Psychiatry Research 242 (2016) 331–335

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Fighting apathy in Alzheimer's dementia: A brief emotional-based intervention

Alberto Di Domenico [a], Rocco Palumbo [a,b,*], Beth Fairfield [a], Nicola Mammarella [a]

[a] Department of Psychological Science, University of Chieti, Italy
[b] Schepens Eye Research Institute, Harvard Medical School, 20 Staniford St, Boston, 02114 MA, USA

ARTICLE INFO

Article history:
Received 10 March 2016
Received in revised form
31 May 2016
Accepted 10 June 2016
Available online 11 June 2016

Keywords:
Apathy
Dementia
Emotional conditioning

ABSTRACT

Lack of motivation, or apathy, is a clinically significant feature among dementia patients. The current study aimed to assess the effectiveness of a brief emotional shaping intervention developed to reduce apathy and increase willingness-to-do in Alzheimer's Dementia patients. To this end, 26 Alzheimer patients diagnosed with apathy according to the Apathy Evaluation Scale (AES, Marin et al.,1991) and 26 healthy older controls performed an emotional shaping task intended to unconsciously foster willingness-to-do. Participants were randomly assigned to either a positive or a neutral conditioning situation. Results showed how the positively conditioned group was associated with improved willingness-to-do in both patients and controls compared to the neutrally conditioned group. Our findings suggest that unconscious emotional processing can be used to treat apathy symptoms and increase willingness-to-do in Alzheimer's Dementia.

© 2016 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Lack of motivation, or apathy, underlies many of the difficulties encountered by individuals across the lifespan and in different contexts (school, work etc.) and is common to different pathological conditions such as dementia and depression (for reviews see Tagariello et al., 2009; Levy, 2012). In particular, lack of motivation is a very common symptom in Alzheimer's Dementia (AD, e.g., Esposito et al., 2010; Tunnard et al., 2011; Theleritis et al., 2014). This lack of or reduced motivation towards initiating goal-directed tasks can have relevant consequences on everyday life of AD patients and often contributes to caregivers' distress. In addition, lack of motivation may also predict progression from mild to more severe cognitive decline conditions (e.g., Richard et al., 2012; Fairfield et al., 2015a; Di Domenico et al., 2014), making it an important index of patient wellbeing. Several studies, in fact, (e.g., Holthoff et al., 2005; Alexopoulos et al., 2013) have underlined the importance of distinguishing between AD patients with and without apathy (e.g., Esposito et al., 2010) and recent studies (e.g., Forstmeier et al., 2012) showed how older adults with high levels of motivation reserve are less likely to develop severe cognitive decline.

Accordingly, patient motivation has also become a central issue in cognitive rehabilitation literature (e.g., Choi and Twamley, 2013, Fairfield et al., 2013; Di Domenico et al., 2015; Altamura et al., 2013) linked to the fact that AD patients often have difficulty adhering to treatments and show lower levels of engagement in activities (Mammarella et al., 2012a, 2013a).

Various cognitive programs that foster goal-oriented behavior in dementia already exist (e.g., Clare et al., 2010). For example, CST, or 'Cognitive Stimulation Therapy', is a brief treatment designed for people with mild to moderate dementia. This therapy aims to actively stimulate and engage people with dementia, whilst providing an optimal learning environment and the social benefits of a group and results of CST appear to be comparable to those reported with currently available anti-dementia drugs (Capotosto et al. 2016; Spector et al., 2010; Orgeta et al., 2014). However, as far as we know, none of these has combined cross-domain techniques involving conditioning and emotional factors. In a classical emotional shaping paradigm, a conditioned stimulus (CS) is typically paired with an unconditioned stimulus (US) in order to change the valence of the CS. Basically, by positively charging the US, the CS valence is expected to move towards the positive pole (for a review see De Houwer et al., 2001; Stella et al., 2014). Interestingly, a series of studies has shown that emotional shaping may occur even without conscious awareness (e.g., Dijksterhuis et al., 2005; Fairfield et al., 2015b; Mammarella et al., 2012b, 2013b, 2016; Altamura et al., 2016), that is, when stimuli are subliminally presented. This is extremely relevant to the study of motivational processes in dementia as numerous studies have shown that automatic unconscious emotional processing is preserved in pathological aging and AD with respect to conscious and more

