PSYCHOGERIATRICS
The Official Journal of the Japanese Psychogeriatric Society

doi:10.1111/j.1479-8301.2010.00323.x PSYCHOGERIATRICS 2010; 10: 206–213

REVIEW ARTICLE

# Overview of non-pharmacological intervention for dementia and principles of brain-activating rehabilitation

**Haruyasu YAMAGUCHI,[1] Yohko MAKI[1,2] and Tetsuya YAMAGAMI[1]**

[1]Gunma University School of Health Sciences and [2]Department of Neurology, Geriatrics Research Institute and Hospital, Maebashi, Japan

*Correspondence:* Professor Haruyasu Yamaguchi MD PhD, 3-39-15 Showa-machi, Maebashi 371-8514, Japan. Email: yamaguti@health.gunma-u.ac.jp

*Received 8 March 2010; accepted 13 May 2010.*

## Abstract

Non-pharmacological interventions for dementia are likely to have an important role in delaying disease progression and functional decline. Research into non-pharmacological interventions has focused on the differentiation of each approach and a comparison of their effects. However, Cochrane Reviews on non-pharmacological interventions have noted the paucity of evidence regarding the effects of these interventions. The essence of non-pharmacological intervention is dependent of the patients, families, and therapists involved, with each situation inevitably being different. To obtain good results with non-pharmacological therapy, the core is not 'what' approach is taken but 'how' the therapists communicate with their patients. Here, we propose a new type of rehabilitation for dementia, namely brain-activating rehabilitation, that consists of five principles: (i) enjoyable and comfortable activities in an accepting atmosphere; (ii) activities associated with empathetic two-way communication between the therapist and patient, as well as between patients; (iii) therapists should praise patients to enhance motivation; (iv) therapists should try to offer each patient some social role that takes advantage of his/her remaining abilities; and (v) the activities should be based on errorless learning to ensure a pleasant atmosphere and to maintain a patient's dignity. The behavioral and cognitive status is not necessarily a reflection of pathological lesions in the brain; there is cognitive reserve for improvement. The aim of brain-activating rehabilitation is to enhance patients' motivation and maximize the use of their remaining function, recruiting a compensatory network, and preventing the disuse of brain function. The primary expected effect is that patients recover a desire for life, as well as their self-respect. Enhanced motivation can lead to improvements in cognitive function. Amelioration of the behavioral and psychological symptoms of dementia and improvements in activities of daily living can also be expected due to the renewed positive attitude towards life. In addition, improvements in the quality of life for both patients and caregivers is an expected outcome. To establish evidence for non-pharmacological interventions, research protocols and outcome measures should be standardized to facilitate comparison among studies, as well as meta-analysis.

***Key words:*** *Alzheimer disease, behavioral and psychological symptoms of dementia (BPSD), dementia, empathy, intersubjectivity, patient-centered rehabilitation.*

## OVERVIEW OF NON-PHARMACOLOGICAL TREATMENT

In tandem with the rapid aging of the population, the prevalence of dementia is increasing steeply. Despite considerable progress in the treatment of causative diseases, such as Alzheimer's disease (AD), dementia remains incurable. Thus, it is of considerable importance to delay disease progression and functional decline; it is expected that non-pharmacological interventions for dementia will have a significant role in this

respect. The American Association for Geriatric Psychiatry (AAGP) position statement proposes a care/treatment model that combines pharmacological and non-pharmacological treatment for patients with AD.[1]

In the present review, we describe recent trends in non-pharmacological treatment for dementia and then propose our brain-activating rehabilitation (BAR).

