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THE COMPREHENSION OF SOCIAL SITUATIONS IN A SMALL GROUP OF PATIENTS WITH FRONTOTEMPORAL DEMENTIA AND ALZHEIMER'S DISEASE

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Background

SUMMARY

'Social understanding' refers to the complex ability to interpret social situations properly in everyday life. It has recently been proposed that the severe social and behavioural problems that often characterize frontotemporal dementia (FTD) and Alzheimer's disease (AD) may be at least partially the result of an impairment in social understanding. The present study was thus designed to investigate the possible presence of defective social understanding in a small group encompassing both FTD and AD patients.

Material/ Methods:

Small groups of dementia patients (n = 12) and matched healthy controls (n = 15) underwent standard clinical, neurological and neuropsychological assessments. Then, the Reading the Mind in the Eyes test was administered to all the participants, along with a validated story completion task encompassing both social and non-social stereotyped situations.

Results:

The dementia patients' performance on both tasks was worse than healthy controls performance. Interestingly, both the non-social and the social parts of the story completion task were significantly impaired, but with the social part being more compromised.

Conclusions:

These preliminary findings suggest the presence of significant difficulties in attributing mental states to others appropriately and interpreting properly stories that explicitly refer to social situations. Our results underline the need for further research to gain a deeper understanding of the possible link between patients' behavioural problems and their social understanding impairment.

Key words: behavioural problems, mental states, social understanding

INTRODUCTION

It has recently been proposed that the severe social and behavioural problems that often characterise neurodegenerative diseases, such as frontotemporal dementia (FTD) and Alzheimer's disease (AD), may be at least partially the result of a significant impairment in social understanding (Adenzato, Cavallo & Enrici, 2010; Kipps & Hodges, 2006). Social understanding refers to the complex ability to understand and interpret social situations properly in everyday life in order to behave appropriately (Frith & Frith, 2006; Tomasello, 1999). FTD and AD are characterised by social and behavioural problems that may lead to substantial worsening in the quality of life of both patients and their families. In particular, FTD is characterised clinically by severe alterations of behaviour and social conduct (Rankin et al., 2003; Neary et al., 1998), and AD involves the presence of a significant impairment in memory and other cognitive domains (McKhann et al., 1984), as well as the presence of behavioural disturbances (Cummings & Victoroff, 1990).

Even if it is now well established that these neurodegenerative diseases typically encompass the presence of significant interpersonal and behavioural disturbances, the exact nature of these symptoms remains unclear. According to the recent proposal that patients' social and interpersonal problems may be at least partially the result of a significant impairment in social understanding ability (Cavallo et al., 2009; Torralva et al., 2007; Lough et al., 2006; Gregory et al., 2002), the present study aimed at investigating the possible impairment of this ability by administering experimental tasks that require the subject to deal with social and non-social situations. The main aim was to test the hypothesis of a higher degree of impairment in patients' comprehension of social situations.

MATERIAL AND METHODS

Participants: The present study involved 12 dementia patients and 15 healthy controls. The dementia patients (eight males and four females, age range 58-78, mean 67.42 ± 7.08 years, years of formal education 8.83 ± 5.80 , mean duration of illness since time of testing 1.96 ± 1.37 years) belonged to two different clinical subgroups: Five FTD patients (three males and two females, age range 59-74, mean 66.20 ± 6.8 years, years of formal education 5.8 ± 1.3 , mean duration of illness since time of testing 2.85 ± 0.83 years), and seven AD patients (five males and two females, age range 58-78, mean 68.29 ± 7.67 years, years of formal education 11.00 ± 6.88 , mean duration of illness since time of testing 1.43 ± 0.43 years). All of the patients were retrospectively recruited from the IRCCS "San Giovanni di Dio - Fatebenefratelli" of Brescia, Italy. Patients underwent routine haematology, biochemistry and neurological examinations. All of them received structural neuroimaging (either CT or MRI). Due to the small number of patients with FTD ($n = 5$) and AD ($n = 7$) recruited, in the statistical analyses FTD and AD patients had been pooled together in a single group.

Healthy controls (eight males and seven females, age range 53-74, mean 63.53 ± 6.01 years, years of formal education 11.07 ± 3.55) were recruited from

a panel of healthy volunteers. None of them were related to the dementia patients involved in the study, and none of them had a positive history of neurological and/or psychiatric disorders, or of alcohol and drug abuse. The study was granted approval by the local Research Ethics Committee.

Neuropsychological assessment: All participants underwent a general neuropsychological assessment.