* Corresponding author at: Schepens Eye Research Institute, Harvard Medical School, 20 Staniford St, Boston, 02114, MA, USA.
E-mail address: rocco_palumbo@meei.harvard.edu (R. Palumbo).

http://dx.doi.org/10.1016/j.psychres.2016.06.009
0165-1781/© 2016 Elsevier Ireland Ltd. All rights reserved.

deliberate processes such as reappraisal (e.g., Henry et al., 2009; Padovan et al., 2002; Mammarella et al., 2015).

Nonetheless, outcomes of non-pharmacological interventions are rare, while evidence for the efficacy of pharmacological treatment of apathy is inconsistent (see Yuen et al., 2014). In this study, we aim to investigate whether a classical behavioral technique like conditioning can be used to develop new interventions to tackle specific aspects of apathy and/or to enhance levels of initiative in a group of Alzheimer patients with apathy. Subsequently, the focus throughout the paper will be on the lack of motivation to initiate a goal-directed activity (often cited among the peculiar symptoms of apathy, e.g., Levy, 2012).

Here, we carried out a proof-of-concept study in order to develop and test the efficacy of a new apathy treatment in AD. Basically, we investigated whether unconsciously shaping the emotional content of an activity or goal-directed behavior can modify the motivational level associated with that activity in AD patients.

To this end, we adopted a procedure already used by Custers and Aarts (2005) who repeatedly found that linking behavioral states to positive emotions automatically increased participants' desire to attain these states. We tested two primary hypotheses. First, we expected both patients and healthy controls to benefit from a positive valence unconscious shaping technique compared to a neutral or control condition. This benefit is indexed by a higher number of positive responses ("yes" responses) when participants are asked whether they are willing to initiate an activity. Second, if we can treat and reduce a motivational states via unconsciously conditioning the valence of goal-directed behavior, we expected AD patients to reach the same levels of motivation as the baseline in healthy controls.

2. Method

2.1. Participants

The study was conducted at the Geropsychology lab, Chieti, Italy over a two-year interval. Referrals for AD were obtained from clinicians (e.g., physicians or neurologists) in affiliated outpatient clinics. In particular, all patients were clinically diagnosed with probable AD based on NINCDS-ADRDA criteria (McKhann et al., 1984), following procedures reported by Bennett et al. (2006). Healthy older adults were recruited on a volunteer basis from Third-Age Universities in Chieti and surroundings. We chose to use healthy older adults instead of AD patients without apathy as our control group because in this study we used a modified version of the original paradigm used by Custers and Aarts (2005). Therefore, we were interested in examining whether the modified increased "motivation to do" with healthy older adults as well. Apathy AD patients were selected from a group of 60 CE patients. In order to select apathy AD participants, we screened the group of 60 CE patients with the Geriatric Depression Scale (GDS, Yesavage, 1988) to for depression. The GDS is a 30-item self-report assessment that asks for a "yes" or "no" response. The grid sets a range of 0–9 as "normal", 10–19 as "mildly depressed", and 20–30 as "severely depressed". To screen for apathy, we used the Apathy Evaluation Scale (AES, Marin et al.,1991). The AES is an 18-item self-report assessment that uses a 4-point Likert-type scale (from "not at all" to "a lot"). High AES scores indicate more apathy. Inclusion criteria for the apathy group were: (1) a score higher than 45 on the AES and (2) absence of major depressive symptoms as measured by the GDS. 26 apathy AD patients corresponded to inclusion criteria.

