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ORIGINAL CONTRIBUTION

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Engaged lifestyle and cognitive function in middle and old-aged, non-demented persons: a reciprocal association?

Engagierter Lebensstil und kognitive Funktion bei nicht-dementen Personen mittleren und höheren Alters: eine reziproke Assoziation?

Summary Some studies have shown that cognitive function is positively affected by an engaged and active lifestyle. However, a recent study found evidence for an opposite causal direction, i.e., persons with good cognitive function more often start to engage in leisure-time activities. Here, we longitudinally examine the causal direction of the association between an engaged lifestyle and cognitive function in middle and old-aged Dutch men and women.

The participants in the prospective cohort study "Maastricht Aging Study" (MAAS) were recruited from a register of 15 family practices in the South of the Netherlands. There were 830 non-demented men and women, aged 49 to 81 in 1993–1995 (baseline phase). They were re-examined three years later (follow-up phase). During both phases, all persons reported on their participation in mental, social, and physical activities. Six separate neuropsychological tests, including the Mini-Mental State Examination, were used to define cognitive function at baseline and follow-up.

All three activities measured were negatively related to cognitive decline between both phases. Effects were moderate, but consistent. Persons participating in all three activities were particularly protected against longitudinal decline. Furthermore, persons with the best baseline cognitive performance were more likely to increase their number of activities during follow-up compared with persons with the poorest scores.

In summary, an engaged lifestyle and cognitive function mutually influence each other in middle and old aged, non-demented persons. This reciprocal association is characterized by simultaneous positive effects of leisure-time activities and good cognitive function on cognitive function and leisure-time activities, respectively. This reciprocal association may create a self-reinforcing, beneficial or adverse life-course in middle and old age.

Key words Engaged lifestyle – cognitive function – longitudinal study

Zusammenfassung Verschiedene Untersuchungen haben ergeben, dass ein engagierter Lebensstil die kognitive Funktion positiv beeinflusst. Jedoch, eine rezente Untersuchung hat eine entgegengesetzte kausale Richtung dargestellt, d. h. dass Personen, die gut kognitiv funktionieren, häufiger und früher Freizeitaktivitäten entwickeln. In dieser Studie haben wir den kausalen Zusammenhang zwischen einem aktiven Lebensstil und der kognitiven Funktion bei älteren und alten niederländischen Männern und Frauen erforscht. Für diese prospektive Kohorten-Untersuchung „Maastricht Aging Study (MAAS)" entnahmen wir die Teilnehmernamen einem ärztlichen Register von 15 Praxen im Süden der Niederlande. In den Jahren 1993–

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1995 untersuchten wir 830 nichtdemente Männer und Frauen im Altersbereich von 49–81 Jahren (erste Phase). Nach drei Jahren wurde die Untersuchung wiederholt (zweite Phase). In beiden Phasen wurden die Personen um ihre mentalen, sozialen und physischen Aktivitäten befragt. Damit das kognitive Funktionieren in der ersten und zweiten Phase festgestellt werden konnte, verwendeten wir sechs unterschiedliche neuropsychologische Tests, einschließlich der Mini Mental State Examination.

Die drei untersuchten Aktivitäten beeinträchtigten, jede für sich die kognitive Leistung zwischen den beiden Phasen. Die Effekte waren zwar bescheiden, aber konsistent. Die Personen, die alle drei Aktivitäten ausübten, waren besonders vor kognitiver Beeinträchtigung geschützt. Die Personen, die ihre Aktivitäten zwischen der ersten und zweiten Phase erweitern, waren auch diejenigen, die in der ersten Phase am besten kognitiv funktionierten.

Kurz gefasst, ein aktiver Lebensstil und die kognitive Funktion beeinflussen sich bei nicht dementen Personen mittleren und höheren Alters gegenseitig und im positiven Sinne. Diese reziproke Assoziation wird durch simultane, positive Effekte von Freizeitaktivitäten auf die kognitive Funktion einerseits, und von der kognitiven Funktion auf die Freizeitaktivitäten andererseits charakterisiert. Diese reziproke Assoziation kann bewirken, dass sich – sich selbst verstärkend – ein positiver oder aber ungünstiger Lebensverlauf in mittlerem und höherem Alter entwickelt.

