REVIEW ARTICLE

Neurocognitive function monitoring

Dilip K. Kulkarni, Srilata Moningi

Abstract

Neuro-cognitive dysfunction quite frequently occurs after major surgery particularly in elderly patients. Cognitive function monitoring becomes an important tool in the perioperative period, especially for patients undergoing neurosurgical procedures as these patients are at a greater risk because of the nature of surgery. Many cognitive assessment tools were described, but selecting a tool or combination of tools to assess depends on preoperative patient condition, availability of informant and post-operative course. The cognitive functioning monitoring is crucial for risk stratification to allow for subsequent prophylaxis, surveillance, and treatment of post-operative cognition dysfunction.

Key words: Anaesthesia, cognitive monitoring tools, post-operative cognitive dysfunction, surgery

INTRODUCTION

Neurocognitive function monitoring is consistently ignored in the perioperative period, despite the fact that both anaesthetics and analgesics primarily act on the brain and spinal cord. The neurocognitive dysfunction following surgery and anaesthesia is of concern, especially in elderly patients, also seen in younger patients. The cognitive dysfunction to some extent is already present in most of the patients undergoing neuroanaesthesia for various operations, particularly patients with head injury, cerebrovascular diseases and cerebral tumours, and it becomes vital to monitor cognition function. The routine pre-operative evaluation does not include the evaluation of baseline cognitive functioning. Assessment of the cognitive status of patients before surgery is useful for risk stratification, subsequent prophylaxis, surveillance and treatment.[1]

Department of Anaesthesiology and Intensive Care, Nizam's Institute of Medical Sciences, Panjagutta, Hyderabad, Telangana, India

Address for correspondence:
Dr. Dilip K. Kulkarni, Department of Anaesthesiology and Intensive Care, Nizam's Institute of Medical Sciences, Panjagutta, Hyderabad - 500 082, Telangana, India.
E-mail: dilipkum@gmail.com

Access this article online	
Quick Response Code:	Website: www.jnaccjournal.org
	DOI: 10.4103/2348-0548.165055

The word cognition is derived from a Latin verb 'cognosco'; literary meaning being 'to conceptualise' or 'to recognise'. Cognitive function can be defined as the processes by which an individual perceives, registers, stores, retrieves and uses information. The hippocampal dentate gyrus and sub-ventricular regions of the lateral ventricles are the regions in the human brain where the neural stem cells are constitutively active. These cells replicate into pro-genitors that segregate into neurons in all age groups. The domino effect of neurogenesis in the dentate gyrus results in neural plasticity, responsible for the cognitive and emotional functions.[2]

Cognition includes all mental aptitudes and activities related to knowledge: Attention, memory and working memory, judgment and evaluation, reasoning and 'computation', problem solving and decision making, comprehension and production of language.[3] The details regarding each entity of cognition with the structures involved are described in Table 1.

With advancing age, the capacity and ability to understand and learn is restrained as there is a gradual reduction in neurogenesis, resulting in cognitive impairment and the elderly being more susceptible for cognitive dysfunction. The following neurocognitive

How to cite this article: Kulkarni DK, Moningi S. Neurocognitive function monitoring. J Neuroanaesthesiol Crit Care 2015;2:246-56.

dysfunctions can occur postoperatively: Delirium, dementia, mild cognitive dysfunction and post-operative cognitive dysfunction (POCD).

DELIRIUM

Delirium is an acute and fluctuating neurological disorder that reflects a change from baseline cognition and is characterised by the cardinal features of inattention and disorganised thinking.

Delirium is one of the most important post-operative complications because: (i) It is common, affecting up to 70% of patients older than 60 undergoing major inpatient surgeries and (ii) it is associated with adverse outcomes, including mortality, persistent cognitive decline, and prolonged intensive care and hospital length of stay. Usually, occurs after 1–2 days after surgery.

The post-operative delirium is a marker of brain vulnerability. The occurrence suggests the possibility of underlying neurological disease, such as early or preclinical dementia.[4,5]

Patients may present with hyperactive (agitated) or hypoactive (lethargic) type of delirium. It fluctuates in its severity and is more severe in the evening and night. The cognitive changes such as memory problems, disorientation or hallucinations can occur. Coma should be ruled out to diagnose delirium.

The risk factors are presented in Table 2.[4-6]

Table 1: The domains of cognition and the concerned brain structures involved

Domains of cognition	Detailed description	Structures involved
Memory	Episodic - personally experienced events; antegrade, retrograde	Hippocampal–diencephalic system
	Semantic - memory for word meaning and general knowledge	Anterior temporal lobe
	Working - very limited capacity which allows us to retain information for a few seconds	Dorsolateral prefrontal cortex
Language	Naming, repetition, comprehension, reading, writing	Frontal lobe - Broca's area, anterior mesial cortex Temporal lobe - Wernicke's area, angular gyrus, supramarginal gyrus, arcuate fasciculus
Executive and frontal lobe functions	Planning, judgement, problem solving, impulse control, and abstract reasoning	(Dorsolateral) frontal lobe function
Performance	Apraxia - The inability to perform a movement with a body part despite intact sensory and motor function	Left parietal and frontal lobes
Visuospatial ability	Dorsal (''where'') stream links visual information with spatial position and orientation	Visual cortex - parietal lobe
	Ventral (''what'') stream links this information to the store of semantic knowledge	Visual cortex - temporal lobe
Orientation	to time, place and person	Parietal lobe
Attention	-	Temporal lobe

Table 2: The risk factors for delirium

Preoperative risk factors delirium	Perioperative triggers
Dementia	Acute pain
Depression	Use of physical restraints
Elderly age group	Malnutrition
Preoperative use of narcotics or benzodiazepines	Addition of three or more medications in 24-48 hours
Self-reported use of alcohol	Use of a urinary bladder catheter
Previous history of delirium	Anaemia
Vision impairment	Electrolyte and fluid abnormalities
Severe illness	Greater surgical blood loss, greater intraoperative transfusion
Blood urea nitrogen/creatinine ratio 0.18	General anaesthesia
Tobacco use	
Vascular surgery	
Depressive symptoms	
Attention deficits	

Prevention and treatment

The only known effective preventative strategy was the Hospital Elder Life Program (HELP) multicomponent intervention demonstrated by Inouye *et al*. in 1999. The intervention, which targeted patients at least 70 years old who were free of delirium and dementia at baseline but judged to be at moderate or high risk for delirium, reduced ward delirium rates from 15% in the usual care group to 9.9% and significantly reduced total number of delirium episodes and delirium days.[7] The HELP model is implemented by an interdisciplinary team that conducts interventions in the domains of cognition, sleep, mobility, vision and hearing adaptations and maintenance of nutrition and hydration.