From a larger group of 60 CE patients, we recruited 26 apathy AD patients. We also recruited 26 healthy controls. As shown in Table 1, AD patients performed worse than control participants on all tests of cognitive functioning. Participants were also screened for depression to ensure that depressive conditions would not affect participant performance and apathy. We used the Geriatric Depression Scale (GDS, Yesavage, 1988) to screen for depression. The GDS is a 30-item self-report assessment that asks for a "yes" or "no" response. The grid sets a range of 0–9 as "normal", 10–19 as "mildly depressed", and 20–30 as "severely depressed". To screen for apathy, we used the Apathy Evaluation Scale (AES, Marin et al.,1991). The AES is an 18-item self-report assessment that uses a 4-point Likert-type scale (from "not at all" to "a lot"). High AES scores indicate more apathy. Inclusion criteria for the apathy group were: (1) a score higher than 45 on the AES and (2) absence of major depressive symptoms as measured by the GDS. Inclusion criteria for healthy controls were: (1) a score lower than 30 on the AES and (2) absence of major depressive symptoms as measured by the GDS. Participants were excluded if they had a neurologic disorder (other than Alzheimer's dementia for the patient groups), a psychiatric disorder (e.g., major depression or anxiety), uncorrected severe vision or hearing impairments, a history of learning disability, impaired basic attention or visuospatial abilities, or impaired comprehension. The two groups were well-matched demographically. There were no significant between-group differences in age, gender, education, and depression. Finally, participants were not concurrently involved in any cognitive or, generally speaking, psychosocial rehabilitative interventions at any time during the study. The Departmental ethics committee approved this study, and written informed consent was obtained from all participants or their caregivers (i.e., legally authorized representatives), where appropriate. All procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Table 1
Demographics by Group.

	AD patients		Controls	
Characteristic/task	M	SD	M	SD
Age	70.46	2.63	70.88	2.94
Gender	(12 M, 14 F)		(12 M, 14 F)	
Education	10.92	4.15	10.54	3.66
MMSE (of 30)*	19.35	1.94	26.77	1.45
Phonemic Word Fluency (of 34)*	7.22	1.08	11.53	1.42
GDS	4.42	2.64	4.00	2.62
AES*	53.46	2.58	23.96	2.27

Note. MMSE=Mini Mental State Exam (Folstein et al., 1975); Word Fluency from Mondini et al. (2011); GDS=Geriatric Depression Scale (Yesavage, 1988); AES=Apathy Evaluation Scale (Marin et al.,1991).

* $p < 0.01$.

2.2. Design

Following referral and screening, participants were assigned to either the AD patients with apathy or the healthy control group. In addition, for both groups, half of the participants were assigned to the positively valenced condition and the other half to the neutral control condition. Participants were randomized to positive or neutral conditions and were blind to the assigned condition.

Participants completed a range of psychological measures first and subsequently took part in the emotional experimental intervention. All AD patients with apathy were able to complete the task since the experimental intervention per sé was very brief. This was a mixed design with a 2 (Conditioned Stimulus: Nonword vs. Activity) within-subject × 2 (Unconditioned Stimulus: Neutral vs. Positive) × 2 (Group: AD patients vs. Controls) between-subjects manipulation.

2.3. Material and procedure

We conducted a pilot study before running the experiment in order to identify a series of neutral activities. In particular, we selected 24 neutral (M=5.15 on a 9-point scale from 1 absolutely negative to 9 absolutely positive) everyday activities (e.g., make a telephone call, put a pair of glasses on, fold a napkin, etc.) to serve as CS and then anagrammed the activities in order to obtain 24 nonwords that would also serve as CS. Furthermore, we selected 12 positive (M=8.11 on a 9-point scale) and 12 neutral (M =4.92) words from the Italian version of the Affective Norms for English Words (The adaptation of the Affective Norms for English Words (ANEW) for Italian, Montefinese et al., 2014). As for the English version, the Italian ANEW provides a set of normative emotional ratings for a large number of words in the Italian language in terms of pleasure, arousal, and dominance as well other three subjective psycholinguist indexes (familiarity, imaginability, and concreteness) and five objective psycholinguistic indexes (e.g., word frequency).

We presented the experimental emotional intervention on an 85-Hz computer screen. Each participant completed a total of 24 trials. 12 trials presented an activity as CS and the same activity at test, while the other half presented a non-word anagram of the activity as CS but the corresponding activity at test. Each activity was randomly presented as CS activity or CS non-word anagram across subjects.