Schlüsselwörter Engagierter Lebensstil – kognitive Funktion – prospektive Untersuchung

Introduction

Life expectancy is increasing in most western countries and neurological and cognitive dysfunctions are rapidly becoming a major concern for public health (1). More and more researchers are therefore trying to find potential determinants of these dysfunctions. Some researchers have hypothesized that age-related decline could be moderated by particular environmental and contextual factors (2–4). One such contextual factor – amenable to change and considered an essential component of successful aging (5, 6) – is a lifestyle characterized by mentally stimulating activities (7, 8). Several researchers have provided evidence in favor of the 'use-it-or-lose-it' hypothesis that participation in cognitively challenging activities keeps persons mentally fit until old age (9–18). Evidence also shows that participation in physical and social activities may equally well promote cognitive health (11, 13, 19–22). This has been interpreted in terms of generally protective effects of an active and engaged lifestyle. However, mental, social, and physical activities have not frequently been examined simultaneously. Furthermore, there remains doubt on whether an engaged or disengaged lifestyle is a cause or a result of differences in cognitive function (15, 16). As one may question whether all previous studies sufficiently controlled for reverse causation, further longitudinal studies are needed to examine the causal direction of the engagement cognitive function association. Here, data from the longitudinal Maastricht Aging Study (MAAS) among middle-aged and older non-demented persons are used to examine the causal direction of the association between activity levels and differences in cognitive function.

Methods

Study population

MAAS is a study on the determinants and consequences of differences in cognitive aging and successful aging in particular. Between 1993 and 1995, participants were selected from a register of 15 family practices in the South of the Netherlands (23). The sample, consisting of both men and women, was stratified for age. The invited persons were between 24 and 81 years old. Furthermore, to allow examination of differences in normal cognitive aging, persons with medical conditions that interfere with normal cognitive aging were not invited to participate. Hence, persons with chronic neurological pathology (e.g., dementia, cerebrovascular disease, epilepsy, parkinsonism and malignancies related to the nervous system), mental retardation, or chronic psychotropic drug use were not included in MAAS. The 1823 participants filled out a questionnaire and participated in a medical and neuropsychological examination. More details on the cross-sectional part can be found elsewhere (24, 25). About three years later (1996–1998), all persons who were 50 years or older and tested at baseline (n = 1069) were again invited to participate in a reassessment of neuropsychological function. Due to refusal (n = 138), death (n = 50), loss-to-follow-up (n = 43), and the development of dementia (n = 8), 830 persons were actually tested and used in the subsequent analyses. Due to the age stratification in the baseline sampling scheme and difficulties in obtaining sufficient numbers in the oldest age stratum (24, 25), there were 143, 136, 135, 132, 131, 112, and 41 persons who were 49 to 51, 54 to 56, 59 to 61, 64 to 66, 69 to 71, 74 to 76, and 79 to 81 years old, respectively. The university review board approved the study and all participants gave their informed consent.

Cognitive function and decline

The following neuropsychological tests were used to determine cognitive function at baseline and follow-up phase: the Stroop Color – Word Test (interference sub-task) (26), the Verbal Learning Test (immediate and delayed recall sub-tasks) (27), the Letter Digit Coding Test (28), the Word Fluency Test (29), and the Mini-Mental State Examination (30). The interference sub-task of the Stroop Color-Word Test involves naming as fast as possible the color of the printing ink of one hundred words for colors; the words do not match the color of the ink with which they are printed. The number of seconds to complete the task is recorded. In the Verbal Learning test, all participants were presented fifteen monosyllabic words and asked to recall the words. This was repeated another four times with the same set of words. The total number of words recalled in the five trials was recorded (immediate recall). Unexpectedly, after 20 min, the participants again had to reproduce the words (delayed recall). In the Letter Digit Coding Test, the participants were presented nine arbitrary letter-digit combinations. Using the correct letter-digit combination, they are then asked to fill in blanks on a sheet with letters. The number of digits correctly written in 90 s was recorded. In the Word Fluency Test, the participants were asked to name as many different animals as possible in 60 s. The number of different animals was recorded. Recently, similar tests were used to determine cognitive function in a study on the cognitive effects of pesticides and operation under general anesthesia (31, 32). The Mini-Mental State Examination is often used as a first screen for dementia. It measures general cognitive function on a scale ranging from 0 (poor) to 30 (good) points. More details on the neuropsychological tests can be found elsewhere (24, 25, 31, 32).

