Impaired recognition of facial emotional expressions in Multiple Sclerosis

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Abstract

This study investigated the ability of patients with Relapsing-Remitting Multiple Sclerosis (RRMS) to recognize emotional facial expressions. Cognitive deterioration, depression, alexithymia and facial expression recognition ability were assessed in fifty-five patients and twenty-one controls. Facial expression recognition ability was measured by a forced-choice labeling procedure of five emotional facial expressions (anger, fear, sadness, happiness, none). RRMS patients exhibited a global impairment in the recognition of facial emotion ($p = .00049$), specifically for anger ($p = .01$), sadness ($p = .0001$), and fear, ($p = .011$). Deficit in emotion recognition was independent from disability (assessed by EDSS score). This deficit was correlated with depression and partially with cognitive deterioration. These results should be discussed in term of global cortico-cortical disconnections.

Keywords: Multiple sclerosis; Emotion facial recognition; Cognition; Alexithymia; Depression

1. Introduction

Multiple Sclerosis (MS) is an inflammatory, degenerative and progressive disease of the Central Nervous System (CNS) and the most frequently diagnosis illness in young adult. This disease is characterized by the production of lesions of the myelin sheath and cause inhibition of axonal transmission in the brain and spinal cord. Because of the widespread development of the lesions, MS results in a broad range of symptoms, which include motor, cognitive and psychiatric disorders (Dutta & Trapp, 2006).

Al though, the patterns of cognitive deficits concerning working memory, and sustained attention, information processing speed, memory retrieval, and also executive functions are increasingly better characterized (Chiaravalotti & DeLuca, 2008), emotion recognition has rarely been investigated in MS so far. Yet, the ability to recognize emotions from facial expressions is crucial for social interaction in everyday life, and it's know that MS patients show impairments in social interaction and affective functions (Kesselring & Klement, 2001). Emotion-specific deficits, described in various CNS disorders like fronto-temporal dementia, Alzheimer's disease, Parkinson's disease (Luzzi, Piccirilli & Provinciali, 2007; Sprengelmeyer et al., 2003; Yip, Lee, Ho, Tsang & Li, 2003; Dujardin et al., 2004), have been explained by disturbed neural processing localized in brain regions, specifically those serving emotion recognition (Adolphs et al., 2002; Kohler et al., 2003). In MS, disconnections in the frontal-subcortical brain tracts, known to be also involved in the processing of emotional signals, are observed (Adolphs, Tranel & Denburg, 2000; Posamentier & Abdi, 2003; Vuilleumier & Pourtois, 2007; Ruffman, Henry, Livingstone & Phillips, 2008).

Several studies have reported some evidence that MS can influence emotion perception, by identifying significant impairment in decoding emotional states (Beatty et al., 1989; Beatty, Orbelo, Sorocco & Ross, 2003; Henry et al., 2009; Jehna et al., 2010; Philips et al., 2010; Prochnow et al., 2011). Beatty et al. (1989) investigated cognitive functions in patients with MS and showed that MS patients had significantly lower scores than healthy controls on the facial recognition test, although authors argued that these results could be due to a general visual impairment. More recently, Prochnow et al. (2011) confirmed that MS patients were impaired in facial affect

recognition on four of the six Ekman basic emotions, except happiness and disgust. Henry et al. (2009) specifically demonstrated deficits in identifying facial expressions of specific basic emotions (anger and fear) in MS, as well as having difficulties in identifying more complex emotional states, with a test designed to assess Theory of Mind (ToM). They also found that problems with emotion perception in MS were correlated with some measures of cognitive performance, particularly processing speed and executive functioning, suggesting that emotion perception difficulties might reflect more general information processing impairments or a specific problem in affective information processing in MS. Poettgen, Dziobek, Reh, Heesen and Gold (2013) highlighted that impairments were more pronounced in identification of emotions than in identification of thoughts or intentions, especially during the early disease stages. Other study (Jehna et al., 2010), confirmed significant decreased reaction-times regarding emotion recognition tests even among patients in the very early state of disease (*clinical isolated syndrome*) compared to HC, associated with worse cognitive abilities in the patients. Nonetheless, those impairments appear not to be exclusively related to face recognition since, Philips et al. (2010) proved specific deficit in decoding static and dynamic information about emotion in MS, as compared to non-emotional information; as well as Beatty, Orbelo, Sorocco and Ross (2003) reported problems in processing prosodic information about emotions in MS, unrelated to peripheral hearing loss, depression, or cognitive impairment. This emotional prosody comprehension deficit was especially found in young patients in the early stage of Relapsing-Remitting Multiple Sclerosis (RRMS; Kraemer et al., 2013). Consequently it exists specific relationships between emotion perception problems and poor social and psychological quality of life. Indeed, ratings of social and psychological aspects of quality of life in MS were related to emotion perception scores, controlling disease severity and duration, age, depression, and cognitive function (Philips et al., 2010), indicating that emotional skills should be considered when evaluating the functioning in MS.