In particular, each trial started with a fixation cross in the center of the screen for 500 ms. followed by a row of *X*s (pre-mask) that remained on the screen for 500 ms. After the pre-mask, the CS activity (e.g., fold a napkin) or a nonword anagram of an activity was presented for 23 ms. followed by another row of *X*s (postmask) for 100 ms. This was followed by the US (a neutral or a positive word) which remained on the screen for 150 ms. Finally, in the successive 23 ms interval either a dot appeared or the screen remained blank. After a delay of 2500 ms, an activity appeared and participants were asked to indicate whether they would like to engage in it or not by pressing a "yes" or "no" key. In addition, participants were instructed to note if a dot had appeared or not before pressing the "yes" or "no" key. The following trial started immediately after the participant's response was recorded. We maintained the temporal windows for the presentation of dots, CS and US as done in the original paradigm. At the end of the intervention session, participants indicated aloud how many dots they had seen. We included this secondary task in order to ensure that participants paid attention to the screen. Response time was self-paced. The whole study involved a single 40 min session that could be divided in two 20 min sessions if participants showed fatigue.

Before the experimental phase, participants competed a series of practice trials with anagrams as CS and neutral words as US stimuli until they fully understood the task. After completing the intervention, participants were thoroughly debriefed and we checked for awareness of the subliminally presented stimuli. All participants were unaware of the presentation of the activity words and of the true nature of the study.

3. Results

All data were analyzed with SPSS version 20 (SPSS Inc., USA). Analyses were conducted using ANOVAs, with Group (AD patients vs. Controls) and Unconditioned Stimulus (Neutral vs. Positive) as a between-subjects factor. Where necessary, post-hoc comparisons were conducted. Results are shown in Table 2.

The proportion of "yes" responses across the 12 wanting questions per CS condition (activity vs. nonword) was subjected to an analysis of variance (ANOVA), according to the design. We found a main effect of the Group, $F(1,48)=54.07$, $p<0.001$, $\eta_p^2=0.529$, since healthy controls showed a higher number of wanting responses compared to patients. We detected a main effect of CS, $F(1,48)=58.91$, $p<0.001$, $\eta_p^2=0.551$, because participants who received an activity as CS showed an increase in wanting compared to participants who were presented with nonwords as CSs. Finally, the ANOVA evidenced a main effect of US, $F(1,48)=11.58$, $p<0.01$, $\eta_p^2=0.194$, showing how participants exposed to positive USs showed a higher number of wanting responses compared with participants who were exposed to neutral USs. The absence of valence in the neutral word inhibits the formation of the motivational link that is instead, created between the positive stimulus and the activity. In fact, as stated, we believe that it is this orientation towards positive emotions that motivates an increase in the desire to engage in everyday activities.

Table 2
Mean scores (standard deviation in parentheses) for each Group according to the Conditioned. (Activity vs. Nonwords) and Unconditioned Stimulus (Positive vs. Neutral).

	AD patients		Controls	
	Positive	Neutral	Positive	Neutral
Activity	0.46 (0.14)	0.18 (0.09)	0.67 (0.16)	0.45 (0.14)
Nonwords	0.22 (0.13)	0.20 (0.07)	0.42 (0.15)	0.48 (0.13)

The interaction CS × US was also significant, $F(1,48)=85.4$, $p<0.001$, $\eta_p^2=0.64$ because when activities were presented as CSs, participants for whom these states were linked to positive USs reported that they wanted to attain those activities more than all other conditions (Tukey test, $p<0.001$). As expected, the three-way interaction was not significant, $F(1,48)=0.08$, $p=0.78$, $\eta_p^2=0.002$, due to the fact that positive words following activities increased motivation in both groups compared to neutral words (planned comparisons $p<0.001$). Noteworthy, the performance of patients with positive words on activities reached the level of performance of controls with neutral words on activities (planned comparisons, $p=0.44$).

4. Discussion

The current proof-of-concept study aimed to test the effectiveness of a new emotional shaping intervention as a brief treatment for apathy in dementia. To this end, we modified a paradigm developed by Custers and Aarts (2005) to include everyday activities and investigated whether apathy patients could be unconsciously conditioned to increase their willingness-to-do. Our findings suggest that our brief experimental intervention was effective in increasing patients' immediate motivation. In particular, the group of apathy patients who were positively conditioned showed a higher number of "yes" responses compared to the group of control patients. In addition, apathy patient motivation reached the level of healthy controls baseline motivation.

