Predicting Cognitive Decline and Dementia in Older Adults Using Neuropsychiatric Measures: A Systematic Review and Meta-Analysis

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INTRODUCTION

Longitudinal studies indicated that neuropsychiatric symptoms can precede the onset of by dementia several years.

However, the predictive risk of neuropsychiatric symptoms for cognitive decline and/or dementia has not yet been systematically evaluated.

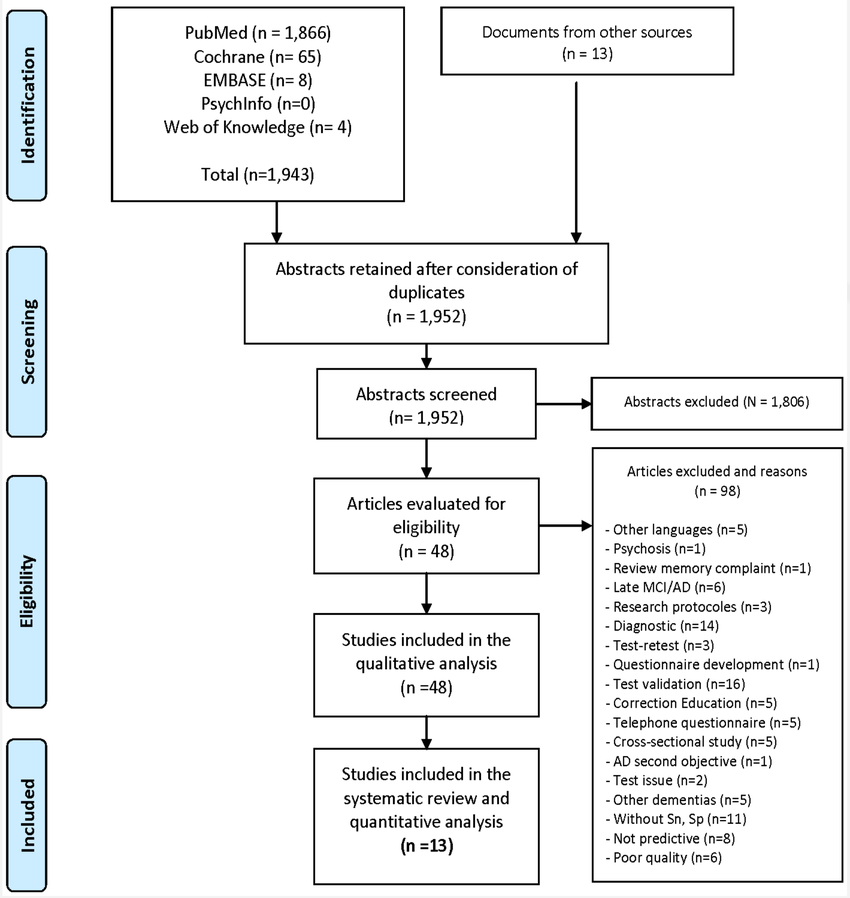
OBJECTIVE

To systematically review and meta-analyze published data on the predictive risk of neuropsychiatric measures regarding cognitive decline or dementia.

METHOD

- Research strategy determined by PICOS method.
- Selection of papers based on PRISMA guidelines.
- Research run on February 2014.

PRISMA Flow Diagram



RESULTS

- ***Depression***: 0.8 to 16.2-fold higher risk for cognitive decline.
- ***Apathy*** : 1.2- to 7-fold increase in the risk for functional decline or Alzheimer's disease.
- ***Anxiety***: One study showed an association with less cognitive decline, and another showed a 4 time increase in the risk of cognitive impairment at 3 years follow-up.
- ***Changes in sleep features*** (duration, efficiency, and excessive daytime sleepiness) : 1.2 to 5-fold increase in the risk of cognitive impairment after one to 10 years.

Table. Sample of studies examining neuropsychiatric disorders or symptoms as risk factors for cognitive decline or dementia