Experimental task: All of the participants were administered the RME task (Baron-Cohen et al., 1997; 2001) and a story completion task based on a task previously used in four neuroimaging studies (Enrici et al., 2011; Walter et al., 2009; Ciaramidaro et al., 2007; Walter et al., 2004).

The RME task consists in the presentation of 36 black and white photographs of the eye region of both male and female human faces. The participants were asked to choose from amongst four words printed on the page on which the picture appears, selecting which word best describes what the person in the photograph is thinking or feeling.

The story completion task consists of 36 comic strip stories subdivided in the two following categories: 1) *Social* stories, depicting both actions with a social goal performed by a single character, where a social interaction is foreseen but has not actually taken place (e.g., preparing six champagne glasses for a toast), and actions with a social goal performed by two characters in a communicative interaction (e.g., a woman shows a boy with muddy hands where to wash them); 2) *Non-Social* stories, depicting both actions performed by a single character with a private goal outside a social interaction (e.g., a single person changing a broken bulb in order to read a book), and situations with a physical interaction between objects (e.g., a boat breaks on a rock).

The story task is composed of simple paper-and-pencil stories. Each story is made up of three black-and-white drawings that are displayed by the examiner one after the other in front of the participant. Then, four additional drawings are provided: Three of them depict unusual and inappropriate conclusions, whereas one of them represent an appropriate ending for the story. The participant is asked to look at the story and choose its most appropriate ending amongst the four additional drawings provided. Examples of the stories used are available at the web address: www.psych.unito.it/csc/pers/adenzato/pdf/neurodegdis.pdf

Statistical analyses were performed using SPSS© (Statistical Package for the Social Sciences) version 18.0. Analyses were as follows: first, group comparisons between dementia patients and healthy controls on the background and experimental variables of interest were performed using unpaired t-tests or Analysis of Variance (ANOVA), as appropriate. To extend the preliminary results reported by Cavallo et al. (2009) – and according to the procedure formalized by Crawford and Garthwaite (2002) to deal with single cases appropriately – comparisons were performed of individual patients' scores with healthy controls' scores were performed on the background and experimental variables of interest.

RESULTS

The present results were presented during the poster session of the Meeting of the World Federation of Neurology Research Group on Aphasia and Cognitive Disorders (Istanbul, May 15-18, 2010).

Dementia patients versus healthy controls

Neuropsychological assessment. The comparison between the two groups (dementia patients and healthy controls), as well as standard clinical cut-off points that indicate significant cognitive impairment, are shown in Table 1. As expected, dementia patients got lower scores than healthy controls on most of the neuropsychological measures. However, when taking into account standard clinical cut-off points, the patients performed above these thresholds in most of the tests administered, suggesting the presence of a relative cognitive integrity in the dementia patients recruited for the present study.

Experimental tasks: On the RME test, dementia patients' performance was significantly worse than healthy controls' performance (16.08 ± 4.27 correct responses out of a possible 36 in the dementia patients' group, vs. 23.80 ± 3.63 in the control group; Student's $t_{(25)} = 5.075$, $p < 0.001$). A bivariate correlation analysis among the RME test score and the background neuropsychological measures showed the presence of a significant correlation of the RME scores

Table 1. Demographic data of dementia patients and healthy controls, and relative performance on general neuropsychological tests. Impaired patients' scores according to standard cut-off thresholds are shown in bold

	Dementia patients (n = 12)	Healthy controls (n = 15)	t-test	Cut-off
Age in years (SD)	67.42 (7.08)	63.53 (6.01)	NS	
Gender (M:F)	8:4	8:7	$\chi^2 = NS$	
Education in years (SD)	8.83 (5.80)	11.07 (3.55)	NS	
MMSE	25.01 (3.40)	27.81 (1.21)	2.975**	24
Digit span	5.24 (0.92)	5.80 (0.87)	NS	3.75
Spatial span	4.07 (0.74)	5.92 (0.95)	NS	3.75
Rey figure copy	20.00 (12.53)	33.50 (1.95)	4.140**	28.88
Rey figure recall	6.45 (7.19)	15.32 (4.40)	NS	9.47
Token test	29.78 (3.73)	34.28 (1.40)	4.327**	26.5
TMT A	75.00 (45.81)	41.27 (13.42)	2.715*	93
TMT B	245.62 (108.43)	94.93 (33.48)	4.886**	282
TMT B-A	188.87 (95.27)	53.43 (30.58)	4.968**	186
RPM	22.75 (8.03)	-	-	18
Prose recall	6.79 (3.65)	-	-	8
Verbal fluency (letter)	25.73 (10.07)	-	-	17
Verbal fluency (category)	26.64 (10.28)	-	-	25

* $p < 0.05$; ** $p < 0.01$; d.f. = degrees of freedom; MMSE = Mini-Mental State Examination; NS = not significant; RPM = Raven's progressive matrices; SD = standard deviation; TMT = Trail Making Test.