We also replicated the large advantage of activities as a conditioned stimuli compared to nonword anagrams, in line with Custers and Aarts (2005). This indicates that it is the activation of activity (rather than of nonsense material) associated with positive affect that instigates this activity automatically. That is, when an activity is linked to positive affect, this link unconsciously operates as motivation for willingness-to-do and the desire to engage in that activity.

Altogether, these results are relevant for two reasons. First, they showed that, differently from controlled and explicit emotional processing, unconscious emotional processing is preserved in

dementia and can be used to increase current motivational states. The implicit nature of this emotional association was guaranteed by the fact that participants were not informed about the true nature of the task, but they knew they were taking part in a study about attention. Moreover, we used a subliminal presentation of stimuli (emotional shaping). Both conditions reduced the intervention of demand characteristics and ruled out the possibility that the association between the activity and positive affect becoming explicit.

Second, results are crucial for the development of new rehabilitation programs since it is clear that cognitive functioning rehabilitation alone is not sufficient for functional improvement in dementia. Targeting motivational aspects before or together with cognitive processing may prove crucial in improving willingness-to-do and help delaying later deterioration stages. In fact, advantages of this conditioning with respect to other more classical interventions are brevity and the use of emotional stimuli to incur emotional shaping that can take place even without conscious awareness. Clinicians should be aware that lack of motivation, or apathy, is a clinically significant feature among dementia patients and that, although there are challenges in distinguishing apathy from depression in AD patients, attention needs to be focused on emotional shaping interventions that can modify patients willingness to do. Moreover, the clinical implications of reducing caregiver stress by increasing the desire to carry out everyday activities in AD patients can have effects on many social and economic implications.

Finally, there were several limitations to the current study. One is the effectiveness of our intervention in terms of long-term effects. We showed, in fact, that apathy patients increased their willingness to do during the current program. However, we do not know whether repetition and later assessments may detect long lasting benefits and even generalization. Moreover, in terms of sample size, the current study was also relatively modest with respect to typical cognitive program studies. Our sample size, however, reflected the difficulty in recruiting AD apathy patients with no history of depression. Also, it must be noted that although different studies have shown that apathy and depression are different constructs (e.g., Levy et al., 1998, Marin, 1991), the GDS (30 items version) is composed of at least 7/8 items that could refer to the loss of motivation toward activities and apathy (as example item 1,3,4,12,19,20,27). Thus, partial scores for items of GDS also may reflect apathy. Future studies need to consider this when distinguishing apathy and depression.

Moreover, in this intervention we used a single task with emotional stimuli, an emotional shaping task. Future studies need to investigate the use of other tasks with emotional stimuli as well and may benefit from incorporating long-term motivational assessments into this intervention and examine more deeply the different apathy factors that are best tackled by this type of treatment.

Another consideration pertains the fact that linking an activity to positive affect may increase people's wanting to attain the activity, but this does not necessarily correspond to actually executing the action. Only if people have the opportunity to accomplish their wanting, then they may engage in that activity. The association with positive affect signals that the activity is desired and worth pursuing but the emergence of an action depends on the situation and it may occur at different time lags. Further studies may help understanding whether Alzheimer's patients are capable of keeping in mind this association and work for execution at different time lags.

In sum, the current study is the first to demonstrate the effectiveness of an emotional shaping intervention for treating apathy in AD patients. We detected a significant improvement in the immediate level of willingness to do in the group of patients that were treated with positively charged emotional stimuli. We believe that lack of motivation is the crucial factor in mediating cognitive and everyday functioning in dementia, and deserve further investigation.

Acknowledgements

We thank all older participants and their caregivers for their participation.

References

Alexopoulos, G.S., Hoptman, M.J., Yuen, G., Kanellopoulos, D., Seirup, J.K., Lim, K.O., Gunning, F.M., 2013. Functional connectivity in apathy of late-life depression: a preliminary study. J. Affect. Disord. 149, 398–405. http://dx.doi.org/10.1016/j.jad.2012.11.023.