Approaches to minimise sedation or anaesthesia are increasingly recognised as important measures to decrease the incidence and duration of delirium. Interesting hypotheses have been advanced that implicate cerebral connectivity and inhibitory tone in the development of delirium.[8] Subsequently, a trial was conducted in which participants undergoing hip fracture surgery were randomised to either light sedation (bispectral index [BIS] >80) or deep sedation (BIS target = 50) with propofol. All procedures were performed with spinal anaesthesia. The authors demonstrated a significantly increased rate of delirium with general anaesthesia (GA) like level of sedation: 40% of the patients receiving deep sedation had an episode of delirium, compared with only 19% of those receiving light sedation.[9]

A handful of studies have been designed to look at the effect of regional anaesthesia (RA) with sedation compared with GA. A meta-analysis of fairly heterogeneous randomised controlled trials of GA versus other anaesthetic methods for a variety of operations found no significant increase in the rate of post-operative delirium with GA.[10] The prophylactic use of haloperidol was evaluated with a dose of 1.5 mg haloperidol versus placebo per day in 430 elderly patients undergoing hip replacement and demonstrated no significant difference in delirium incidence but significantly shorter duration of delirium and hospital length of stay in the haloperidol group compared with the placebo group.[11]

Guidelines are published by National Institute for Health and Clinical Excellence in delirium: Diagnosis, prevention and management of delirium.[12] All patients presenting to a hospital or for long-term care should be assessed for four major risk factors: Age >65, pre-existing cognitive impairment, current hip fracture and severe illness. To minimise the effects of cognitive impairment and the potential for disorientation, patients should be provided appropriate lighting and time orientation (e.g., a 24-h clock in critical care settings); frequent re-orientation to place, person and situation; cognitive stimulation and visits from family and friends, if possible. As dehydration, malnutrition and constipation can contribute to delirium, appropriate fluid, feeding and bowel regimens must be used. Expert consultation should be considered in situations where fluid management can be challenging, as in patients with congestive heart failure or renal disease. Patients should be closely monitored for infection, hypoxemia and pain.

Focusing on changes noted in the past few hours or days, patients or caregivers should be asked about new or fluctuating cognitive impairment, abnormal perception (e.g., visual or auditory hallucinations), reduction in physical function and alteration in social behaviour (e.g., unusual social withdrawal, uncooperativeness and changes in mood). Randomised controlled trials of pharmacologic interventions, subcomponents of the successful multicomponent interventions that have been described and even delirium screening itself in various medical settings will be interesting future directions for the field. Rigorous studies of intraoperative interventions, such as haemodynamic targets, anaesthetic techniques and brain monitoring are likely to be instructive.

POST-OPERATIVE DEMENTIA AND COGNITIVE IMPAIRMENT

Memory loss is a normal part of the ageing process and usually involves a decreased ability to retrieve information. Memory loss due to ageing does not impact activities of daily living. People with memory loss often make use of adaptive strategies such as list making and sticky notes to preserve independence and safety. Mild cognitive impairment is a syndrome defined as cognitive decline greater than expected for an individual's age and education level that does not interfere notably with activities of daily living. It is not a diagnosis of any type. People with mild cognitive impairment are at higher risk to progress to dementia.

Dementia is a disorder characterised by problems with memory and at least one other cognitive function (learning, reasoning, language, spatial ability and orientation and handling complex tasks) that are severe enough to interfere with activities of daily living. Dementia may have different aetiologies, e.g. Alzheimer's disease.

Cognitive impairment includes both mild cognitive impairment and dementia. Here, in this review article, we will be dealing with cognition, changes following anaesthesia and surgery and tools for assessment in the perioperative period.[3]

The incidence of POCD 1-week after non-cardiac surgery in patients older than 18 years is between 15% and 41%.[13,14] This is often underestimated, usually associated

with increased morbidity and mortality. Age has shown to be a major predictor of POCD following both cardiac and non-cardiac surgeries. An increased POCD rate (10%) 3 months after surgery is only detected in patients older than 60 years.[14] Cardiac surgery carries the highest risk for POCD (30–36%).[15]

Dementia refers to a series of chronic organic brain syndromes associated with irreversible pathology. The failure of the cholinergic transmission is associated with dementia and anticholinesterases are used in some patients to improve cognitive function. Usually, dementia presents as a global deterioration of cognitive ability in the absence of clouding of consciousness. For example, the patient when initially introduced responds appropriately but later during the interview, is confused as to where he or she is, when asked for.[6]

There are a number of diseases in which dementia is a feature like Alzheimer's disease. Decline in cognitive dysfunction can also occur in Parkinson's disease and widespread cerebrovascular disease.[6]

Structural changes in the brain

The brain volume, both the white and grey matter starts decreasing with age, maximum by 85 years.[16] Along with the decrease in brain volume, changes in the permeability of blood brain barrier (BBB) contribute to the white matter disease.[17] Contributing factors include hypertension, hyperlipidaemia, diabetes mellitus and adverse drug reactions.[18] This in turn affects the ischaemia response and drug entry of BBB.[17] The arteriosclerotic changes in both the small and large vessels along with the age-related changes are responsible for the changes in cognition, including attention, psychomotor speed and executive function. Functional imaging depicts the greater variability of connection strengths between networks with increasing age across time at rest. Higher order neurons show a selective inversion of this effect during the implementation of cognitive control.[18]

There is a link between peripheral immune system and central nervous system (CNS) inflammatory response which is mediated by the microglia, astrocytes and CNS-associated macrophages.[19] Lower levels of effector memory CD4(+) T cells with corresponding higher numbers of naive CD8(+) T cells and B cells were correlated to have better cognitive performance.[20] Thus, immune dysregulation can reflect as alterations in behaviour or cognition in response to stress.[21,22] In the perioperative period, any peripheral stimuli with impaired anti-inflammatory activity in the ageing brain may result in exaggerated cytokine release and cognitive impairment.[23]