The correct identification of emotions may be seen as a complex cognitive process, requiring the functional integrity of a number of cognitive domains, including working memory, visual attention, visuospatial perception and executive functions. Moreover, depression (Asthana, Mandal, Khurana & Haque-Nizamie, 1998; Persad & Polivy, 1993; Surguladze et al., 2004; Bourke, Douglas & Porter, 2010) and alexithymia (Parker, Taylor & Bagby, 1993; Mann, Wise, Trinidad & Kohanski, 1994; Lane et al., 1996; Lane, Sechrest, Riedel, Shapiro & Kaszniak, 2000; Zonnevijlle-Bender, van Goozen, Cohen-Kettenis, van Elburg & van Engeland, 2002; Kucharska-Pietura & Masiak, 2004; Ridout, Thom & Wallis, 2010) are two dimensions

which might influence or modify the identification or the expression of emotion.

This study, therefore, had two aims. The first was to investigate whether MS patients, with relapsing-remitting form of the disease, was associated with impaired ability to decode emotional facial expressions. Second aim was to test the hypothesis that problems with emotion perception in MS would relate to cognitive, mood and emotional disorders. RRMS is the most common MS form, achieved in younger patients who might benefit more favorably from procedure-specific support, particularly in patients with early disease. To substantiate our hypotheses, MS patients' data were compared to those of healthy controls.

2. Method

2.1. Participants

For the MS sample, individuals were recruited during neurological consultation. Patients were not specifically addressed for specific cognitive complaints or for a neuropsychological assessment. None patient was hospitalized. This sample included 55 participants with clinically defined RRMS, according to McDonald's criteria (McDonald et al., 2001). Inclusion was done remotely at least six weeks of an acute relapse and four weeks of a bolus of corticosteroids. These patients were all diagnosed and treated at the Department of Neurology of St Philibert Hospital (GHICL, North of France). The average number of year since the diagnosis was 7.52 (SD = 2.81). Participants' median EDSS (*Expanded Disability Status Scale*: Kurtzke, 1983) score, which ranges from 0 (normal) to 10 (death), was 2 (1-3), indicating thus a moderate mobility disability.

Twenty-one healthy participants matched for age (± 3 years) and educational level were recruited from the general community via advertisements.

In Table 1, means and standard deviations of demographic and clinical characteristics of all participants, as well as the results of inferential statistical tests are presented. The mean age in years of patients did not differ significantly from the healthy participants ($t[74] = 1.473$, $p = .145$). Both the MS and control groups were mainly women (80% and 62.9%, respectively, $\chi^2[1] = 2.654$, $p = .103$), and did not significantly differ in the number of years of education ($t[74] = 0.929$, $p = .356$). Most of the patients received an immunomodulatory treatment (44/55).

Table 1. Demographic and clinical characteristics of RRMS patients and healthy participants

	RRMS* patients		Health participants		*t* tests
Characteristics	M	SD	M	SD	*p* value
Age (years)	39.84	8.74	36.38	10.14	.145
Female/male	44/11	–	13-ago	–	.103
Education (years)	13.49	2.81	14.14	2.54	.356
EDSS**, median (range)	2 (0-6)	–	–	–	–
Disease duration (years)	7.52	5.93	–	–	–

* Relapsing-Remitting Multiple Sclerosis; ** Expanded Disability Status Scale.