Table 2. Bivariate correlation analysis among the RME test score and the background neuropsychological measures administered

	RME	MMSE	DIGIT SPAN	SPAT SPAN	REY COPY	REY REC	TOKEN	TMT A	TMT B	TMT B-A	RPM	PROSE REC	VF LET	VF CAT
RME	-	0.58 **	0.36	0.67 **	0.58 **	0.51 **	0.64 **	-0.47 *	-0.47 *	-0.46 *	0.39	0.69 *	0.68 *	0.50

* p < 0.05; ** p < 0.01; MMSE = Mini-Mental State Examination; PROSE REC = Prose recall; REY COPY = Rey figure copy; REY REC = Rey figure recall; RME = Reading the Mind in the Eyes test; RPM = Raven's progressive matrices; SPAT SPAN = Spatial span; TMT = Trail Making Test; VF LET = Verbal fluency (letter); VF CAT = Verbal fluency (category).

with most of the measures administered (Table 2). The participants' performance on the story completion task is reported in Table 3. The patients' performance on both social and non-social stories was worse than the healthy controls' performance. Interestingly, the patients' performance on the social stories was much worse than their own performance on non-social stories (Fisher's $F = 10.267$, $p < 0.01$). The results of interest regarding the story completion tasks are shown graphically in Figure 1. A bivariate correlation analysis among the story completion task score (social – non-social stories) and the background neuropsychological measures showed the presence of a significant correlation of the story completion task with the Token test, the TMT-B, the TMT B-A and the Spatial span only (data not shown).

Single case analyses: Individual patients versus healthy controls

Neuropsychological assessment. For the sake of clarity, FTD patients are denoted by numbers 1-5, and AD patients by numbers 6-12. Comparison of individual patients' scores with controls' means (Crawford & Garthwaite, 2002) showed significant impairment on the MMSE in patients 1, 6 and 7 ($p < 0.001$) and in patients 3 and 5 ($p < 0.01$); on the Digit span and the Spatial span, in patient 6 only ($p < 0.01$); on the Rey complex figure test copy, in patient 1 ($p < 0.01$) and in patients 2-3, 5, 7-8,10 and 12 ($p < 0.001$); on the Rey complex figure test recall, in patients 7, 8,10 and 12 ($p < 0.01$). Finally, impaired performance was identified on the Token test in patients 3 and 6 only ($p < 0.001$); on the TMT A, in patients 1 and 7 only ($p < 0.001$); and on the TMT B and TMT B-A, in patients 4, 8-10 and 12 ($p < 0.001$).

Experimental tasks: Comparison of individual patients' scores with the control means for the RME task showed the presence of a significant difference in patients 1, 5, 6 and 12 ($p < 0.05$) and in patients 3, 4 and 7 ($p < 0.01$). Individual patients' scores on the RME test, expressed as Z scores, are shown in Figure 2.

Table 3. The story completion task. Comparison between correct responses in the non-social and social stories. Values (range 0-18) represent correct responses

	Non-social stories 0-18 (SD)	Social stories 0-18 (SD)	F value
Dementia patients (n = 12)	10.75 (3.60)	7.83 (4.17)	10.267 *
Healthy controls (n = 15)	17.33 (1.05)	17.27 (1.44)	NS

* p < 0.01; NS = not significant; SD = Standard deviation.