Engagement

Leisure-time activities were measured with self-report items in the baseline self-administered questionnaire. All persons were asked to report how many hours per week they engaged in 1) physically active sports (e.g., ball sports, fitness training), 2) mentally active sports (e.g., chess, puzzles), and 3) organizational memberships (e.g., clubs). These three indicators of physical, mental, and social activities were dichotomized so that 0 is "no engagement in activity" and 1 is "at least one hour per week engagement in activity". There were 356 persons (43%) reporting physical activities, 446 persons (54%) reporting mental activities, and 434 persons (52%) reporting social activities. Activities were summed to provide an overall score and to study the cumulative effect of the activities (zero activities: 126 persons (15%); one activity: 303 persons (37%); two activities: 270 persons (33%); three activities: 131 persons (16%).

Statistical methods

Percentages of persons participating in the activities were computed and compared between baseline and follow-up phase using the McNemar test. Basic statistics (mean and standard deviation) of the six cognitive tests were similarly computed and compared between baseline and follow-up using paired t-tests. First, using ordinary least-squares regression analysis, the activities at baseline were related to longitudinal cognitive decline with adjustment for baseline age, sex, attained educational level, length of follow-up interval, and baseline cognitive function (activities → cognitive function). Attained educational level had eight ordinal categories ranging from primary education to university education. Second, using logistic regression analyses, cognitive function at baseline (in thirds) was related to whether or not persons increased their number of activities during follow-up and to whether or not they started any of the three activities. Baseline age, sex, attained educational level, length of follow-up interval, and baseline activity level were controlled for (cognitive function → activities).

Results

Activity levels generally decreased during follow-up. The percentage of persons participating in physical and social activities decreased from 43 to 30 and from 52 to 48, respectively. The small decline in mental activities (from 54 to 53%) was not statistically significant. Cognitive function also declined during follow-up. This was not significant for the Word Fluency test. Although the three-year decline was small on average, there was a wide variation in this decline. For example, the average Mini-Mental State score at baseline was 28.0 compared with 27.8 at follow-up (mean decline = 0.2, standard deviation = 1.8) and total recalled words decreased from 42.5 to 41.8 words (mean decline = 0.8, standard deviation = 7.3).

Although not consistently statistically significant, all activities were in each case related to cognitive decline in the expected direction (Table 1). For example, compared with persons not participating in physical activities, active persons had 2.9 seconds less slowing (Stroop Color-Word Test) during follow-up. Similarly, their score on the Letter Digit Coding Test decreased 0.82 points less compared with inactive persons. The activities had cumulative effects on cognitive decline. There was an almost linear association between the number of activities and cognitive decline. Persons with three activities had statistically significant less cognitive decline compared with persons with no activities (according to the Letter Digit Coding Test and the Mini-Mental State Examination). For example, persons with three activities showed 1.79 points less longitudinal decline on the Letter Digit Coding Test compared with inactive persons ($p<0.01$). The effects of the continuous measure (number of activities) underlined these findings and the effect became additionally significant for the delayed recall and Word Fluency measure ($p<0.05$).

Table 2 shows that – with few exceptions – cognitive function at baseline was related to longitudinal change in the activities, even when controlled for baseline activities. Persons with good cognitive function at baseline more often became (more) engaged during follow-up compared with persons with poor baseline cognitive function (independent of their baseline activities). Although not consistently statistically significant, the direction of the association is as expected for practically all associations. For example, persons in the best scoring tertile of the Stroop Color Word Test had a 2.82 higher probability of increasing their number of activities ($p<0.01$) and a 1.40 (not significant), 2.15 ($p<0.05$), and 3.32 ($p<0.01$) higher probability of starting physical, mental, and social activities during follow-up, respectively, compared with persons in the poorest scoring tertile of the baseline Stroop task.

The participation at the follow-up phase was related to baseline activity levels and cognitive function. For example, 30% of the persons who at baseline engaged in none of the activities was non-participant at follow-up compared with 17% of the persons who engaged in all three activities. Furthermore, the mean baseline Mini-Mental score for the follow-up participants was 28.0 (sd = 1.72) compared with 26.6 (2.56) for the non-participants.