Patients and healthy participants were all Caucasian. Exclusion criteria for both groups were: (a) a history of neurological disease (other than MS for the MS participants), (b) a history of major psychiatric illness, except depressive episodes, (c) a premorbid history of alcohol or drug abuse, (d) motor disturbances that would interfere with testing, (e) an acute relapse for MS patients. Because all measures of emotion recognition used in the present study also impose demands on perceptual function, vision testing was conducted binocularly, for the MS participants, with both eyes open, using standard Snellen acuity letter charts. Tests for opthalmoplegia were also conducted. None of the MS participants included in the study had visual disturbances that would interfere with testing. All participants provided informed consent. The study has been approved by the local Ethics Committee of Catholic Institute of Lille (ICL), and was in compliance with the regulations of the University of Medicine of Lille (North of France).

2.2. Procedure and measures

All participants first provided demographic information, and then completed several cognitive measures, and self-report measures of depression, anxiety and alexithymia, which has been completed by a clinical assessment. This was followed by measures of facial emotion recognition.

The same psychologist conducted an extensive neuropsychological examination for each participant to identify cognitively impaired participants. The test battery (BCcogSEP) was constructed based on previously published neuropsychological findings (Dujardin et al., 2004) and was designed to assess a wide range of cognitive abilities. This battery, based on the *Brief Repeatable*

Battery for Neuropsychological Examination (BRB-N: Rao, Leo, Bernardin & Unverzagt, 1991), was used to assess several dimensions of cognitive functioning in patients, particularly in areas of cognitive deficits often observed in MS patients. This battery consisted of eight tests with: the *Selective Reminding Test* (SRT: Buschke & Fuld, 1974) allowing to assess learning and consolidating information capabilities in verbal modality, a test of visual-spatial learning (the 10/36 adapted of Barbizet & Cany, 1968), an adaptation of the Digit-symbol coding subtest of the WAIS-R, the *Paced Auditory Serial Addition Task* (PASAT: Gronwall, 1977), with three and two seconds interstimulus, direct and reverse digit spans, semantic and phonemic fluency (using the probes: *p* and animals, respectively), the Crossed Tapping (Godefroy et al., 1992) and Go / No Go non-computerized (Dubois, Slachevsky, Litvan & Pillon, 2000). Fourteen scores were obtained from this battery. For each score, participants were classified as passing or failing the task using the cut-off of the fifth percentile.

The *TAS-20 Questionnaire* (Bagby, Parker & Taylor, 1994; Loas et al., 1996) was used to assess the level of alexithymia among participants. This questionnaire consisted of 20 items divided into three factors "Ability to identify feelings and to distinguish them", "Ability to describe feelings to other people" and "Externally oriented thinking" (Zech, Luminet, Rimé & Wagner, 1999). The subject self-assessed for each item on a scale rating from 1 to 5 (1 = "Completely disagree" and 5 = "Complete agreement"). The total score was analyzed (with a threshold of 56), as well as the scores of the three factors.

The *Beck Depression Inventory* (BDI-II: Beck, Ward, Mendelson, Mock & Erbaugh, 1961) was used for the evaluation of depressive disorders among the participants. The BDI-II is a self-administered questionnaire consisting of 21 items rated from 0 (no problem) to 3 (maximum severity of symptoms). The total score, sum of different items scores, determined the intensity of the depressive symptoms on an ordinal scale of increasing intensity (12-19: slight depression, 20-27: moderate depression, > 27: severe depression). Each participant also completed a forced-choice labeling of facial expressions. In this task, black and white photographs of 10 models (5 females / 5 males) were selected from the Ekman and Friesen (1976) pictures of Facial Affect series. Each model displayed five facial expressions corresponding to four emotional facial expressions (anger, fear, sadness, happiness) and one neutral facial expression. The 10 models were selected so that each emotion was well recognized by Ekman & Friesen's normative sample. A forced-choice labeling procedure was adopted. Pictures were presented individually in random order during 1.5 seconds, followed by the label of emotions during 2.5 seconds. Participants were asked to select one of the five emotion labels that best described the facial expression shown; no feedback was given about accuracy of the response. A total number of correct recognitions for each subtype of emotions was recorded.