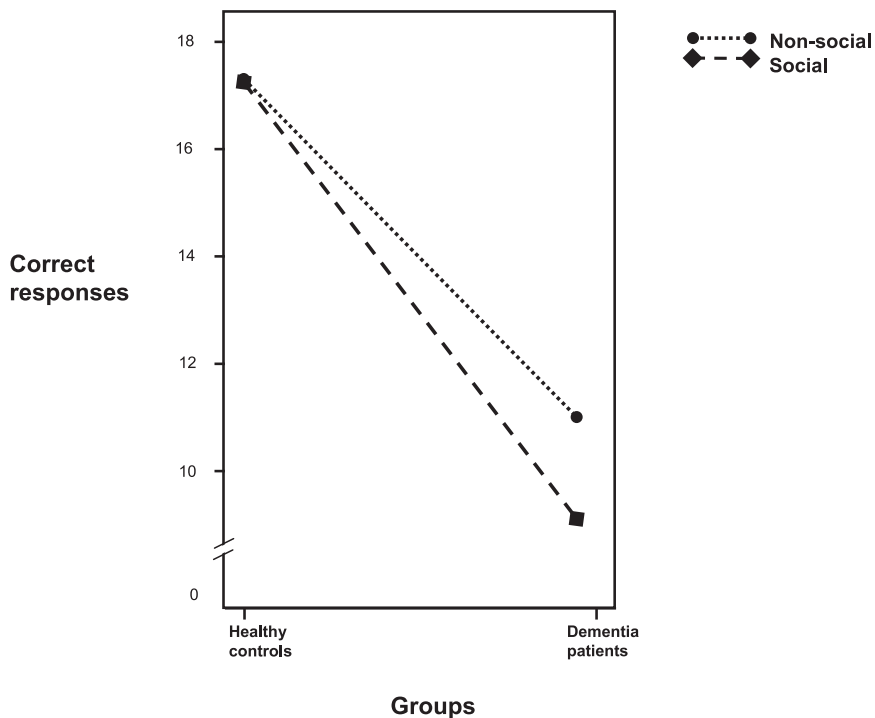
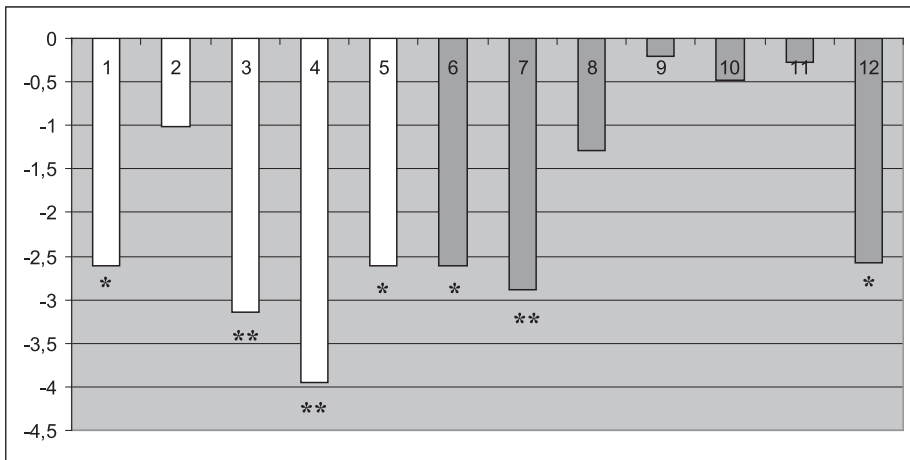


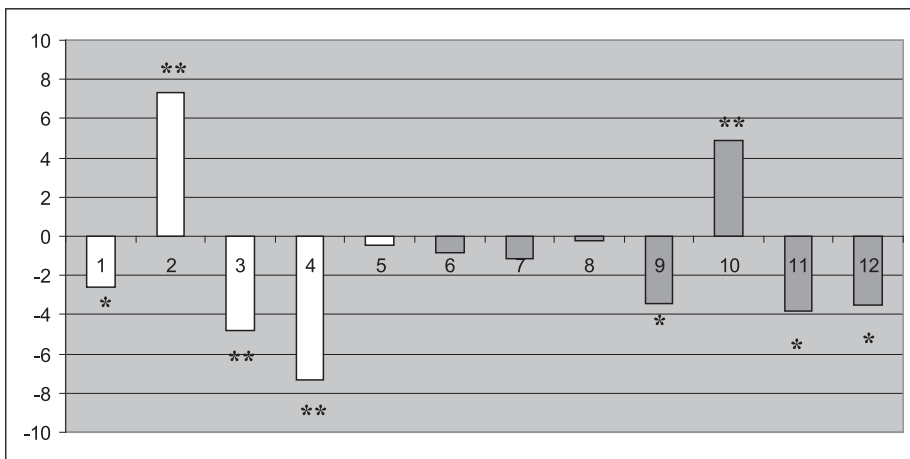
Figure 1. Visual projection of the interaction 'group' (dementia patients/healthy controls) x 'experimental dimension' (social/non-social stories)

Regarding the story completion task, the individual patients' differences between social and non-social categories (social – non-social stories) were compared with the analogous difference in the healthy controls group (Crawford & Garthwaite, 2005). The comparison showed the presence of a difference in the direction of the experimental hypothesis (non-social > social) in 10 out of 12 patients, and this difference was statistically significant in patient 1, 9 (p < 0.01), 3, 4, 11 and 12 (p < 0.001). Conversely, a significant difference in the opposite direction (social > non-social) was observed in patients 2 and 10 only (p < 0.001). The individual patients' difference, expressed as Z scores, are shown in Figure 3.