Study	Country	Risk Factor / Test instrument	Outcome	Study Design	Population Number Characteristics	Data Source Assessment	Recruitment Follow-up Participation Attrition	Risk measure (HR, RR, OR) Sensitivity, Specificity, Other results	95 % Confidence Interval P-value	Particularities Covariates Signification	Risk of bias
Stepaniuk et al. 2008	Canada	*Depression* NPI 3MS **CAMDEX – H for NPI[3]** Clinical exam	MCI or Alzheimer's disease (DSM-III-R)	Longitudinal population-based study	10 263 subjects 88% community 12% institutionalized	Canadian Study of Health and Aging (CSHA-3) Random sample	Before 2008 FU[1] 5-years 42 cases of possible or probable AD at 5-years	*Cognitive status* and MCI/AD: **OR = 29.20** Change personality: OR=2.35 Changes In mood: OR=0.52 Irritability/anger: OR=0.69 Loss of interest: OR = 0.10 *Depression:* **OR=16.16**	*Cognitive status* and MCI/AD:: (6.37-133.94) **P < 0.0001** Change personality: (0.60-9.20) P = 0.22 Changes In mood: (0.05-5.04) p=0.57 Irritability/anger: (0.11-4.5) P = 0.69 Loss of interest: (0.01-1.74) P = 0.11 *Depression:* **(1.12-232.94) P = 0.04**	Covariates (cognitive status)	***Unknown*** (possibility of differential selection bias, comorbidity different in community vs. institutionalized participants. Miss-classification possible with use of 3MS < 78 and depressive at baseline, use of use of proxy, no control for age, sex, education)
Palmer et al. 2010	Italy	*Apathy and Depression* **NPI** ADL, IADL MMSE, MBD, Cognitive battery	Alzheimer's disease CDR < 0.5 at baseline NINCDS-ADRDA Neurologist examination	Longitudinal study	131 subjects newly diag. **aMCI** Baseline: - 36.6% had depression - 10.7% had Apathy Men (59%) Women (41%) Mean age: 70.8	3 memory clinics	Before 2010 FU[1] 4-years Participation: 76% Attrition: 24%	Depression: HR=0.6 Depression per symptoms: HR=1.0 **Apathy: HR=6.9 Apathy per symptom: HR=1.2 Cut-off 2+ for symptoms vs < 2 (ref)**	Depression: (0.2-1.8) P > 0.05 Depression per symptoms: (0.7-1.3) P > 0.05 **Apathy: (2.3-20.6) P < 0.05 Apathy per symptom: (1.0-1.6) P = 0.05 Sensitivity: 70.6 Specificity: 65.9**	Covariates (age, gender, education, baseline global cognitive and functional status and depression (for apathy), baseline MMSE, and baseline diagnosis of depression or apathy, ADL and IADL)	***Low*** (selection and characteristics of subjects and dropout well documented, battery test well elaborated, standardized measures, neurologist evaluation, analyses of depression and apathy per symptoms, multivariate analyses)
Sinoff et al. 2003	Israel	*Anxiety and Depression* Tucker's short interview < 70 (no depression) SAST anxiety ≥ 24 = anxiety MMSE > 24 SCC[a] : loss of memory – few question ADL Barthel's	Dementia / cognitive decline	Longitudinal Study community-based	137 subjects randomly selected ≥ 60 years, from 700 persons in database (61 with anxiety, 76 control) Control: Mean =78.9 years Case: Mean =75.9 years	HaGefen community based geriatric assessment unit in Haifa, Israel	Between 1995 and 2000 FU[1] 1 to 5-years (mean 3.2) Participation to final analysis: Control= 58 % Anxious= 42 %	*Presence vs absence of anxiety at T1 and risk of cognitive impairment at T2:* **RR = 3.96**	*Presence vs absence of anxiety at T1 and risk of cognitive impairment at T2:* (1.69 - 9.08) P < 0.001 Loss of memory was correlated with anxiety (p <0.01) Anxiety was correlate with cognitive decline (p<0.05)	Covariates (loss of memory, anxiety, depression, age family status, living condition, education, profession, complaints, MMSE, ADL)	*Unknown* (Subject referred by physicians family or self-referred could cause selection bias, seen at baseline and FU, FU variable cause misclassification , and some lost to FU due to cognitive decline)
Potvin et al. 2012	Canada	*Sleep disorders* (plus mood and anxiety) MMSE ≥ 22 at baseline PSQI[a] (0 -3 = worse score) *3 word recall from MMSE (score 0 or 1 considered amnestic type)*	Incident cognitive impairment (was defined according to a follow-up MMSE score below the 15[th] percentile according to normative data and of at least 2 point below baseline) DSM-IV mood and anxiety disorders section	Population-based, prospective cohort study	2,785 subjects (1,664 intact) ≥ 65 years (65-96) Men (69.7%) Women (30.3%)	ESA Study	Recruitment in 2005-2006 FU[1] 1-year Participation: 76.5% Attrition: 23.5%	*Global PSQI in men:* **OR = 1.17** *Women :* Sleep disturbance: **OR = 2.62** (nonamnestic risk) Sleep ≥ 9 hr: **OR = 3.70** (amnestic risk) *Men:* Sleep ≤ 5 hr: **OR = 4.95** (amnestic risk) Habitual sleep efficiency : **OR = 1.94** (general cognitive impairment)	*Global PSQI in men:* **(1.05-1.30)** *Women :* Sleep disturbance: **(1.41-4.86) P = 0.002** (nonamnestic risk) Sleep ≥ 9 hr: **(1.49-9.17) P = 0.005** (amnestic risk) *Men:* Sleep ≤ 5 hr: **(1.72-14.27) P = 0.003** (amnestic risk) Habitual sleep efficiency : **(1.42-2.66) P = 0.002** (general cognitive impairment)	Covariates (age, education, baseline MMSE score, psychotropic drug use, anxiety, depressive episodes, cardiovascular conditions, chronic disease)	**Low** (Low risk of selection bias due to random dialing method and representative of 16 regions , good response rate of 76% and high number of answer, FU well describe, linkage with administrative data, low risk of misclassification with liked scale, adjusted norms and used of DSM-IV criteria, adjusted for covariates)

DISCUSSION

Depression, **apathy**, **anxiety**, and **sleep changes** all predict cognitive decline or dementia in older adults.

The present results may be used to construct a battery of instruments that will contribute to a better identification of persons at risk for future cognitive decline.

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