Discussion

Our findings show that participation in certain leisure-time activities and cognitive function mutually influence each other in middle and old aged, non-demented persons. This reciprocal association is, first, based upon good cognitive function causing persons to increase their participation in leisure-time activities and, second, leisure-time activities being protective against cognitive deterioration. The reciprocal association between activity levels and cognitive function thus creates a self-reinforcing beneficial or adverse life-course in middle and old age. These findings

Table 1 Unstandardized regression coefficients of the association between baseline activities and longitudinal cognitive decline, adjusted for age (years), sex, educational level, length of follow-up interval, and baseline cognitive function [a, b]

	Stroop interference (n = 808)	Letter Digit Coding (n = 826)	Word Fluency animals (n = 824)	Total recall (n = 827)	Delayed recall (n = 827)	Mini-mental state examination (n = 818)
Physical activities						
Yes	–2.90*	0.82**	0.33	0.09	0.08	0.11
Mental activities						
Yes	–0.49	1.18***	0.61*	0.36	0.18	0.40***
Social activities						
Yes	–1.22	0.36	0.24	0.94**	0.30**	0.08
Number of activities						
One activity	–1.71	–0.14	0.25	–0.38	–0.08	0.13
Two activities	–1.92	0.73	0.70	0.59	0.22	0.26
Three activities	–4.70*	1.79***	0.91	0.77	0.38	0.53***
Number of activities						
Continuous measure (ranging from 0 to 3)	–1.31	0.66***	0.34**	0.40*	0.16**	0.17***

* $p<0.10$; ** $p<0.05$; *** $p<0.01$

[a] Persons with no activities are the reference category

[b] Negative coefficients on the Stroop Test (seconds needed to complete the task) and positive coefficients on the other neuropsychological tests indicate less cognitive decline compared to the inactive reference group

Table 2 Odds ratios (95% confidence intervals) of the association between cognitive function at baseline (in thirds: poor, moderate, good) and within person increase of the number of activities and starting physical, mental, and social activities during follow-up, adjusted for age, sex, educational level, length of follow-up interval, and baseline activities

	Number	Increasing number of activities during follow-up	Starting physical activities during follow-up	Starting mental activities during follow-up	Starting social activities during follow-up
Percentage		17	7	9	11
Stroop interference	820				
Poor	273	1.00	1.00	1.00	1.00
Moderate	273	2.16 (1.28–3.65)***	1.08 (0.51–2.29)	1.40 (0.71–2.79)	2.50 (1.25–5.00)***
Good	274	2.82 (1.59–5.02)***	1.40 (0.64–3.07)	2.15 (1.03–4.51)**	3.32 (1.58–7.01)***
Letter Digit Coding	826				
Poor	285	1.00	1.00	1.00	1.00
Moderate	279	0.93 (0.56–1.56)	0.54 (0.26–1.12)*	1.37 (0.67–2.82)	0.62 (0.32–1.20)
Good	262	1.73 (0.98–3.07)*	0.79 (0.36–1.73)	3.76 (1.67–8.47)***	1.24 (0.60–2.58)
Word Fluency	828				
Poor	327	1.00	1.00	1.00	1.00
Moderate	261	1.17 (0.73–1.88)	2.25 (1.12–4.53)**	0.77 (0.39–1.50)	0.76 (0.43–1.37)
Good	240	1.47 (0.88–2.44)	1.66 (0.76–3.61)	1.76 (0.91–3.40)*	0.96 (0.51–1.83)
Total recall	829				
Poor	289	1.00	1.00	1.00	1.00
Moderate	286	1.76 (1.08–2.84)**	1.19 (0.59–3.42)	1.14 (0.61–2.14)	1.48 (0.79–2.77)
Good	254	1.68 (0.97–2.89)*	1.29 (0.60–2.80)	1.75 (0.87–3.55)	2.00 (1.02–3.95)**
Delayed recall	828				
Poor	365	1.00	1.00	1.00	1.00
Moderate	215	1.36 (0.83–2.20)	1.51 (0.75–3.03)	1.22 (0.65–2.31)	0.89 (0.46–1.71)
Good	248	1.67 (1.01–2.75)**	1.43 (0.68–2.98)	1.67 (0.87–3.22)	2.08 (1.14–3.80)**
Mini-mental state	818				
Poor	436	1.00	1.00	1.00	1.00
Moderate	207	1.34 (0.83–2.16)	1.00 (0.49–2.02)	1.67 (0.91–3.06*	1.06 (0.57–1.96)
Good	175	1.31 (0.75–2.28)	0.92 (0.41–2.05)	1.15 (0.51–2.59)	1.78 (0.90–3.48)*