* p < 0.05; ** p < 0.01; RME = Reading the Mind in the Eyes test.

Figure 2. Individual dementia patients' score on the RME task. Scores are expressed as Z scores. FTD patients are associated with numbers 1-5 and shown in white, AD patients are associated with numbers 6-12 and shown in grey



* p < 0.01; ** p < 0.001

Figure 3. Individual patient difference between social and non-social categories on the story completion task. Differences are expressed as Z scores. FTD patients are associated with numbers 1-5 and shown in white, AD patients are associated with numbers 6-12 and shown in grey

DISCUSSION

According to the recent proposal that the social and interpersonal problems which often characterise dementia patients may be at least partially the result of a significant impairment in social understanding ability, the present study investigated patients' ability to understand social situations appropriately.

Before focusing on the results of interest, it is important to note that the dementia patients involved in the present study attained scores higher than the standard cut-off thresholds on most of the neuropsychological measures administered, allowing us to conclude that from a cognitive standpoint the patients recruited were relatively preserved.

Regarding the experimental tasks used in the present study, the dementia patients' performance on the RME was poorer than the healthy controls' performance. Furthermore, when individual patients' score were taken into account, dementia patients were found to get a lower score compared with healthy controls, extending the findings of previous studies (Torralva et al., 2007; Gregory et al., 2002; Lough & Hodges, 2002) and supporting the view that dementias appear to be associated with a defective performance on the ability measured by this task. The bivariate correlation analysis among the RME test score and the background neuropsychological measures showed the presence of a significant association of the RME score with most of the measures administered, suggesting that performance on the RME test seems to be significantly associated with performance on most of the cognitive tasks administered.

The story completion task was designed to explicitly assess the patients' ability to interpret and understand social and non-social situations properly. The dementia patients' performance was poorer than that of the healthy controls in both the experimental conditions (social and non-social): however, a significant difference in the direction stated by the experimental hypothesis emerged (social < non-social), showing that the social stories were more challenging to deal with than the non-social stories. In addition, in order to verify that the deficits in social understanding showed by the group comparisons really depend on a genuine and specific pattern of results in this direction, and not on the mere presence of a single outlier, individual scores were taken into due account. The results showed that the vast majority of patients (10 out of 12) presented with a profile following the experimental hypothesis: more precisely, four out of five FTD patients and six out of seven AD patients showed the hypothesized profile of results. Thus, our findings support the view that both FTD and AD patients seem to be significantly impaired in understanding social situations appropriately, as compared to healthy controls. Interestingly, a bivariate correlation analysis between the story completion task score (social – non-social stories) and the background neuropsychological measures showed a significant correlation of the story completion task with few neuropsychological measures, suggesting that the performance on the story completion task seems not to be associated significantly with performance on the neuropsychological tasks administered.

The study has some limitations. First, the small sample size requires us to consider these results as preliminary evidence of a possible social understanding deficit in dementias. Secondly, due to the small number of FTD and AD patients recruited, a direct comparison between the two subgroups of patients was not performed: however, it would be interesting to compare their performances in studies involving larger samples of participants. Lastly, although the patients in-

volved in the current study were relatively well preserved from a neuropsychological point of view, it is not possible to rule out completely the possibility that the general cognitive deficits typically associated with dementia might have played a role in influencing the patients' performance on the specific experimental tasks proposed. Thus, in the near future it would be extremely interesting to investigate social understanding abilities in a different neurodegenerative condition that presents important and well established links with dementia but is not characterized by the same degree of cognitive impairment (e.g., amyotrophic lateral sclerosis).