Cognitive reserve is defined in terms of the passive and active reserve. The passive reserve speaks about the quantal decrease in the brain volume and the active reserve about the functional qualitative capacity of cognition. Education further enhances the active reserve. Hence, we see a late decline in the acquired knowledge (active reserve) after 60 years of age and an early fall in cognition regarding spatial ability, reasoning and memory from adulthood (passive reserve).[24] The chain of nor adrenergic activity, with its set of neurocognitive correlates (such as arousal, sustained attention, response to novelty and awareness), right hemispheric involvement, frontoparietal localisation and working memory, is responsible for the protective effects of cognitive reserve.[25]

COGNITION DRIFTS AND ANAESTHESIA

Most anaesthetic agents target either excitatory (e.g. N-methyl-D-aspartate [NMDA]) and or inhibitory (e.g., glycine, gamma-aminobutyric acid) postsynaptic ligand-gated ion channels for their action[26-28] [Table 3]. There are many theories depicting the underlying mechanism of POCD following surgery. Anaesthesia and surgery are associated with inflammatory changes. The underlying mechanisms of degeneration in the elderly brain with anaesthesia have been studied. Liberation of pro-inflammatory mediators will lead to the oxidative metabolism of tryptophan to Kynurenines and other inflammatory markers. These modulate NMDA receptor function and are found to be one of the predictors for POCD.[29] The other theory for cognitive decline following anaesthesia in the geriatric population is found to be a complex and variable interaction of the anaesthetic agent and specific ion channel, especially involving the acetylcholine.[30-32] Loss of functional cholinergic neurons in the frontal area is associated with significant cognitive decline. Some studies have shown that exposure to anaesthesia leads to oligomerisation of amyloid beta peptide. Excess production and deposition of these oligomerised products leads to changes in brain cognition in elderly patients.[33,34] Recent reports suggest that GAs may result in hyperphosphorylation and aggregation of

Table 3: The anaesthetic agents and the receptors

Anaesthetic agents	Receptors
Propofol, Etomidate	GABA
Dexmedetomidine	α_2
Ketamine	N-methyl D-Aspartate
Opioids	Acetyl choline, adenosine and dopamine
Inhalational agents	GABA, glycine, acetylcholine, glutamate and serotonin

GABA: Gamma amino butyric acid

microtubule-associated protein (tau protein) resulting in intra-neuronal neurofibrillary tangles, which correlates well with the cognitive dysfunction.[35] Tau pathology has been implicated for POCD linked with hypothermia, insulin dysfunction and inhalational anaesthesia.[34,36-38]

Several factors have been implicated in the development of POCD [Table 4]. Pre-operative cognitive impairment is a strong predictor for POCD.[39] This shows a strong correlation of anaesthetic agents and POCD, especially in elderly patients. Presence of co-morbidities such as hypertension, vascular insufficiency, diabetes and multiple sclerosis will increase the severity of POCD.[40] General anaesthesia compared to regional anaesthesia has shown a positive correlation with POCD. Cognitive impairment following inhalational anaesthesia does not vary much with different agents.[41] Total intravenous anaesthesia has shown to have a negligent effect on cognitive impairment both in young and elderly patients.[42-44] Inadequate post-operative pain management causes up-regulation of NMDA receptors in the hippocampal region and leads to memory decline after surgery and anaesthesia.[45]

Multimodal anaesthesia and analgesic protocols, use of ultrashort-acting agents with intraoperative cerebral function monitoring should be instituted to target optimum depth of anaesthesia.[46-48] Novel agents such as dexmedetomidine have a neuroprotective effect due to its anti-inflammatory effect.[49,50]

Use of other anti-inflammatory drugs such as statins and minocycline may reduce the incidence of POCD.[14]

INTRAOPERATIVE MONITORING AND COGNITIVE IMPAIRMENT

Stress associated with anaesthesia and surgery has shown a definitive role in the implications of POCD.[51] The triad of cerebral oxygenation, perfusion and depth of anaesthesia plays a pivotal role in cognition and its decline following this stress. Depth of anaesthesia monitoring has shown to have conflicting results for POCD outcome.[52-54] Different modalities include electroencephalogram based indices (entropy, modified sample entropy and BIS monitor), evoked potentials, cerebral saturation and minimal alveolar concentration values.[55,56] Intraoperative burst suppression was associated with POCD following cardiac surgery.[57] Continuous auditory evoked potential monitoring has resulted in lesser consumption of anaesthetic agents with lesser incidence of haemodynamic instability and POCD.[58] Prolonged regional cerebral oxygen (rSO2) desaturation has shown positive correlation with cognitive impairment.[59] Intraoperative cerebral oximetry monitoring is an important monitoring tool that can be adopted in routine practice to decrease the incidence of cognitive decline, especially in anaesthetised patients undergoing on pump cardiac surgery. Cerebral hypoperfusion detected by transcranial Doppler, correlated with clinical indicators in patients with delirium superimposed on dementia.[60] In contrast, some studies were inconclusive with specific to cerebral perfusion/oxygenation and cognitive decline.[61]

Table 4: Predisposing factors for post-operative cognitive dysfunction (POCD)

	Predisposing factors
Preoperative	General
	Age
	Alcohol dependence
	Presence of other co-morbidities- diabetes, vascular insufficiency, hypertension, multiple sclerosis
	Smoking
	Sedentary life style
	Obesity, elevated cholesterol
	Polypharmacy
	H/o depression
	Lower education
	Higher American Society of Anaesthesiologists (ASA) scores
	Previous h/o stroke or delirium
	Specific
	Age related structural changes in the brain
	Cerebrovascular accidents
	Inflammation of the brain
	Decreased cognition reserve
	Pre-operative cognitive impairment
Intraoperative	General
	Stress following surgery and anaesthesia
	After major surgeries - cardiac surgery, emergency surgeries, major non-cardiac surgeries,
	Increased duration of anaesthesia
	Haemodynamic insults (ischaemia, hypoperfusion)
	Anaesthesia and its neurodegerative effects
	Dysregulation of cerebral circulation
	Increased depth of anaesthesia
	Thromboembolism
	Polypharmacy
	Specific
	Anaesthetic agents
	Cerebral hypoperfusion/desaturation
	Carotid endarterectomy
Postoperative	Inadequate pain relief
	Prolonged hospital stay
	Thromboembolism
	Prolonged ventilator support

PERIOPERATIVE SURVEILLANCE

The cognitive impairment following anaesthesia delays post-operative recovery increases hospital stay with increased cost burden, thus, has shown to increase the morbidity and mortality in elderly frail patients.