* $p<0.10$; ** $p<0.05$; *** $p<0.01$

are similar to a recent study of Hultsch and colleagues who have also reported reciprocal associations between activities and cognitive function (15). Our findings provide evidence that reverse causation, i.e., cognitive function influencing activity levels, cannot be excluded and therefore deserves detailed attention in studies examining protective effects of an engaged lifestyle. Without such attention, reported protective effects of engagement may be seriously overstated and the finding that cognitive dysfunction and engagement mutually influence each other may be left unnoticed. It is noteworthy that the effects of leisure-time activities on cognitive function were stronger when the engaged lifestyle moved beyond participation in mental activities and persons thus participated in multiple activities. This supports the broader 'engagement' hypothesis, which emphasizes additional beneficial effects of activities other than mental per se (5, 6, 10, 11).

There are several methodological considerations. First, having excluded demented cases (eight incident cases only), our findings indicate that engagement predicts differences in normal aging and the risk of cognitive impairment without dementia, rather than the incidence of dementia. Second, non-participants at follow-up were less active persons at baseline and had worse baseline cognitive performance scores than their participating counterparts. Assuming similar associations between activity levels and cognitive function in participants and non-participants at follow-up, this is likely to have resulted in underestimated associations. Third, our findings are unlikely to be confounded by socioeconomic status, because educational differences were controlled for. Eductional differences are – particularly in the Netherlands – a strong proxy for socioeconomic differences. Fourth, leisure-time activities were measured somewhat crudely. Only one indicator for each activity domain was available and items were dichotomized, because about half of the people did not spend time on the activity. Finally, the wide age range in our sample (49 to 81 years) raises the question of whether findings were similar in the 50 and 80-year olds. Age-specific analyses and multiplicative interaction terms, however, did not reveal any age-specific patterns (not shown). This indicates a similar reciprocal association between activity levels and cognitive function in the 50 and 80-year olds.

Conclusion

An engaged lifestyle and cognitive function mutually influence each other in middle and old aged, non-demented persons. This reciprocal association is characterized by simultaneous positive effects of leisure-time activities and good cognitive function on cognitive function and leisure-time activities, respectively. This reciprocal association may create a self-reinforcing, beneficial or adverse life-course in middle and old age. Stimulating persons to participate in leisure-time activities may thus prevent the development of an adverse vicious circle in the life-course of middle and old aged persons.