## APPROACHES TO COGNITIVE SYMPTOMS

Time–place disorientation and memory deficits are the most prominent features of AD from the early stages, and cognitive rehabilitation, such as reality orientation and memory training, is widely used. However, cognitive rehabilitation inevitably identifies what patients are not capable of. Patients' realization of their disorientation and/or memory deficits can devastate their self-confidence, leading to depression and withdrawal. Until the mid-1980s, reality orientation training was conducted in a confrontational atmosphere, with adverse effects reported, including frustration, anxiety, depression, and a lowering of self-esteem.[2,3] Thus, the consensus statement of the AAGP warned of the potentially harmful effects of reality orientation training.[4] Now, a consensus has been reached that training must be conducted in a person-centered manner.[5]

Errorless learning was proposed in consideration of patients' dignity. Errorless learning is a teaching technique that prevents learners from making mistakes.[6,7] Therapists should be careful to ensure that patients succeed in any attempt; if errors are made, the therapists should not point out these errors. For patients with memory deficits, trial-and-error learning is not effective. One can learn from errors only when prior errors can be compared with the present results. However, recollection of past errors is difficult for patients with memory deficits, and the errors can be reinforced by priming effects.[8]

Another challenge in cognitive rehabilitation is the relevance to daily living. Cognitive training is meaningless unless it serves to enhance cognitive function in daily living. However, memory skills recovered by cognitive rehabilitation are hardly generalized in daily living.[7] Thus, the benefits to patients may be rather small, even after a great deal of time and effort have been invested in memory training.[9] To deal with the issue, tailor-made therapy has been proposed to meet each patient's specific needs (e.g. to put names to faces of business associates).[10] Tailor-made therapy needs to be conducted in a manner that is most consistent with the patient's wishes; thus, the intervention programs should not be fixed, but improved to fit the current functioning of the patient and their particular situation.

## APPROACHES TO THE BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA

The AAGP model recommends non-pharmacological treatment as the first-line management strategy for behavioral and psychological symptoms of dementia (BPSD),[1] and positive evidence has been accumulated regarding non-pharmacological approaches.[11,12] Interventions for BPSD have focused on the patients themselves. However, BPSD can result from an interaction between the patients and their caregivers, including families.[13] A discrepancy between a patient's capabilities and the demands of his/her caregivers may trigger BPSD. Changes in caregivers' attitudes towards patients can ameliorate BPSD; thus, there is a strong need for caregiver education.[14–16] The AAGP states that caregivers' behavior is the most effective therapy, the benefits of which could last for months for neuropsychiatric symptoms such as agitation, aggression, delusions, hallucinations, repetitive vocalizations, and wandering.[1] Conversely, BPSD has a significant impact on caregivers' burden and stress.[17,18] Thus, caregivers, especially families, also require counseling in addition to education, and the quality of life (QOL) of families is considered as main the outcome in addition to the QOL of patients.[14–16]

Consideration of patients' emotion, the concept of tailor-made therapy, and family education and care are the important issues common to non-pharmacological approaches regardless of differences in aims and techniques. Thus far, research has focused on categorizing approaches and evaluating the efficacy of each approach. However, Cochrane Reviews on non-pharmacological interventions have highlighted the insufficiency of the available evidence.[19–22] It should be necessary to change the strategy in considering non-pharmacological interventions as follows

## BRAIN-ACTIVATING REHABILITATION

The essence of non-pharmacological intervention is intersubjectivity among patients, families, and therapists, with each situation being unique. This is an

**Table 1** Principles of brain-activating rehabilitation for dementia

1. Enjoyable and comfortable activities in an accepting atmosphere
2. Activities associated with empathetic two-way communication between therapists and patients, as well as between patients
3. Therapists should praise patients to enhance their motivation
4. Therapists should try to offer each patient some social role that takes advantage of his/her remaining abilities
5. Errorless learning for a pleasant atmosphere and to maintain patients' dignity

intrinsic difference between non-pharmacological and pharmacological interventions, in which study designs are strictly regulated. To obtain good results with non-pharmacological therapy, the core is not 'what' approach is taken but 'how' the therapists communicate with their patients. The therapeutic effects of non-pharmacological intervention can be highly influenced by therapists' attitudes, therefore we propose new therapeutic principles for non-pharmacological intervention (i.e. BAR).

## Criteria and principles of BAR

The five principles of BAR are given in Table 1. Any approaches associated with these five principles are considered to be BAR.