Recognition of the cognitive status of the patient pre-operatively, proper counselling, decreasing or modifying the anaesthetic burden with appropriate monitoring and stepwise assessment of the cognitive status postoperatively and timely intervention are the keys to perioperative surveillance of these patients. Initial screening is done, especially to ascertain the presence or absence of impairment. Evaluation of the cognitive status preoperatively and postoperatively helps in tracking the changes incurred over time with the stress of surgery and anaesthesia. Detailed interview from the patient and the informant separately helps us to gain maximum knowledge, and any different views from both helps us in obtaining information, especially pertaining to language and co-operation domains. Assessment of the functional status of the patient adds on to the overall cognitive assessment. This provides an insight regarding the performance of daily activities of living by the patient which may be constrained by cognitive impairment.

NEUROCOGNITIVE ASSESSMENT TOOLS

There are no well-defined criteria established for the diagnosis of post-operative cognitive disorders due to the inconsistency of different studies. Preferably, an optimal cognitive assessment tool should have the following idealistic characteristics [Table 5]. There are some limitations which include place of examination, ageing, and education, and culture, presence of primary psychiatric disorders or sensory deficits. A battery of neuropsychological tests is required for the assessment of different domains of cognitive function.

Before administration of any test, some factual methods need to be employed: Making the patient comfortable, checking for any dependence on sensory aids, gaining patient's confidence, permission for asking questions, interview of the informant separately and history of polypharmacy.

DELIRIUM

Delirium is usually assessed by the short Confusion Assessment Method (CAM). While there are both a long (10-item) and short (4-item) CAM, and both have acceptable sensitivity, the short version has been more widely applied in clinical practice. The short CAM is recommended for routine clinical applications; however, the longer 10-item CAM is preferred where more definitive or research diagnoses for delirium are required.[12]

The short CAM includes two parts. First part deals with the questionnaire pertaining to screening for overall cognition. Second part deals with the main four features namely: 1. Acute onset and fluctuating course, 2. Inattention, 3. Disorganised thinking and 4. Altered level of consciousness that distinguishes delirium or reversible confusion from other types of cognitive impairment.[62,63] The diagnosis of delirium is established by the presence of both features 1 and 2, with either feature of 3 or 4.

COGNITIVE IMPAIRMENT

Mini-Mental State Examination (MMSE), The Mini cog, The General Practitioner Assessment of Cognition (GPCOG), memory impairment screen (MIS), Alzheimer's disease 8 (AD8) Test and Short form of Informant Questionnaire on Cognitive Decline in the Elderly (Short IQCODE) are the most commonly used tools to screen and assess the post-operative cognition decline. The algorithm for assessment of cognitive function impairment is depicted in Figure 1.[64]

Mini mental state examination

This is the most widely used bedside global validated tool for evaluation of cognitive function.[65] A total of 20 questions addressing 11 aspects of cognition, carry a total score of 30 in a patient with normal cognition. The cognition variables include orientation (time – 5 points; place – 5 points) and attention/concentration/calculation (5 points) with lower emphasis on registration memory (3 points) and recall (3 points). Others include naming (2 points), repetition (1 point), following a three-stage command (3 points), reading (1 point), writing (1 point) or copying intersecting pentagons (1 point). The total score will be 30. Score of 26–28 indicates mild cognitive impairment and score below 26 indicates there is an increased risk of developing dementia.

Other modified forms of MMSE are available. They include standardised MMSE and modified MMSE. The modified MMSE was devised by Teng and Chui.[66] This has, in addition, four more components: Personal information, verbal fluency, abstraction or conceptual thinking and long-term recall with some minor modifications in the actual questionnaire.

Table 5: Cognitive Assessment Tool: Ideal Criteria stated by the Research Committee of the American Neuropsychiatric Association

Takes less time (<15 minutes) and easy to administer by any clinician
Should address all components of cognition: memory, attention/concentration, executive function, visual-spatial skills, language, and orientation
Needs to be reliable with satisfactory test re-test and inter-rater validity
Should be able to detect cognition disorders commonly encountered by neuropsychiatrists
Easy to interpret