Altamura, M., Padalino, F.A., Mammarella, N., Fairfield, B., Balzotti, A., Di Domenico, A., Bellomo, A., 2013. Are all forms of feature binding disturbed in schizophrenia? evidence from a central vs. peripheral distinction in working memory. Psychiatry Res. 209 (1), 9–14. http://dx.doi.org/10.1016/j.psychres.2012.11.015.

Altamura, M., Padalino, F.A., Stella, E., Balzotti, A., Bellomo, A., Palumbo, R., Fairfield, B., 2016. Facial emotion recognition in bipolar disorder and healthy aging. J. Nerv. Ment. Dis. . http://dx.doi.org/10.1097/NMD.0000000000000453

Bennett, D.A., Schneider, J.A., Aggarwal, N.T., Arvanitakis, Z., Shah, R.C., Kelly, J.F., Wilson, R.S., 2006. Decision rules guiding the clinical diagnosis of Alzheimer's disease in two community based cohort studies compared to standard practice in a clinic-based cohort study. Neuroepidemiology 27, 169–176. http://dx.doi.org/10.1159/000096129.

Choi, J., Twamley, E.W., 2013. Cognitive rehabilitation therapies for Alzheimer's disease: a review of methods to improve treatment engagement and self-efficacy. Neuropsychol. Rev. 23, 48–62. http://dx.doi.org/10.1007/s11065-013-9227-4.

Clare, L., Linden, D.E., Woods, R.T., Whitaker, R., Evans, S.J., Parkinson, C.H., Rugg, M. D., 2010. Goal-oriented cognitive rehabilitation for people with early-stage Alzheimer disease: a single blind randomized controlled trial of clinical efficacy. Am. J. Geriatr. Psychiatry 18, 928–939. http://dx.doi.org/10.1097/JGP.0b013e3181d5792a.

Custers, R., Aarts, H., 2005. Positive affect as implicit motivator: on the nonconscious operation of behavioral goals. J. Personal. Soc. Psychol. 89, 129–142. http://dx.doi.org/10.1037/0022-3514.89.2.129.

De Houwer, J., Thomas, S., Baeyens, F., 2001. Association learning of likes and dislikes: a review of 25 years of research on human evaluative conditioning. Psychol. Bull. 127, 853–869. http://dx.doi.org/10.1037/0033–2909.127.6.853.

Di Domenico, A., Fairfield, B., Mammarella, N., 2014. Aging and others' pain processing: implications for hospitalization. Curr. Gerontol. Geriatr. Res. . http://dx.doi.org/10.1155/2014/737291

Di Domenico, A., Palumbo, R., Mammarella, N., Fairfield, B., 2015. Aging and emotional expressions: is there a positivity bias during dynamic emotion recognition? Front. Psychol. 6. http://dx.doi.org/10.3389/fpsyg.2015.01130.

Dijksterhuis, A., Aarts, H., Smith, P.K., 2005. The power of the subliminal: on subliminal persuasion and other potential applications. In: Hassin, R.R., Uleman, J. S., Bargh, J.A. (Eds.), The New Unconscious. Oxford University Press, New York, pp. 77–106.

Capotosto, E., Gardini, S., Faggian, S., Piras, F., Belacchi, C., Mantoan, V., Salvaiolo, E., Pradelli, S., Borella, E., 2016. Cognitive Stimulation Therapy in the Italian context: its efficacy in cognitive and non- cognitive measures in older adults with dementia. Int. J. Geriatr. Psychiatry http://dx.doi.org/10.1002/gps.4521.

Esposito, F., Rochat, L., Van der Linden, A.C.J., Lekeu, F., Quittre, A., Charnallet, A., Van der Linden, M., 2010. Apathy and executive dysfunction in Alzheimer disease. Alzheimer Dis. Assoc. Disord. 24, 131–137. http://dx.doi.org/10.1097/WAD.0b013e3181c9c168.