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References

1. Menken M, Munsat TL, Toole JF (2000) The global burden of disease study: implications for neurology. Archives of Neurology 57:418–420
2. Pientka L (2001) Erkenntnisse zur Verlängerung behinderungsfreier Lebenszeit. Zeitschrift für Gerontologie und Geriatrie 34:38–43
3. Schaie KW (1996) Intellectual development in adulthood: the Seattle Longitudinal Study. Cambridge University Press, New York
4. Schooler C (1990) Psychosocial factors and effective cognitive functioning in adulthood. In: Birren JE, Schaie KW (eds) Handbook of the psychology of aging. Academic Press, San Diego, CA, pp 347–358
5. Rowe JW, Kahn RL (1997) Successful aging. Gerontologist 37:433–440
6. Wahl HW (1998) Alltagskompetenz: Ein Konstrukt auf der Suche nach einer Identität. Zeitschrift für Gerontologie und Geriatrie 31:243–249
7. Orrel M, Sahakian B (1995) Education and dementia. Research evidence supports the concept "use it or lose it". British Medical Journal 310:951–952
8. Swaab DF (1991) Brain aging and Alzheimer's disease. "Wear and tear" versus "Use it or lose it". Neurobiology of Aging 12:317–324
9. Albert MS, Jones K, Savage CR, Berkman L, Seeman T, Blazer D, Rowe JW (1995) Predictors of cognitive change in older persons: MacArthur studies of successful aging. Psychology and Aging 10:578–589
10. Arbuckle TY, Maag U, Pushkar D, Chaikelson JS (1998) Individual differences in trajectory of intellectual development over 45 years of adulthood. Psychology and Aging 13:663–675
11. Bassuk SS, Glass TA, Berkman LF (1999) Social disengagement and incident cognitive decline in community-dwelling elderly persons. Annals of Internal Medicine 131:165–173
12. Christensen H, Korten AE, Jorm AF, Henderson AS, Scott R, Mackinnon AJ (1996) Activity levels and cognitive functioning in an elderly community sample. Age and Ageing 25: 72–80
13. Fabrigoule C, Letenneur L, Dartigues JF, Zarrouk M, Commenges D, Barberger-Gateau P (1995) Social and leisure activities and risk of dementia: a prospective longitudinal study. Journal of the American Geriatric Society 43:485–490
14. Gold DP, Andres D, Etezadi J, Arbuckle T, Schwartzman A, Chaikelson J (1995) Structural equation model of intellectual change and continuity and predictors of intelligence in older men. Psychology and Aging 10:294–303
15. Hultsch DF, Hertzog C, Small BJ, Dixon RA (1999) Use it or lose it: engaged lifestyle as a buffer of cognitive decline in aging? Psychology and Aging 14:245-263
16. Pushkar D, Etezadi J, Andres D, Arbuckle T, Schwartzman AE, Chaikelson J (1999) Models of intelligence in late life: comment on Hultsch et al (1999). Psychology and Aging 14: 520–527
17. Schooler C, Mulatu MS, Oates G (1999) The continuing effects of substantively complex work on the intellectual functioning of older workers. Psychology of Aging 14:483–506
18. Stevens FCJ, Kaplan CD, Ponds RWHM, Jolles J (2001) The importance of active lifestyles for memory performance and memory self-knowledge. Basic and Applied Social Psychology 23:137–145
19. Dustman RE, Emmerson RY, Ruhling RO, Shearer DE, Steinhaus LA, Johnson SC, Bonekat HW, Shigeoka JW (1990) Age and fitness effects on EEG, ERPs, visual sensitivity, and cognition. Neurobiology of Aging 11:193–200
20. Fratiglioni L, Wang HX, Ericsson K, Maytan M, Winblad B (2000) Influence of social network on occurrence of dementia: a community-based longitudinal study. Lancet 355:1315–1319
21. Rogers RL, Meyer JS, Mortel KF (1990) After reaching retirement age physical activity sustains cerebral perfusion and cognition. Journal of the American Geriatric Society 38: 123–128
22. Van Boxtel MP, Paas FG, Houx PJ, Adam JJ, Teeken JC, Jolles J (1997) Aerobic capacity and cognitive performance in a cross-sectional study. Medicine and Science in Sports and Exercise 29:1357–1365
23. Metsemakers JFM, Hoppener P, Knottnerus JA, Kocken RJJ, Limonard CBG (1992) Computerized health information in the Netherlands: A registration network of family practices. British Journal of General Practice 42:102–106
24. Jolles J, Houx PJ, Van Boxtel MPJ, Ponds RWHM (1995) Maastricht Aging Study; Determinants of cognitive aging. Neuropsych Publishers, Maastricht
25. Van Boxtel MPJ, Buntinx F, Houx PJ, Metsemakers JF, Knottnerus A, Jolles J (1998) The relation between morbidity and cognitive performance in a normal aging population. Journal of Gerontology: Medical Sciences 53: M147–M154
26. Stroop JR (1935) Studies of interference in serial verbal reactions. Journal of Experimental Psychology 18: 643–662

27. Rey A (1964) L'examen psychologique dans les cas d'encepholopathie traumatique. Presses Universitaires de France, Paris
28. Smith A (1986) The Symbol Digit Modalities Test: A neuropsychological test for eco-nomic screening of learning and other cerebral disorders. Learning Disorders 36:83–91
29. Luteijn F, Van der Ploeg FAE (1983) Handleiding Groninger Intelligentie-test (GIT). Swets and Zeitlinger, Lisse
30. Folstein MF, Folstein SE, McHugh PR (1975) 'Mini-Mental State': A practical method for grading the cognitive state of patients for the clinician. Journal of Psychiatric Research 12:189-198
31. Bosma H, Van Boxtel M, Ponds R, Houx P, Jolles J (2000). Pesticide exposure and risk of mild cognitive dysfunction. Lancet 356:912–913
32. Møller JT, Cluitmans P, Rasmussen LS, Houx P, Rasmussen H, Canet J, Rabbitt P, Jolles J, Larsen K, Hanning CD, Langeron O, Johnson T, Lauven PM, Kristensen PA, Biedler A, Van Beem H, Fraidakis O, Silverstein JH, Beneken JE, Gravenstein JS (1998) Long-term postoperative cognitive dysfunction in the elderly ISPOCD1 study. ISPOCD investigators. International Study of Post-Operative Cognitive Dysfunction. Lancet 351:857–861