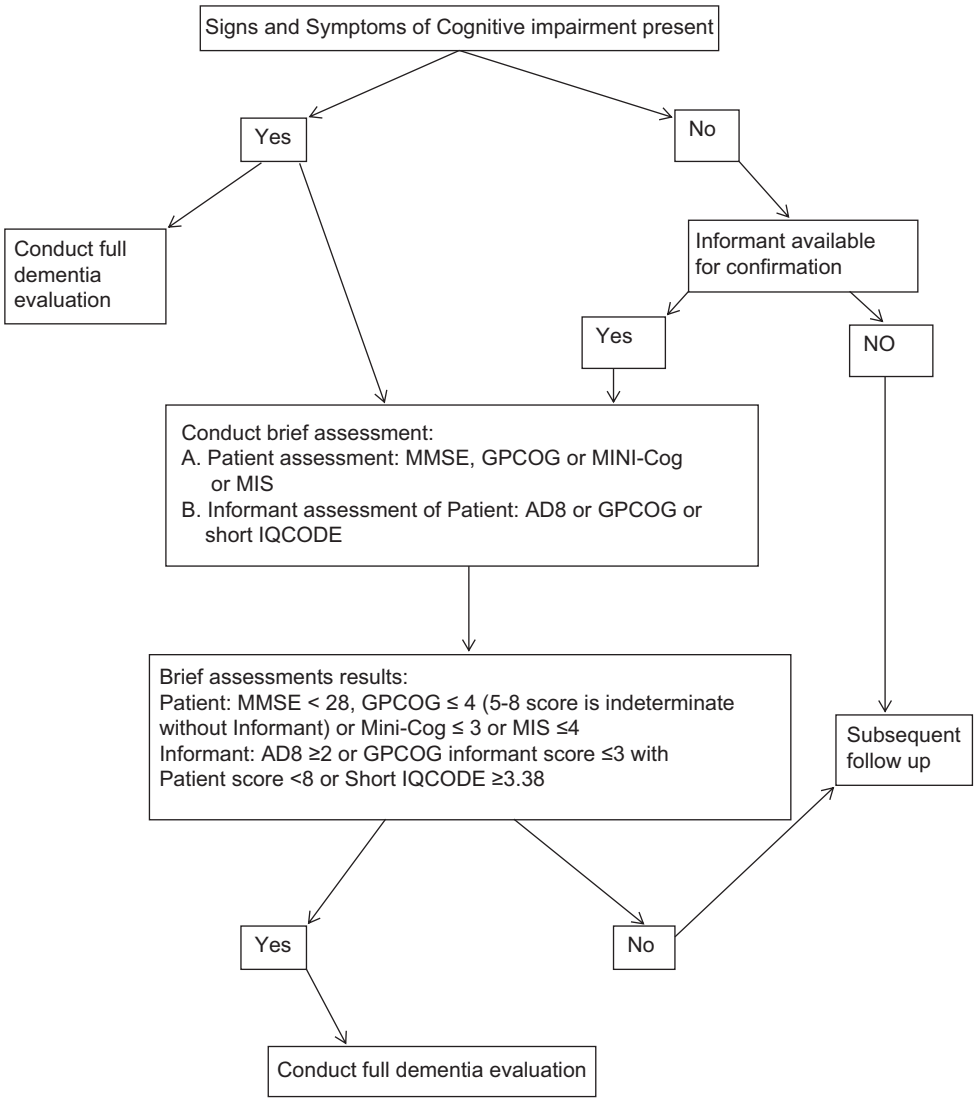

Figure 1: Algorithm for assessment of cognitive function

Mini-cog

This test is used to screen and monitor cognitive impairment in its earlier stages.[67] It is simple, effective, easy to administer and requires minimal training. This consists of 3-item recall task and a simple clock-drawing task.[68] But, this needs to be supplemented with other functional tests to complete the evaluation.

After obtaining comfortable criteria for examination and interview, the patient is initially asked to remember three unrelated words (Step 1), later to be tested for recall of these words. This is mainly to ensure the functional ability of the learning domain. List of words tested for recall were validated in different studies.

This is followed by the Clock-Drawing Test (CDT) (Centres for Disease Control) (Step 2). First, the patient is asked to draw the face of the clock with the appropriate numbers, and second to draw hands to point out the time – 10 past eleven or 20 past eight.

Finally, the patient is asked to recall those three words (Step 3) from Step 1. If patient is able to recall 3 words or 1–2 recalled words with normal CDT, the test is considered negative for cognitive impairment. If the patient is not able to recall all the 3 words or able to recall 1–2 recalled words with abnormal CDT, this indicates positive for cognitive impairment.

The general practitioner assessment of cognition

The GPCOG[69] is a brief screening test for cognitive impairment. Both the patient and the informant are examined, with a maximum score of 9 to the patient and 6 to the informant. The patient is under examination for time orientation, clock-drawing, reporting a recent event and a word recall task. The informant is asked about the patient's memory of recent conversations, misplacing objects, word finding difficulties, and ability to manage money, ability to manage medication and need for travel assistance. The

patient score of 9 indicates no cognitive impairment and if score lies between 5 and 8, the informant should be examined. The patient score of 4 or lower or the informant section score of 3 or lower suggests cognitive impairment.[70]

Memory impairment screen

MIS comprises 4-item, takes 4 min to administer and uses free and cued-recall.[71] The subject is asked to read the four target (to-be-remembered) aloud from a printed page. Category cues are presented then one at a time and subject is asked to identify the target word that matched the category cue (e.g. FRUIT–PEACH). The words sheet is then removed. After a non-sematic interference task lasting 2–3 min, the subject is asked to recall as many of the four target words as possible (free recall) and presented with category cues for items not recalled freely (cued-recall). The maximum score for the MIS is 8 and score ≤ 4 indicates the possibility of cognitive impairment.

AD8 Test

AD8 is a brief tool used to screen dementia, which was developed from Washington University in St. Louis.[72] It is capable of screening very mild dementia in a general population. If the screening result score of AD8 is 0–1 it is considered normal, 2 and above, the individual would be considered having dementia.[73] AD8 can be administered to the patient and also to the informant of demented patients.[74]

Short form of the Informant Questionnaire on Cognitive Decline in the elderly

Among the validated informant tools, this is the most widely used. This testing tool compares the different domains of cognition such as memory and intelligence of the patient currently with that of 10 years before. The final score is given as the sum of the scores of all the questions divided by the total number of questions, and it ranges from 1 to 5. A score of ≥3.38 indicates cognitive impairment. To increase the sensitivity and specificity, the test needs to be supplemented with other patient tests such as MMSE for improved accuracy for recognition of cognitive impairment.[75]

The comparison of the commonly used cognitive assessment tools with respect to the time taken for these

Table 6: Comparison of Cognitive Assessment Tools

Assessment tools	Time to administer	Sensitivity (%)	Specificity (%)	Strengths	Limitations
Confusion Assessment Method (CAM)	< 5 minutes	94-100	90-95	Closely correlates with DSM-IV criteria for delirium, MMSE, Visual Analog Scale for Confusion and the digit span test	Does not assess the severity of the condition
Mini Mental State Examination (MMSE)	5-10 minutes	76.9	89.9	An effective screening instrument; Validated tool; easy to administer	Only includes 5 domains of cognition; patients with sensory deficit, intubated, low literacy and communication disorders may not perform well
Mini-cog	3-5 minutes	99	93	Simple, easy to administer, requires minimal training	Needs to be supplemented with other tests for complete evaluation
GPCOG	4-6 minutes	85	86	Incorporates functional status; short administration time	Cannot be used without an informant
MIS	4 minutes	80	96	Age, education, and sex did not significantly affect performance	Used for memory testing only
AD8 test	4-5 minutes	84	80	Screening very mild dementia	Better used with informant
Short IQCODE	quick	86%	39%	High reliability and measures a single general factor of cognitive decline Unaffected by education and pre-morbid ability or by proficiency in the culture's dominant language	Variable performance; affected by informant characteristics such as depression and anxiety and the quality of the relationship between the informant and the subject

DSM: Diagnostic and Statistical Manual of Mental Disorders; GPCOG: The General Practitioner Assessment of Cognition; MIS: Memory Impairment Screen; AD: Alzheimer's disease; IQCODE: Informant Questionnaire on Cognitive Decline in the Elderly

tools to administer, sensitivity and specificity of the tests with their strengths and limitations are presented in Table 6.