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REFERENCES

- Adenzato, M., Cavallo, M. & Enrici, I. (2010). Theory of Mind ability in the behavioural variant of frontotemporal dementia: an analysis of the neural, cognitive, and social levels. *Neuropsychologia*, *48*, 2-12.
- Baron-Cohen, S., Jolliffe, T., Mortimore, C. & Robertson, M. (1997). Another advanced test of theory of mind: evidence from very high functioning adults with autism or Asperger syndrome. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *38*, 813-822.
- Baron-Cohen, S., Wheelwright, S., Hill, J., Raste, Y. & Plumb, I. (2001). The "Reading the Mind in the Eyes" Test revised version: a study with normal adults, and adults with Asperger syndrome or high-functioning autism. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *42*, 241-251.
- Cavallo, M., Enrici, I., Abrahams, S., MacPherson, S.E., Cotelli, M., Frisoni, G. & Adenzato M. (2009). Knowing how to behave properly: preliminary evidence of defective 'social understanding' in neurodegenerative diseases. *Confinia Neuropsychiatria*, *4*, 7-14.
- Ciaramidaro A, Adenzato M., Enrici I., Erk S, Pia L, Bara BG, Walter H. (2007). The intentional network: how the brain reads varieties of intentions. *Neuropsychologia*, *45*, 3105-3113.
- Crawford, J.R. & Garthwaite, P.H. (2002). Investigation of the single case in neuropsychology: Confidence limits on the abnormality of test scores and test scores differences. *Neuropsychologia*, *40*, 1196-1208.
- Crawford J.R., & Garthwaite, P.H. (2005). Testing for suspected impairments and dissociations in single-case studies in neuropsychology: Evaluation of alternatives using Monte Carlo simulations and revised tests for dissociations. *Neuropsychology*, *19*, 318-331.
- Cummings, J.L. & Victoroff, J. (1990). Noncognitive neuropsychiatric syndromes in Alzheimer's disease. *Neuropsychiatry, Neuropsychology and Behavioral Neurology*, *3*, 140-158.
- Enrici, I., Adenzato, M., Cappa, S., Bara, B.G. & Tettamanti, M. (2011). Intention processing in communication: a common brain network for language and gestures. *Journal of Cognitive Neuroscience*. doi:10.1162/jocn.2010.21594.
- Frith, C.D. & Frith, U. (2006). How we predict what other people are going to do. *Brain Research*, *1079*, 36-46.
- Gregory, C., Lough, S., Stone, V., Erzincioğlu, S., Martin, L., Baron-Cohen, S. et al. (2002). Theory of mind in patients with frontal variant frontotemporal dementia and Alzheimer's disease: theoretical and practical implications. *Brain*, *125*, 752-64.
- Kipps, C.M. & Hodges, J.R. (2006). Theory of mind in frontotemporal dementia. *Social Neuroscience*, *1*, 235-244.

- Lough, S. & Hodges, J.R. (2002). Measuring and modifying abnormal social cognition in frontal variant frontotemporal dementia. *Journal of Psychosomatic Research*, *53*, 639-646.
- Lough, S., Kipps, C.M., Treise, C., Watson, P., Blair, J.R. & Hodges, J.R. (2006). Social reasoning, emotion and empathy in frontotemporal dementia. *Neuropsychologia*, *44*, 950–958.
- McKhann, G., Drachman, D., Folstein, M., Katzman, R., Proce, D. & Stadlan, E.M. (1984). Clinical diagnosis of Alzheimer's disease. *Neurology*, *34*, 939–944.
- Neary, D., Snowden, J.S., Gustafson, L., Passant, U., Stuss, D., Black, S., et al. (1998). Frontotemporal lobar degeneration. A consensus on clinical diagnostic criteria. *Neurology*, *51*, 1546-1554.
- Rankin, K.P., Kramer, J.H., Mychack, P. & Miller, B.L. (2003). Double dissociation of social functioning in frontotemporal dementia. *Neurology*, *60*, 266-271.
- Tomasello, M. (1999). *The cultural origins of human cognition*. Harvard: Harvard University Press.
- Torralva, T., Kipps, C.M., Hodges, J.R., Clark, L., Bekinschtein, T., Roca, M. et al. (2007). The relationship between affective decision-making and theory of mind in the frontal variant of frontotemporal dementia. *Neuropsychologia*, *45*, 342-349.
- Walter, H., Adenzato, M., Ciaramidaro, A., Enrici, I., Pia, L. & Bara, B.G. (2004). Understanding intentions in social interaction: the role of the anterior paracingulate cortex. *Journal of Cognitive Neuroscience*, *16*, 1854-1863.
- Walter, H., Ciaramidaro, A., Adenzato, M., Vasic, N., Ardito, R.B., Erk, S. et al. (2009). Dysfunction of the social brain in schizophrenia is modulated by intention type: An fMRI study. *Social Cognitive and Affective Neuroscience*, *4*, 166–176.

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