### *Activities should be enjoyable and comfortable, to make the patients–therapist interaction as pleasant as possible*

A happy feeling accompanied by a smile motivates patients. A comfortable and pleasant atmosphere is important because their lives are filled with unpleasant things due to their cognitive deficits. Activities with errorless learning are conducive to a pleasant atmosphere and to maintain a patient's dignity. A positive emotion presumably activates brain areas related to reward, which plays a critical role in motivation.[23] The dopamine system is an essential component of the brain reward circuitry.[24–27] The release of dopamine is stimulated by happy feelings and this release enhances motivation; dopamine release is not evoked by a negative mood.[28,29]

Happy feelings could relieve patients' relentless stress. Chronic exposure to stress hormones has an impact on brain structures. Animal studies have revealed that, particularly in old age, the hippocampus is highly vulnerable to the effects of the stress hormone glucocorticoid.[30] Regarding humans, a longitudinal study reported that basal glucocorticoid levels were higher in AD patients than in a control group,[31] with the magnitude of the increase in glucocorticoid levels strongly correlated with hippocampal atrophy and memory deficits.[32] In addition to the hippocampus, the frontal lobe is sensitive to glucocorticoid in aged humans.[33] Pleasant activities relieve patients' relentless stress, even if only during the therapy sessions.

### *Activities should be associated with two-way communication between the therapist and patient, as well as between patients*

Because of memory deficits and disorientation, AD patients suffer from discommunication with others even from the early stages of the disease. Communicating with them while taking into consideration their feelings makes them feel relieved.

For AD patients, the importance of empathetic non-verbal communication increases with the progression of the disease because it becomes more difficult to verbalize what they think and feel due to the amnesic and transcortical sensory aphasia. Patients with AD enjoy talking together, but what they say is not always comprehensible. For them, the purpose of communication is not to get information, but to enjoy exchanges of affection and empathy. Such emotional empathy exchange enhances relationships between therapists and patients because patients feel accepted and understood.

Therapists' smiles could be a pleasant stimulus for patients. The perception of others' smiles results in spontaneous activation of homologous muscles related to smiling in the observer; the mirror neuron system is the physiological basis for this phenomenon.[34] Then, a happy feeling is evoked by afferent feedback from the neural structures involved in the facial movement (facial feedback hypothesis[35]). In this manner, a happy feeling is evoked as an automatic reaction to seeing others smile; thus, therapists' smiles can make patients feel happy.

According to the Functional Assessment Staging of Alzheimer Disease (FAST),[36] the ability to smile at others (e.g. families and caregivers) remains even at Stage 7e (advanced stage), just before consciousness is lost. Patients with AD lose function in reverse order of development after birth.[36] At the developmental stage, a social smile is acquired at around 4 months of age, after the disappearance of the neonatal smile;

infants smile in response to a caregivers' smiles (in most cases, mothers' smiles). This could be the primary intersubjective communication by which positive feelings are shared. Stern defines such affective interactions as 'mirroring' or 'empathetic responsiveness'.[37] Thus, an exchange of smiles is effective, even for patients at advanced stages.

Regarding empathy, the validation method[38] is useful. The therapists/caregivers should pay close attention to recognize and confirm patients' emotions. For example, therapists/caregivers should not point out a patient's disorientation; a patient's self-esteem is restored in the context of the 'reality' in which they perceive themselves to be in.

### *Therapists should praise patients and recognize their individuality*

Being publicly praised and appreciated is a typical social reward. Social rewards also recruit the dopaminergic reward system and stimulate motivation.[39–41] For demented patients, a series of failures may provoke reproach from families or caregivers and so these patients are rarely praised in daily living. Therefore, public praise during rehabilitation sessions may enhance patients' motivation and restore their self esteem. Therapists should help patients regain their self-confidence, despite their failures. Self-efficacy is the belief that one is capable of achieving certain goals, regardless of whether the belief is true or not.[42] One of the components affecting self-efficacy is social persuasion (i.e. praise and encouragement). In the phase of learning or training in some skills, errorless learning[6,7] is efficient.

As mentioned above in 'approaches to cognitive symptoms', a patient's mood may be lowered by 'excess disability'.[43] In constrast, the experience of being praised could be a pump-priming effect to lift the patient from a vicious cycle of failure and 'excess disability' to a virtuous cycle of willingness and the manifestation of potential capacity.