2.3. Data analysis

Statistical analysis was completed with SPSS 18.0. Variables were compared between groups using the *chi-square* test for nominal data, the Mann-Whitney *U*-tests (Z) for non-normally distributed quantitative data and the Student's *t*-tests for normally distributed quantitative data, as appropriate (homogeneous in between-group variance was assessed by Levenes Test). Significance was accepted at a conservative $p < .05$. Effect sizes were calculated based on means with Cohen's d.

A two-step data analysis was performed. The first stage was descriptive statistics of neuropsychological and psychological functioning, by group analyses in order to compare patients and healthy participants. In the second stage, a regression analysis was performed for analyzing the specific cognitive or mood variables responsible for the accuracy of solving the facial emotion recognition using the number of correct answers as covariate.

3. Results

3.1. Between groups analysis

In Table 2, the *Means* (M) and *Standard Deviation* (SD) and the results of inferential statistical tests comparing RRMS and healthy participants are presented for each cognitive assessment of the BCcogSEP. RRMS patients exhibited a lower score than healthy participants for each variable of cognitive assessment, except for selective reminding test (mean number of words, learning index and delay recall).

In Table 3, the *Means* (M) and *Standard Deviation* (SD) and the results of inferential statistical tests comparing RRMS and healthy participants are presented for the BDI-II and TAS-20. Applying Bonferonni corrections to the five pair-wise comparisons yields an adjusted critical *p* value of .01. Using this criterion, RRMS patients exhibited a higher score than healthy participants for depression (BDI-II) ($U[74] = 4.45$, $p < .001$), alexithymia (TAS-20) ($U[74] = 3.76$, $p = .0001$), "Ability to identify feelings and to distinguish emotion" (first factors of the TAS-20) ($U[74] = 4.66$, $p = .0001$) and "Ability to describe feelings to other people" (second factor of the TAS-20) ($U[74] = 2.7$, $p = .008$), but not for "Externally oriented thinking" (third factor of the TAS-20) ($U[74] = 1.7$, $p = .089$).

Table 2. Comparison on measures of cognitive functions obtained by RRMS patients and healthy participants in different test of BCcogSEP

	RRMS patients		Healthy participants		*t* tests
	M	SD	M	SD	*p* value
SRT Mean number of words	12.11	1.20	12.52	0.55	NS
SRT Learning index	76.54	13.96	83.08	9.52	NS
SRT Delay recall	13.98	1.61	14.62	0.74	NS
10/36 Recall	43.58	10.13	51.00	5.81	.03
10/36 Delay recall	33.51	9.97	43.57	7.65	.04
Digit-symbol coding subtest of the WAIS-R	18.44	5.29	21.38	4.80	.0005
PASAT 3 sec.	6.73	2.41	8.00	2.19	.002
PASAT 2 sec.	59.15	12.25	69.86	9.47	.00008
Direct digit span	6.65	1.70	8.05	1.72	.002
Reverse digit span	5.89	1.93	7.33	1.68	.003
Semantic fluency	20.40	4.83	23.43	4.46	.01
Phonemic fluency	13.65	3.95	18.19	4.29	.00004
Crossed taping	0.62	1.19	0.00	0.00	.02
Go / No Go	0.73	1.11	0.14	0.36	.02

Table 3. Comparison on measures of depression (using the BDI-II) and alexithymia (using the TAS-20, total score and factor's scores) obtained by RRMS patients and healthy participants

	RRMS patients		Healthy participants		*t* tests
	M	SD	M	SD	*p* value
BECK depression (BDI-II)	12.84	10.18	2.57	4.02	< .001
TAS-20	50.22	13.25	37.43	8.43	< .001
Factor 1	18.04	6.53	10.29	3.57	< .001
Factor 2	13.47	4.59	10.33	3.81	NS
Factor 3	18.71	4.84	16.81	3.31	NS

Table 4. Performance of RRMS patients and healthy participants in forced-choice labeling of facial expressions task

	RRMS patients		Healthy participants		*t* tests
Measure	M	SD	M	SD	*p* value
Forced-choice labeling of facial expressions task					
Total score (/50)	43.47	4.28	47.05	2.13	< .001
Happy (/10)	9.95	0.23	10	0	.083
Anger (/10)	8.36	1.44	9.1	0.89	.01
Sadness (/10)	7.95	1.73	9.05	1.07	.001
Fear (/10)	8.42	1.97	9.57	0.75	.01
Neutral (/10)	8.8	1.39	9.33	0.66	.027

In Table 4, the *Means* (M) and *Standard Deviation* (SD), and the results of inferential statistical tests comparing RRMS and healthy participants are presented for the task of forced-choice labeling of facial expressions.