Fairfield, B., Mammarella, N., Di Domenico, A., 2013. Centenarians holy memory: is being positive enough? J. Gen. Psychol. 174 (1), 42–50. http://dx.doi.org/10.1080/00221325.2011.636399.

Fairfield, B., Mammarella, N., Di Domenico, A., 2015a. Motivated goal pursuit and working memory: are there age-related differences? Motiv. Emot. 39 (2), 201–215. http://dx.doi.org/10.1007/s11031-014-9428-z.

Fairfield, B., Mammarella, N., Di Domenico, A., Palumbo, R., 2015b. Running with emotion: when affective content hampers working memory performance. Int. J. Psychol. 50 (2), 161–164. http://dx.doi.org/10.1002/ijop.12101.

Folstein, M.F., Folstein, S.E., McHugh, P.R., 1975. Mini-mental state. A practical method for grading the cognitive state of patients for the clinician. J. Psychiatr. Res. 12 (3), 189–198. http://dx.doi.org/10.1016/0022-3956(75)90026-6.

Forstmeier, S., Maercker, A., Maier, W., van den Bussche, H., Riedel-Heller, S., Kaduszkiewic, H., Pentzek, M., Weyerer, S., Bickel, H., Tebarth, F., Luppa, M., Wollny, A., Wiese, B., Wagner, M., AgeCoDe Study Group, 2012. Motivational reserve: Motivation-related occupational abilities and risk of mild cognitive impairment and Alzheimer disease. Psychol. Aging 27, 353–363. http://dx.doi.org/10.1037/a0025117.