### *Patients should play a social role*

The loss of their own role increases a patient's feeling of alienation, which drives demented patients to withdraw from social life. Social roles could help patients confirm their identity and regain their dignity. Thus, therapists should pay attention to what each patient is good at, and attach meaning and significance to whatever he/she can do (e.g. to sing a song to please other participants; to applaud performers etc.). By acting out social roles, patients may start to care about each other and become aware that they are appreciated by doing what they can for others. As such, social contact has been proven to reduce the risk of dementia.[44–46]

## An example of a BAR program: Activity reminiscence therapy

We will explain how the principles of BAR are realized with an example of activity reminiscence therapy. Activity reminiscence therapy is a therapeutic method that combines reminiscence and activity. In ordinary reminiscence therapy,[47] elderly people talk about their memories and experiences, which the therapists listen to attentively with an empathetic attitude. In activity reminiscence therapy based on BAR principles, the patients teach therapists or caregivers how to use old-style tools that are familiar to them because they used such tools in their childhood or as housewives (Fig. 1).

The advantage of this method is the 'role-reversal'; the patients are teaching the therapists or caregivers who help them in daily living (the fourth principle). Patients may feel timid or even inferior to the therapists or caregivers in daily living; thus, this sort of role-reversal helps them regain their self-confidence. Through this process, patients recover their sense of social function to pass on knowledge to younger generations. Because of this role-reversal, the patients may enjoy playing the leading role in the therapy (the first principle) and the therapists can praise the patients naturally (the third principle). Regarding the second principle of two-way communication, therapist–patient and patient–patient communication becomes much smoother with tools. Therapists should accept and share the world of the patients, regardless of whether it is 'true' or not. Conversation is based on memories; activities to use old-style tools recruit procedural memories, which remain after the loss of episodic memory.[48] Thus, it is expected that participants will enjoy conversations.

## Effects of BAR

### *Effects on cognitive ability*

Although BAR does not directly focus on cognitive enhancement as such, it is naturally expected that enhanced motivation will lead to improved cognitive


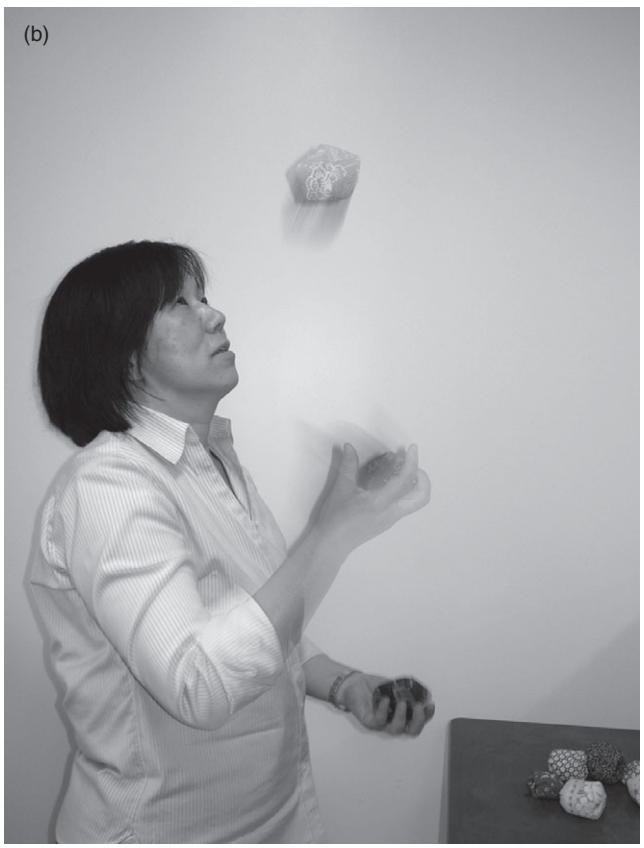


**Figure 1** Activity reminiscence therapy. (a) Washing sheets using a washboard. Before electric washing machines became common, housewives did the laundry using washboards and basins. However, the younger generations rarely use washboards. Being appreciated and praised, Alzheimer's disease (AD) patients really enjoy their role of teaching and passing on their knowledge to younger generations. (b) Beanbag juggling: A beanbag is a palm-sized sack with beans inside, played with by tossing and catching (i.e. 'beanbag juggling'). Concerning the physical aspects of this activity, beanbag juggling requires rhythmic visuomotor coordination. Because the procedural memories remain robust, AD patients enjoy beanbag juggling with younger staff. Emotion-based communication over a game is enjoyable even for participants with impaired verbal skills.

ability. One of the key perspectives considering approaches to dementia is that the cognitive status does not necessarily correspond to the degree of pathological lesions in the brain. Regarding the brain's resistance to neuropathological damage, the 'cognitive reserve hypothesis' has been proposed, as described below.