Neurocognitive dysfunction assessment is of great significance particularly in neuroanaesthesia because the cognitive function likely to be effected by the pre-operative diseases conditions and the surgical procedures the patient undergoes. A lot of cognitive assessment tools have been studied and analysed for their application in perioperative care. Choosing an exact and specific tool (or combination of two), suitable for day to day cognitive assessment and practical application of the same depends on various factors such as patient condition, availability of informants, education level, time for administration and specific requirements *per se* MMES and mini-cog are suitable tools for perioperative assessment of cognitive dysfunction and short CAM is for delirium. Pre-operative identification of the patients at risk, scoring the risk and explaining the risk to the patient and their relatives and risk involved with surgery and anaesthesia would solve the major problem of legal implications, especially in elderly patients. Second, safe administration of anaesthesia, attenuation of surgical stress with intraoperative monitoring with optimum depth of anaesthesia and monitoring the cognition changes with the same assessment tool in the post-operative period will guide the perioperative physician regarding the outcome. Though research articles with biomarkers for cognition impairment have reported upon, still substantial evidence has not surfaced to identify specific risk patients. In order to curtail the cognition changes following anaesthesia and surgery, neurocognitive assessment tools should be made mandatory as a part of the routine perioperative clinical practice.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Long LS, Shapiro WA, Leung JM. A brief review of practical preoperative cognitive screening tools. Can J Anaesth 2012;59:798-804.
2. Couillard-Despres S, Iglseder B, Aigner L. Neurogenesis, cellular plasticity and cognition: The impact of stem cells in the adult and aging brain – A mini-review. Gerontology 2011;57:559-64.
3. Alzheimer's Association. 2012 Alzheimer's disease facts and figures. Alzheimers Dement 2012;8:131-68.
4. Deiner S, Silverstein JH. Postoperative delirium and cognitive dysfunction. Br J Anaesth 2009;103 Suppl 1:i41-6.
5. Mashour GA, Woodrum DT, Avidan S. Neurological complications of surgery and anaesthesia. Br J Anaesth 2014;8:1-10.
6. Fines DP, Severan AM. Anaesthesia and cognitive disturbance in elderly. Anaesth Crit Care Pain 2006;6:37-40.
7. Inouye SK, Bogardus ST Jr, Charpentier PA, Leo-Summers L, Acampora D, Holford TR, *et al*. A multicomponent intervention to prevent delirium in hospitalized older patients. N Engl J Med 1999;340:669-76.
8. Sanders RD. Hypothesis for the pathophysiology of delirium: Role of baseline brain network connectivity and changes in inhibitory tone. Med Hypotheses 2011;77:140-3.
9. Sieber FE, Zakriya KJ, Gottschalk A, Blute MR, Lee HB, Rosenberg PB, *et al.* Sedation depth during spinal anesthesia and the development of postoperative delirium in elderly patients undergoing hip fracture repair. Mayo Clin Proc 2010;85:18-26.
10. Mason SE, Noel-Storr A, Ritchie CW. The impact of general and regional anesthesia on the incidence of post-operative cognitive dysfunction and post-operative delirium: A systematic review with meta-analysis. J Alzheimers Dis 2010;22 Suppl 3:67-79.
11. Kalisvaart KJ, de Jonghe JF, Bogaards MJ, Vreeswijk R, Egberts TC, Burger BJ, *et al.* Haloperidol prophylaxis for elderly hip-surgery patients at risk for delirium: A randomized placebo-controlled study. J Am Geriatr Soc 2005;53:1658-66.
12. Greer N, Rossom R, Anderson P, MacDonald R, Tacklind J, Rutks I, *et al*. Delirium: Screening, prevention, and diagnosis - A systematic review of the evidence. VA-ESP Project #09-009; 2011. p. 1-51. Available from: http://www.hsrd.research.va.gov/publications/esp/delirium-REPORT.pdf. [Last cited on 2015 May 22].
13. Shoair OA, Grasso Ii MP, Lahaye LA, Daniel R, Biddle CJ, Slattum PW. Incidence and risk factors for postoperative cognitive dysfunction in older adults undergoing major noncardiac surgery: A prospective study. J Anaesthesiol Clin Pharmacol 2015;31:30-6.
14. Ida M, Kawaguchi M. Postoperative cognitive dysfunction after non-cardiac surgery. Masui 2014;63:1228-34.
15. van Harten AE, Scheeren TW, Absalom AR. A review of postoperative cognitive dysfunction and neuroinflammation associated with cardiac surgery and anaesthesia. Anaesthesia 2012;67:280-93.
16. Hedman AM, van Haren NE, Schnack HG, Kahn RS, Hulshoff Pol HE. Human brain changes across the life span: A review of 56 longitudinal magnetic resonance imaging studies. Hum Brain Mapp 2012;33:1987-2002.
17. Zeevi N, Pachter J, McCullough LD, Wolfson L, Kuchel GA. The blood-brain barrier: Geriatric relevance of a critical brain-body interface. J Am Geriatr Soc 2010;58:1749-57.
18. Aine CJ, Sanfratello L, Adair JC, Knoefel JE, Caprihan A, Stephen JM. Development and decline of memory functions in normal, pathological and healthy successful aging. Brain Topogr 2011;24:323-39.
19. Fakhoury M. Role of immunity and inflammation in the pathophysiology of neurodegenerative diseases. Neurodegener Dis 2015;15:63-9.
20. Serre-Miranda C, Roque S, Santos NC, Portugal-Nunes C, Costa P, Palha JA, *et al*. Effector memory CD4(+) T cells are associated with cognitive performance in a seniorpopulation. Neurol Neuroimmunol Neuroinflamm 2015;2:e54.
21. Prenderville JA, Kennedy PJ, Dinan TG, Cryan JF. Adding fuel to the fire: The impact of stress on the ageing brain. Trends Neurosci 2015;38:13-25.
22. Pukhal'skii AL, Shmarina GV, Aleshkin VA. Immune dysfunction and cognitive deficit in stress and physiological aging. Part II: New approaches to cognitive disorder prevention and treatment. Vestn Ross Akad Med Nauk 2014;7-8:30-7.
23. Corona AW, Fenn AM, Godbout JP. Cognitive and behavioral consequences of impaired immunoregulation in aging. J Neuroimmune Pharmacol 2012;7:7-23.

