAMP we found that men with erectile dysfunction and no sexual activity at baseline were more likely to have declines in their MMSE scores over time, suggesting the possibility that poor sexual function might lead to a decline in cognitive function. We also found evidence of a temporal relationship between decline in erectile function and frequency of sexual activity and decline in cognitive function which suggest that a bidirectional relationship may exist between sexual and cognitive function in older men. Unfortunately, we were unable to examine whether baseline cognitive impairment predicts declines in sexual function over time because sexual function was based on responses to questionnaires and the validity of such responses in participants with cognitive impairment is likely to be poor.

It has been suggested that biological correlates of sexual function such as testosterone and estrogen may have an effect on the cognitive function in older adults.[19] This hypothesis was supported by our previous study findings in which decline in androgen status over time is associated with cognitive decline in older men.[15] However, the adjustment for circulating reproductive hormones in this study had minor influence on the observed relationship. Sexual inactivity may affect cognition decreasing production of certain neurotransmitters that may be a mediators of the association; for example dopamine has potential cognitive enhancing effects [20, 21] and has been shown to be associated with improved working memory and executive function in older adults.[22] Reduced oxytocin production with ageing may also explain the association; however this has not been researched extensively in this context.[23]

Further studies are needed to explore the influence of these other biological factors in the association between sexual and cognitive function.

A major strength of our study was the use of longitudinal data to provide a temporal framework to not only investigate sexual function as a predictor of cognitive function across 3 time-points over 5 years, but also to examine the contemporaneous associations between changes in sexual function and cognitive function. Our study also included detailed assessment of cognitive status at baseline which allowed us to exclude men with dementia from our analyses. Another strength of the CHAMP study is that it includes a large and representative group of older Australian men.[24]

However, our study has some limitations. Longitudinal studies are subject to attrition (loss at follow-up), due to non-participation, a potential source of bias.[25] We recorded 20% loss to follow-up from baseline to 2-year and a further 30% loss from 2-years to 5-years. However, loss to follow up in cohort studies of older people is inevitable because of the high mortality rate, which accounted for over a third of the loss in our cohort over 5-years. Our study was limited to community living men, as women and institutionalized men were not invited. The MMSE provides a measurement for cognitive impairment but does not discriminate between different cognitive functions and domains.

This study suggests there is a temporal relationship between erectile dysfunction and sexual inactivity and cognitive function in older men. Whether engagement in

sexual activity makes a positive contribution and have any clinical significance in cognitive function requires further longitudinal observational studies to examine.

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Conflict of interest disclosures: B.H., V.H., L.M.W., V.N., F.M.B., D.G.L.C., M.J.S., R.G.C., and D.J.H. have nothing to declare.

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TABLE 1. Descriptive characteristics of the analytic sample (Mean (SD) or N (%))

	Baseline (n=986)	2-year (n=829)	5-year (n=595)	Non-participation* at 2-year (n=157)	Non-participation* at 5-year (n=391)
Age (yr)	77.5 (5.7)	79.1 (5.4)	81.6 (4.7)	80.3 (6.5)	80.0 (6.1)
BMI (kg/m ²)	27.4 (4.1)	27.4 (4.0)	27.1 (3.8)	26.9 (4.3)	27.2 (4.5)
Education (yr)	15.5 (1.6)	15.5 (1.6)	15.6 (1.4)	15.3 (1.8)	15.3 (1.8)
MMSE (score)	27.9 (2.4)	28.1 (2.1)	27.9 (2.7)	26.7 (3.6)	27.0 (3.0)
Comorbidity	2.6 (1.8)	2.6 (1.7)	2.5 (1.6)	3.0 (2.0)	3.0 (1.9)
Testosterone (ng/ml)	4.2 (1.9)	4.2 (1.9)	3.4 (1.8)	3.8 (1.9)	3.9 (2.0)
DHT (ng/ml)	0.4 (0.3)	0.4 (0.2)	0.3 (0.2)	0.3 (0.2)	0.3 (0.2)
Estradiol (pg/ml)	24.8 (9.5)	24.1 (9.9)	36.0 (15.4)	24.2 (11.5)	24.2 (10.8)
Current smoker	41 (4%)	18 (2%)	16 (3%)	12 (6%)	19 (4%)
Living with partner	755 (72%)	610 (71%)	419 (69%)	132 (65%)	290 (65%)
Poor self-rated health	263 (26%)	203 (24%)	144 (24%)	60 (35%)	134 (34%)
Depression	125 (12%)	108 (13%)	62 (10%)	50 (25%)	83 (19%)
Erectile dysfunction	615 (65%)	504 (70%)	357 (79%)	114 (70%)	268 (71%)
Sexual inactivity	563 (60%)	460 (63%)	287 (63%)	119 (74%)	282 (75%)
Low sexual satisfaction	402 (46%)	300 (44%)	232 (54%)	59 (40%)	143 (42%)
Low sexual desire	661 (70%)	512 (70%)	313 (70%)	113 (69%)	267 (71%)

*The data for non-participation at 2-year and 5-year are their baseline descriptive characteristic.

TABLE 2. The temporal associations between deterioration in sexual function and changes in MMSE scores across three time-points over 5-years.

	Unadjusted		Age-adjusted		Multivariable-adjusted*	
	β (95%CI)	P-value	β (95%CI)	P-value	β (95%CI)	P-value
Erectile dysfunction	-0.317	<0.001	-0.211	0.01	-0.209	0.009
Sexual inactivity	-0.575	<0.001	-0.393	<0.001	-0.360	<0.001
Low sexual satisfaction	0.001	0.9	-0.009	0.9	-0.061	0.4
Low sexual desire	-0.052	0.5	0.026	0.8	-0.092	0.3

*multivariable model adjusted for age, BMI, comorbidity, self-rated health, smoking, education, ethnicity, marital status, depression, number of medications, testosterone, estradiol, dihydrotestosterone