The cognitive reserve refers to the observation that the degree of brain pathology or brain damage does not directly explain the clinical manifestation or cognitive performance of patients. Thus, people with a greater cognitive reserve are able to withstand a greater pathological AD burden without becoming demented by adopting alternative cognitive strategies and/or recruiting compensatory brain networks.[49–54] Increasing evidence indicates the presence of plastic changes in the synaptic efficacy in mature brains, which could be the physiological underpinning of this phenomenon.[55] A good example of 'the cognitive reserve' is the Nun study,[56] which reported non-linear associations between AD pathology in the postmortem brain and cognitive status in participants. Some participants in the study were cognitively intact, although their brains fulfilled the criteria for AD pathology. In a recent community-based study, minimal to moderate AD pathology was found in most brains of older people without dementia who were 80 years or older.[57] Enhanced cognitive ability was reported after activity reminiscence therapy intervention based on BAR principles.[58] The improvement was observed in the overall scores for immediate and delayed recall on the Wechsler Memory Scale-Revised after 1-h interventions once a week for 12 weeks.

### *Effects on BPSD*

Behavioral and psychological symptoms of dementia often result from the relationship between patients

and their families. Patients with AD tend to overestimate their cognitive and functional abilities compared with what their families report.[59] Because of this discrepancy in evaluation of cognitive ability between patients and families, the patients may feel that they are not understood and accepted by their families, which may accelerate BPSD. In such cases, we recommend that families participate in the therapy session. By participating in the therapy, the families come to understand the underlying reasons for the patient's behavior.

### *Effects on daily living*

Improvements in the activities of daily living (ADL) are also seen after BAR. Deficits in instrumental ADL are caused by a decline in cognitive functions such as executive function. Although disuse syndrome can account for a considerable part of the deficits in basic ADL, there remains room for beneficial effects following intervention with BAR. Patients may lose motivation due to numerous failures and reproach from their families', which suppresses brain function and accelerates disuse syndrome. Cooperation with families is indispensable to maintain enhanced motivation induced by BAR in daily living.

### *Family care and the QOL of both patients and their caregivers*

The final effect of BAR is to make patients feel happy in their daily lives. Thus, it is crucial that patients' families understand the difficulties of living with dementia and learn how to help patients feel happy or smile by participating in BAR. At the same time, families also suffer with patients; thus, therapists should also praise and appreciate the efforts of the families. The BPSD service pack of the International Psychogeriatric Association (IPA) recommends that families and/or caregivers reward themselves for achieving certain goals to ameliorate BPSD.[60] It is desirable that therapists' attitudes towards families become their reward.

## EVIDENCE FOR THE EFFICACY OF NON-PHARMACOLOGICAL TREATMENT

The efficacy of BAR should be verified on the basis of evidence. The protocol of any study investigating the efficacy of non-pharmacological treatment should reflect the characteristics of these interventions (i.e. intersubjectivity).

With regard to the outcomes, the broadening of outcome measures, including well-being, mood, and QOL, is desirable to consider the impact of non-pharmacological treatments on families and other caregivers.

For comparisons and meta-analyses among studies, it is desirable to use standardized outcome measures and protocols. In 2008, a European consensus on outcome measures for psychosocial intervention research in dementia care was published to enable meaningful comparisons between different studies and interventions.[61] We hope that the Japanese Psychogeriatric Society promotes the establishment of consensus guidelines for non-pharmacological interventions.