24. O'Shea DM, Fieo RA, Hamilton JL, Zahodne LB, Manly JJ, Stern Y. Examining the association between late-life depressive symptoms, cognitive function, and brain volumes in the context of cognitive reserve. Int J Geriatr Psychiatry 2015;30:614-22.
25. Robertson IH. Right hemisphere role in cognitive reserve. Neurobiol Aging 2014;35:1375-85.
26. Franks NP. General anaesthesia: From molecular targets to neuronal pathways of sleep and arousal. Nat Rev Neurosci 2008;9:370-86.
27. Uhrig L, Dehaene S, Jarraya B. Cerebral mechanisms of general anesthesia. Ann Fr Anesth Reanim 2014;33:72-82.
28. Son Y. Molecular mechanisms of general anesthesia. Korean J Anesthesiol 2010;59:3-8.
29. Forrest CM, Mackay GM, Oxford L, Millar K, Darlington LG, Higgins MJ, *et al.* Kynurenine metabolism predicts cognitive function in patients following cardiac bypass and thoracic surgery. J Neurochem 2011;119:136-52.
30. Pa J, Berry AS, Compagnone M, Boccanfuso J, Greenhouse I, Rubens MT, *et al.* Cholinergic enhancement of functional networks in older adults with mild cognitive impairment. Ann Neurol 2013;73:762-73.
31. Fodale V, Quattrone D, Trecroci C, Caminiti V, Santamaria LB. Alzheimer's disease and anaesthesia: Implications for the central cholinergic system. Br J Anaesth 2006;97:445-52.
32. Schifilliti D, Santamaria LB, Rosa G, Di Nino G, Mandal PK, Fodale V. Cholinergic central system, Alzheimer's disease, and anesthetics liaison: A vicious circle? J Alzheimers Dis 2010;22 Suppl 3:35-41.
33. Fodale V, Santamaria LB, Schifilliti D, Mandal PK. Anaesthetics and postoperative cognitive dysfunction: A pathological mechanism mimicking Alzheimer's disease. Anaesthesia 2010;65:388-95.
34. Jiang J, Jiang H. Effect of the inhaled anesthetics isoflurane, sevoflurane and desflurane on the neuropathogenesis of Alzheimer's disease (review). Mol Med Rep 2015;12:3-12.
35. Whittington RA, Bretteville A, Dickler MF, Planel E. Anesthesia and tau pathology. Prog Neuropsychopharmacol Biol Psychiatry 2013;47:147-55.
36. Craddock TJ, St George M, Freedman H, Barakat KH, Damaraju S, Hameroff S, *et al.* Computational predictions of volatile anesthetic interactions with the microtubule cytoskeleton: Implications for side effects of general anesthesia. PLoS One 2012;7:e37251.
37. Bretteville A, Marcouiller F, Julien C, El Khoury NB, Petry FR, Poitras I, *et al.* Hypothermia-induced hyperphosphorylation: A new model to study tau kinase inhibitors. Sci Rep 2012;2:480.
38. El Khoury NB, Gratuze M, Papon MA, Bretteville A, Planel E. Insulin dysfunction and Tau pathology. Front Cell Neurosci 2014;8:22.
39. Silbert B, Evered L, Scott DA, McMahon S, Choong P, Ames D, *et al.* Preexisting cognitive impairment is associated with postoperative cognitive dysfunction after hip joint replacement surgery. Anesthesiology 2015;122:1224-34.
40. Arora SS, Gooch JL, García PS. Postoperative cognitive dysfunction, Alzheimer's disease, and anesthesia. Int J Neurosci 2014;124:236-42.
41. Meineke M, Applegate RL 2nd, Rasmussen T, Anderson D, Azer S, Mehdizadeh A, *et al.* Cognitive dysfunction following desflurane versus sevoflurane general anesthesia in elderly patients: A randomized controlled trial. Med Gas Res 2014;4:6.
42. Ilvan G, Özköse HZ. The effect of total intravenous anesthesia on the postoperative cognitive functions of young and elderly patients after lumbar disk surgery. Turk J Med Sci 2015;45:191-6.
43. Tang N, Ou C, Liu Y, Zuo Y, Bai Y. Effect of inhalational anaesthetic on postoperative cognitive dysfunction following radical rectal resection in elderly patients with mild cognitive impairment. J Int Med Res 2014;42:1252-61.
44. Xu D, Yang W, Zhao G. Effect of propofol and inhalation anesthesia on postoperative cognitive dysfunction in the elderly: A meta-analysis. Nan Fang Yi Ke Da Xue Xue Bao 2012;32:1623-7.
45. Chi H, Kawano T, Tamura T, Iwata H, Takahashi Y, Eguchi S, *et al.* Postoperative pain impairs subsequent performance on a spatial memory task via effects on N-methyl-D-aspartate receptor in aged rats. Life Sci 2013;93:986-93.
46. Zywiel MG, Prabhu A, Perruccio AV, Gandhi R. The influence of anesthesia and pain management on cognitive dysfunction after joint arthroplasty: A systematic review. Clin Orthop Relat Res 2014;472:1453-66.
47. Muravchick S. The elderly outpatient: Current anesthetic implications. Curr Opin Anaesthesiol 2002;15:621-5.
48. Kapila AK, Watts HR, Wang T, Ma D. The impact of surgery and anesthesia on post-operative cognitive decline and Alzheimer's disease development: Biomarkers and preventive strategies. J Alzheimers Dis 2014;41:1-13.
49. Ding L, Zhang H, Mi W, He Y, Zhang X, Ma X, *et al.* Effects of dexmedetomidine on recovery period of anesthesia and postoperative cognitive function after robot-assisted laparoscopicradical prostatectomy in the elderly people. Zhong Nan Da Xue Xue Bao Yi Xue Ban 2015;40:129-35.
50. Chen J, Yan J, Han X. Dexmedetomidine may benefit cognitive function after laparoscopic cholecystectomy in elderly patients. Exp Ther Med 2013;5:489-94.
51. Mu DL, Li LH, Wang DX, Li N, Shan GJ, Li J, *et al.* High postoperative serum cortisol level is associated with increased risk of cognitive dysfunction early after coronary artery bypass graft surgery: A prospective cohort study. PLoS One 2013;8:e77637.
52. Jildenstål PK, Rawal N, Hallén JL, Berggren L, Jakobsson JG. Perioperative management in order to minimise postoperative delirium and postoperative cognitive dysfunction: Results from a Swedish web-based survey. Ann Med Surg (Lond) 2014;3:100-7.
53. Shepherd J, Jones J, Frampton G, Bryant J, Baxter L, Cooper K. Clinical effectiveness and cost-effectiveness of depth of anaesthesia monitoring (E-Entropy, Bispectral Index and Narcotrend): A systematic review and economic evaluation. Health Technol Assess 2013;17:1-264.
54. Radtke FM, Franck M, Lendner J, Krüger S, Wernecke KD, Spies CD. Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction. Br J Anaesth 2013;110 Suppl 1:i98-105.
55. Wang Y, Liang Z, Voss LJ, Sleigh JW, Li X. Multi-scale sample entropy of electroencephalography during sevoflurane anesthesia. J Clin Monit Comput 2014;28:409-17.
56. Chan MT, Cheng BC, Lee TM, Gin T; CODA Trial Group. BIS-guided anesthesia decreases postoperative delirium and cognitive decline. J Neurosurg Anesthesiol 2013;25:33-42.
57. Soehle M, Dittmann A, Ellerkmann RK, Baumgarten G, Putensen C, Guenther U. Intraoperative burst suppression is associated with postoperative delirium following cardiac surgery: A prospective, observational study. BMC Anesthesiol 2015;15:61.
58. Jildenstål PK, Hallén JL, Rawal N, Gupta A, Berggren L. Effect of auditory evoked potential-guided anaesthesia on consumption of anaesthetics and early postoperative cognitive dysfunction: A randomised controlled trial. Eur J Anaesthesiol 2011;28:213-9.
59. Colak Z, Borojevic M, Bogovic A, Ivancan V, Biocina B, Majeric-Kogler V. Influence of intraoperative cerebral oximetry monitoring on neurocognitive function after coronary artery bypass surgery: A randomized, prospective