Henry, J.D., Rendell, P.G., Scicluna, A., Jackson, M., Phillips, L.H., 2009. Emotion experience, expression, and regulation in Alzheimer's disease. Psychol. Aging 24, 252–257. http://dx.doi.org/10.1037/a0014001.
Holthoff, V.A., Beuthien-Baumann, B., Kalbe, E., Lüdecke, S., Lenz, O., Zündorf, G., Herholz, K., 2005. Regional cerebral metabolism in early Alzheimer's disease with clinically significant apathy or depression. Biol. Psychiat. 57, 412–421. http://dx.doi.org/10.1016/j.biopsych.2004.11.035.
Levy, M.L., Cummings, J.L., Fairbanks, L.A., Masterman, D., Miller, B.L., Craig, A.H., Paulsen, J.S., Litvan, I., 1998. Apathy is not depression. J. Neuropsychiatry Clin. Neurosci. 10 (3), 314–319. http://dx.doi.org/10.1176/jnp.10.3.314.
Levy, R., 2012. Apathy: a pathology of goal-directed behaviour. A new concept of the clinic and pathophysiology of apathy. Rev. Neurol. 168, 585–597. http://dx.doi.org/10.1016/j.neurol.2012.05.003.
Mammarella, N., Fairfield, B., Di Domenico, A., 2012b. Comparing different types of source memory attributes in dementia of alzheimer's type. Int. Psychogeriatr. 24 (4), 666–673. http://dx.doi.org/10.1017/S1041610211002274.
Mammarella, N., Fairfield, B., Di Domenico, A., 2013a. When spatial and temporal contiguities help the integration in working memory: “A multimedia learning” approach. Learn Individ. Differ. 24, 139–144. http://dx.doi.org/10.1016/j.lindif.2012.12.016.
Mammarella, N., Fairfield, B., Di Domenico, A., 2015. Commentary: spacing as the friend of both memory and induction in young and older adults. Front. Aging Neurosci. 15. http://dx.doi.org/10.3389/fnagi.2015.00226.
Mammarella, N., Fairfield, B., Frisullo, E., Di Domenico, A., 2013b. Saying it with a natural child's voice! when affective auditory manipulations increase working memory in aging. Aging Ment. Health 17 (7), 853–862. http://dx.doi.org/10.1080/13607863.2013.790929.
Mammarella, N., Fairfield, B., De Leonardis, V., Carretti, B., Borella, E., Frisullo, E., Di Domenico, A., 2012a. Is there an affective working memory deficit in patients with chronic schizophrenia? Schizophr. Res. 138 (1), 99–101. http://dx.doi.org/10.1016/j.schres.2012.03.028.
Mammarella, N., Di Domenico, A., Palumbo, R., Fairfield, B., 2016. Noradrenergic modulation of emotional memory in aging. Ageing Res Rev 27, 61–66. http://dx.doi.org/10.1016/j.arr.2016.03.004.
Marin, R.S., Biedrzycki, R.C., Firinciogullari, S., 1991. Reliability and validity of the apathy evaluation scale. Psychiatry Res. 38, 143–162. http://dx.doi.org/10.1016/0165-1781(91)90040-V.
McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., Stadlan, E.M., 1984. Clinical diagnosis of Alzheimer's disease Report of the NINCDS-ADRDA work group* under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease. Neurology 34 (7) 939-939.
Mondini, S., Mapelli, D., Vestri, A., Arcara, G., Bisiacchi, P.S., 2011. Esame Neuropsicologico Breve 2. Raffaello Cortina Editore, Milano.
Montefinese, M., Ambrosini, E., Fairfield, B., Mammarella, N., 2014. The adaptation of the Affective Norms for English Words (ANEW) for Italian. Behav. Res. Methods 46 (3), 887–903. http://dx.doi.org/10.3758/s13428-013-0405-3.
Orgeta, V., Qazi, A., Spector, A.E., Orrell, M., 2014. Psychological treatments for depression and anxiety in dementia and mild cognitive impairment. Cochrane Database Syst. Rev. 1, CD009125. http://dx.doi.org/10.1002/14651858.
Padovan, C., Versace, R., Thomas-Antérion, C., Laurent, B., 2002. Evidence for a selective deficit in automatic activation of positive information in patients with Alzheimer's disease in an affective priming paradigm. Neuropsychologia 40, 335–339. http://dx.doi.org/10.1016/S0028-3932(01)00101-4.
Richard, E., Schmand, B., Eikelenboom, P., Yang, S.C., Ligthart, S.A., Moll van Charante, E.P., 2012. Symptoms of apathy are associated with progression from mild cognitive impairment to Alzheimer's disease in non-depressed subjects. Dement. Geriatr. Cogn. Disord. 33, 204–209. http://dx.doi.org/10.1159/000338239.
Spector, A., Orrell, M., 2010. Using a biopsychosocial model of dementia as a tool to guide clinical practice. Int. Psychogeriatr. 22 (6), 957–965. http://dx.doi.org/10.1017/S1041610210000840.
Stella, F., Radanovic, M., Aprahamian, I., Canineu, P.R., de Andrade, L.P., Forlenza, O. V., 2014. Neurobiological correlates of apathy in Alzheimer's disease and mild cognitive impairment: a critical review. J. Alzheimers Dis. 39, 633–648. http://dx.doi.org/10.3233/JAD-131385.
Tagariello, P., Girardi, P., Amore, M., 2009. Depression and apathy in dementia: same syndromeor different constructs? A critical review. Arch. Gerontol. Geriatr. 49, 246–249. http://dx.doi.org/10.1016/j.archger.2008.09.002.
Theleritis, C., Politis, A., Siarkos, K., Lyketsos, C.G., 2014. A review of neuroimaging findings of apathy in Alzheimer's disease. Int. Psychogeriatr. 26, 195–207. http://dx.doi.org/10.1017/S1041610213001725.
Tunnard, C., Whitehead, D., Hurt, C., Wahlund, L.O., Mecocci, P., Tsolaki, M., Simmons, A., 2011. Apathy and cortical atrophy in Alzheimer's disease. Int. J. Geriatr. Psychiatry 26, 741–748. http://dx.doi.org/10.1002/gps.2603.
Yesavage, J.A., 1988. Geriatric Depression Scale. Psychopharmacol. Bull. 24 (4), 709–711.
Yuen, G.S., Gunning, F.M., Woods, E., Klimstra, S.A., Hoptman, M.J., Alexopoulos, G.S., 2014. Neuroanatomical correlates of apathy in late-life depression and antidepressant treatment response. J. Affect. Disord. 166, 179–186. http://dx.doi.org/10.1016/j.jad.2014.05.008.