## ACKNOWLEDGMENTS

The research into BAR by the authors was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports, Culture and Technology of Japan (18650196) and a Research Grant for Longevity Sciences (21A-12) from the Ministry of Health, Labour and Welfare. The authors thank R. Shinohara and Y. Tsunoda (Gunma University, Maebashi, Japan) for technical assistance.

## REFERENCES

1 Lyketsos CG, Colenda CC, Beck C *et al*. Task Force of American Association for Geriatric Psychiatry. Position statement of the American Association for Geriatric Psychiatry regarding principles of care for patients with dementia resulting from Alzheimer disease. *Am J Geriatr Psychiatry* 2006; **14**: 561–572.
2 Dietch JT, Hewett LJ, Jones S. Adverse effects of reality orientation. *J Am Geriatr Soc* 1989; **37**: 974–976.
3 Woods B. Reality orientation: A welcome return? *Age Ageing* 2002; **31**: 155–156.
4 Small GW, Rabins PV, Barry PP *et al*. Diagnosis and treatment of Alzheimer disease and related disorders: Consensus statement of the American Association for Geriatric Psychiatry, the Alzheimer's Association and the American Geriatric Society. *J Am Med Assoc* 1997; **278**: 1363–1371.
5 Kitwood T. *Dementia Reconsidered: The Person Comes First*. Buckingham: Open University Press, 1997.
6 Page M, Wilson BA, Shiel A, Carter G, Norris D. What is the locus of the errorless-learning advantage? *Neuropsychologia* 2006; **44**: 90–100.
7 Clare L, Wilson BA, Carter G, Breen K, Gosses A, Hodges JR. Intervening with everyday memory problems in Dementia of Alzheimer type: An errorless learning condition approach. *J Clin Exp Neuropsychol* 2000; **22**: 132–146.
8 Baddeley A, Wilson BA. When implicit learning fails: Amnesia and the problem of error elimination. *Neuropsychologia* 1994; **32**: 53–68.