study. Eur J Cardiothorac Surg 2015;47:447-54.
60. Caplan GA, Lan Z, Newton L, Kvelde T, McVeigh C, Hill MA. Transcranial Doppler to measure cerebral blood flow in delirium superimposed on dementia. A cohort study. J Am Med Dir Assoc 2014;15:355-60.
61. Zheng F, Sheinberg R, Yee MS, Ono M, Zheng Y, Hogue CW. Cerebral near-infrared spectroscopy monitoring and neurologic outcomes in adult cardiac surgery patients: A systematic review. Anesth Analg 2013;116:663-76.
62. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horwitz RI. Clarifying confusion: The confusion assessment method. A new method for detection of delirium. Ann Intern Med 1990;113:941-8.
63. Klich-Raczka A, Piotrowicz K, Grodzicki T. Delirium in the light of the most recent guidelines. Przegl Lek 2009;66:187-91.
64. Cordell CB, Borson S, Boustani M, Chodosh J, Reuben D, Verghese J, *et al.* Alzheimer's Association recommendations for operationalizing the detection of cognitive impairment during the Medicare Annual Wellness Visit in a primary care setting. Alzheimers Dement 2013;9:141-50.
65. Folstein MF, Folstein SE, McHugh PR. Mini-mental state. A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-98.
66. Tombaugh TN. Test-retest reliable coefficients and 5-year change scores for the MMSE and 3MS. Arch Clin Neuropsychol 2005;20:485-503.
67. Carolan Doerflinger DM. How to try this: The mini-cog. Am J Nurs 2007;107:62-71.
68. Michieletto F, Binkin N, Saugo M, Boorson S, Scanlan J; Gruppo Studio Argento. Use of the Mini-Cog test as a screening method for dementia in the Italian population: The Argento Study results. Ig Sanita Pubbl 2006;62:159-72.
69. Brodaty H, Pond D, Kemp NM, Luscombe G, Harding L, Berman K, *et al.* The GPCOG: A new screening test for dementia designed for general practice. J Am Geriatr Soc 2002;50:530-4.
70. Brodaty H, Kemp NM, Low LF. Characteristics of the GPCOG, a screening tool for cognitive impairment. Int J Geriatr Psychiatry 2004;19:870-4.
71. Buschke H, Kuslansky G, Katz M, Stewart WF, Sliwinski MJ, Eckholdt HM, *et al.* Screening for dementia with the memory impairment screen. Neurology 1999;52:231-8.
72. Galvin JE, Roe CM, Powlishta KK, Coats MA, Muich SJ, Grant E, *et al.* The AD8: A brief informant interview to detect dementia. Neurology 2005;65:559-64.
73. Yang YH, Galvin JE, Morris JC, Lai CL, Chou MC, Liu CK. Application of AD8 questionnaire to screen very mild dementia in Taiwanese. Am J Alzheimers Dis Other Demen 2011;26:134-8.
74. Galvin JE, Roe CM, Xiong C, Morris JC. Validity and reliability of the AD8 informant interview in dementia. Neurology 2006;67:1942-8.
75. Jorm AF. A short form of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): Development and cross-validation. Psychol Med 1994;24:145-53.