9 Cahn-Weiner DA, Malloy PF, Rebok GW, Ott BR. Results of a randomized placebo-controlled study of memory training for mildly impaired Alzheimer's disease patients. *Appl Neuropsychol* 2003; **10**: 215–223.
10 Clare L, Wilson BA, Carter G, Roth I, Hodges JR. Relearning face–name associations in early Alzheimer's disease. *Neuropsychology* 2002; **16**: 538–547.
11 Ayalon L, Gum AM, Feliciano L, Areán PA. Effectiveness of nonpharmacological interventions for the management of neuropsychiatric symptoms in patients with dementia: A systematic review. *Arch Intern Med* 2006; **166**: 2182–2188.
12 Ballard CG, Gauthier S, Cummings JL *et al*. Management of agitation and aggression associated with Alzheimer disease. *Nat Rev Neurol* 2009; **5**: 245–255.
13 Brodaty H, Finkel S. *International Psychogeriatric Association: Introduction to Behavioral and Psychological Symptoms of Dementia (Revised)*. Available from: http://www.ipa-online.org/ipaonlinev3/ipaprograms/bpsdarchives/bpsdrev/toc.asp [Accessed 17 June 2010].
14 Gitlin LN, Winter L, Dennis MP, Hauck WW. A nonpharmacological intervention to manage behavioral and psychological symptoms of dementia and reduce caregiver distress: Design and methods of project ACT3. *Clin Interv Aging* 2007; **2**: 695–703.
15 Gitlin LN, Winter L, Vause Earland T *et al*. The Tailored Activity Program to reduce behavioral symptoms in individuals with dementia: Feasibility, acceptability, and replication potential. *Gerontologist* 2009; **49**: 428–439.
16 Woods RT, Bruce E, Edwards RT *et al*. Reminiscence groups for people with dementia and their family carers: Pragmatic eight-centre randomised trial of joint reminiscence and maintenance versus usual treatment: A protocol. *Trials* 2009; **10**: 64.
17 Buhr GT, White HK. Difficult behaviors in long-term care patients with dementia. *J Am Med Dir Assoc* 2006; **7**: 180–192.
18 Fauth EB, Zarit SH, Femia EE, Hofer SM, Stephens MA. Behavioral and psychological symptoms of dementia and caregivers' stress appraisals: Intra-individual stability and change over short-term observations. *Aging Ment Health* 2006; **10**: 563–573.
19 Woods B, Spector A, Jones C, Orrell M, Davies S. Reminiscence therapy for dementia. *Cochrane Database Syst Rev* 2005; **2**: CD001120.
20 Neal M, Briggs M. Validation therapy for dementia. *Cochrane Database Syst Rev* 2003; **3**: CD001394.
21 Clare L, Woods RT, Moniz Cook ED, Orrell M, Spector A. Cognitive rehabilitation and cognitive training for early-stage Alzheimer's disease and vascular dementia. *Cochrane Database Syst Rev* 2003; **4**: CD003260.
22 Forbes D, Forbes S, Morgan DG, Markle-Reid M, Wood J, Culum I. Physical activity programs for persons with dementia. *Cochrane Database Syst Rev* 2008; **3**: CD006489.
23 Berridge KC. Pleasures of the brain. *Brain Cogn* 2003; **52**: 106–128.
24 Schultz W, Tremblay L, Hollerman JR. Reward processing in primate orbitofrontal cortex and basal ganglia. *Cerebral Cortex* 2000; **10**: 272–284.
25 Wise RA. Brain reward circuitry: Insights from unsensed incentives. *Neuron* 2002; **36**: 229–240.
26 Berridge KC. The debate over dopamine's role in reward: The case for incentive salience. *Psychopharmacology* 2007; **191**: 391–431.
27 Delgado MR. Reward-related responses in the human striatum. *Ann N Y Acad Sci* 2007; **1104**: 70–88.
28 Burgdorf J, Panksepp J. The neurobiology of positive emotions. *Neurosci Biobehav Rev* 2006; **30**: 173–187.
29 Mitchell RL, Phillips LH. The psychological, neurochemical and functional neuroanatomical mediators of the effects of positive and negative mood on executive functions. *Neuropsychologia* 2007; **45**: 617–629.
30 Lupien SJ, de Leon M, de Santi *et al*. The effects of stress and stress hormones on human cognition: Implications for the field of brain and cognition. *Brain Cogn* 2007; **65**: 209–237.
31 Giubilei F, Patacchioli FR, Antonini G *et al*. Altered circadian cortisol secretion in Alzheimer's disease: Clinical and neuroradiological aspects. *J Neurosci Res* 2001; **66**: 262–265.
32 Lupien SJ, Maheu F, Tu M, Fiocco A, Schramek TE. Cortisol levels during human aging predict hippocampal atrophy and memory deficits. *Nat Neurosci* 1998; **1**: 69–73.
33 Dai J, Buijs R, Swaab D. Glucocorticoid hormone (cortisol) affects axonal transport in human cortex neurons but shows resistance in Alzheimer's disease. *Br J Pharmacol* 2004; **143**: 606–610.
34 Gallese V. Before and below 'theory of mind': Embodied simulation and the neural correlates of social cognition. *Philos Trans R Soc Lond B Biol Sci* 2007; **362**: 659–669.
35 Tomkins SS. *Affect Imagery and Consciousness: Vol. 1. The Positive Affects*. New York: Springer, 1962.
36 Reisberg B. Dementia: A systematic approach to identifying reversible causes. *Geriatrics* 1986; **41**: 30–46.
37 Stern D. *The Interpersonal World of the Infant*. New York: Basic Books, 1985.
38 Feil N. *The Validation Breakthrough: Simple Techniques for Communicating with People with 'Alzheimer's-Type Dementia'*. Baltimore, MD: Health Promotion Press, 1993.
39 Rilling J, Gutman D, Zeh T, Pagnoni G, Berns G, Kilts C. A neural basis for social cooperation. *Neuron* 2002; **35**: 395–405.
40 Izuma K, Saito DN, Sadato N. Processing of social and monetary rewards in the human striatum. *Neuron* 2008; **58**: 284–294.
41 Zink CF, Tong Y, Chen Q, Bassett DS, Stein JL, Meyer-Lindenberg A. Know your place: Neural processing of social hierarchy in humans. *Neuron* 2008; **58**: 273–283.
42 Bandura A. Toward a unifying theory of behavioral change. *Psychol Rev* 1977; **84**: 191–215.
43 Reifler BV, Larson E. Excess disability in dementia of the Alzheimer's type. In: Light E, Lebowitz BD eds. *Alzheimer's Disease Treatment and Family Stress*. New York: Hemisphere, 1990; 363–382.
44 Fratiglioni L, Wang HX, Ericsson K, Maytan M, Winblad B *et al*. Influence of social network on occurrence of dementia: A community-based longitudinal study. *Lancet* 2000; **355**: 1315–1319.
45 Bennett DA, Schneider JA, Tang Y, Arnold SE, Wilson RS. The effect of social networks on the relation between Alzheimer's disease pathology and level of cognitive function in old people: A longitudinal cohort study. *Lancet Neurol* 2006; **5**: 406–412.
46 Carlson MC, Helms MJ, Steffens DC, Burke JR, Potter GG, Plassman BL. Midlife activity predicts risk of dementia in older male twin pairs. *Alzheimers Dement* 2008; **4**: 324–331.
47 Butler RN. The life review: An interpretation of reminiscence in the aged. *Psychiatry* 1963; **26**: 65–76.
48 Ribot T. *Les maladies de la mémoire [Disease of Memory]*. Paris: Encyclopédie psychologique, 1881.
49 Katzman R. Education and the prevalence of dementia and Alzheimer's disease. *Neurology* 1993; **43**: 13–20.

50 Bennett DA, Wilson RS, Schneider JA *et al*. Education modifies the relation of AD pathology to level of cognitive function in older persons. *Neurology* 2003; **60**: 1909–1915.
51 Whalley LJ, Deary IJ, Appleton CL, Starr JM. Cognitive reserve and the neurobiology of cognitive aging. *Ageing Res Rev* 2004; **3**: 369–382.
52 Mortimer JA, Borenstein AR, Gosche KM, Snowdon DA. Very early detection of Alzheimer neuropathology and the role of brain reserve in modifying its clinical expression. *J Geriatr Psychiatry Neurol* 2005; **18**: 218–223.
53 Roe CM, Xiong C, Grant E, Miller JP, Morris JC. Education and reported onset of symptoms among individuals with Alzheimer disease. *Arch Neurol* 2008; **65**: 108–111.
54 Roe CM, Mintun MA, D'Angelo G, Xiong C, Grant EA, Morris JC. Alzheimer disease and cognitive reserve: Variation of education effect with carbon 11-labeled Pittsburgh Compound B uptake. *Arch Neurol* 2008; **65**: 1467–1471.
55 Eriksson PS, Perfilieva E, Björk-Eriksson T *et al*. Neurogenesis in the adult human hippocampus. *Nat Med* 1998; **4**: 1313–1317.
56 Snowdon DA. Nun Study. Healthy aging and dementia: Findings from the Nun Study. *Ann Intern Med* 2003; **139**: 450–454.
57 Bennett DA, Schneider JA, Arvanitakis Z *et al*. Neuropathology of older persons without cognitive impairment from two community-based studies. *Neurology* 2006; **66**: 1837–1844.
58 Yamagami T, Oosawa M, Ito S *et al*. Effect of activity reminiscence therapy as brain-activating rehabilitation for elderly people with and without dementia. *Psychogriatrics* 2007; **7**: 69–75.
59 Farias ST, Mungas D, Jagust W. Degree of discrepancy between self and other-reported everyday functioning by cognitive status: Dementia, mild cognitive impairment, and healthy elders. *Int J Geriatr Psychiatry* 2005; **20**: 827–834.
60 The International Psychogeriatric Association (IPA). Behavioral and Psychological Symptoms of Dementia (BPSD) Educational Pack. Available from: http://www.ipa-online.org/ipaonlinev3/ipaprograms/bpsdarchives/bpsdrev/1BPSDfinal.pdf [Accessed 17 June 2010].
61 Moniz-Cook E, Vernooij-Dassen M, Woods R *et al*. INTERDEM group. A European consensus on outcome measures for psychosocial intervention research in dementia care. *Aging Ment Health* 2008; **12**: 14–29.