These data were analyzed with a 2*5 mixed ANOVA with the between-subjects variable of *group* (RRMS, healthy) and the within-subjects variable of *emotion type* (happiness, anger, sadness, fear, neutral). The results indicated that there was a main group effect ($F[1, 74] = 13.3$, $p = .00049$), a main emotion type effect ($F[4, 296] = 13.13$, $p = .00001$), but without an interaction between group and emotion type ($F[4, 296] = 2.12$, $p = .079$). To identify which specific emotions differed between the two groups, a series of *t* tests were carried out. Applying Bonferonni corrections to the five pair-wise comparisons yields an adjusted critical *p* value of .01. These revealed that recognition of anger ($t[74] = 2.66$, $p = .01$, $d = 1.14$), sadness ($t[74] = 3.34$, $p = .0001$, $d = 0.76$) and fear ($t[74] = 3.7$, $p = .011$, $d = 0.77$) were disrupted in the RRMS participants, but that there were no group differences in the recognition of happiness ($t[74] = 1.76$, $p = .08$) and neutral ($t[74] = 2.25$, $p = .03$). Deficit in emotion recognition was independent from disability (assessed by EDSS score).

3.2. Regression analysis in RRMS group

Finally, it was assessed whether the performance on facial emotion recognition task was related to more general cognitive function and mood parameters in the MS group. More important cognitive deterioration (assessed by

number of score under the 5th percentile in neuropsychological evaluation, BCcogSEP) was significantly associated with weak number of total (Bêta = -0.428, $p < 0.0005$) and fear (Bêta = -0.544, $p < 0.000009$) recognitions in emotional facial recognition task. We observed a significant association between the number of total emotional facial recognitions and the learning capacity, in verbal (Bêta = 0.378, $p < 0.0008$) and visuo-spatial (Bêta = 0.44, $p < 0.0003$) modality. A significant association was also found between the number of fear recognitions, verbal episodic memory (Bêta = 0.401, $p < 0.0007$) and phonemic fluency (Bêta = 0.239, $p < 0.05$). Whereas, intensity of depression (assessed by BDI-II score) was significantly related with weak number of total (Bêta = -0.389, $p < 0.002$) and anger (Bêta = -0.327, $p < 0.02$) recognitions. None of the other emotional facial recognition (happy, sadness and neutral) showed a significant correlation with neuropsychological and emotional data.

4. Discussion

The aim of the current study was to clarify the nature of the facial expression recognition impairment among patients in the early phase of relapsing-remitting MS, the most frequent form, with less extended cognitive disorders. Our results showed a global impairment in the recognition of facial emotion in RRMS patients, especially for emotion with negative valence (i.e., anger, sadness and fear).

(1) *Emotional facial expressions recognition in Relapsing-Remitting Multiple Sclerosis* – These data are consistent with previous studies. For instance, Krause et al. (2009) showed that decreased recognition performance was limited to unpleasant facial expressions (sad, fearful, anger). Henry et al. (2009) showed specific disturbance in the decoding of specific facial emotion like fear and anger, in MS patients. Our results complete those studies by evidencing specific deficits in recognition of emotion with negative valence, also in patients in the early stage of relapsing-remitting disease course. Although, we have not specifically evaluated this aspect, this result cannot only be explained by a deficit of facial recognition. Indeed, Berneiser, Wendt, Dressel, Kessler and Hamm (cited by Krause et al., 2009) have identified clear deficits in emotion recognition using the *Florida Affect Battery*, while their patients showed no impairments in the facial identification task. Moreover, in our MS patients, no deficit was found neither in the recognition of happy expression, nor in the recognition of neutral expression. This preservation

of the recognition of happy and neutral expressions seems to emphasize the preservation of some level of face and emotional expressions processing.

(2) *Emotional facial expressions recognition, cognitive impairment and emotional disorders* – Furthermore, cognitive abnormalities appear to be related to the elevated incidence of facial emotional recognition deficit, specifically for fear recognition. In the study of Henry et al. (2009), deficits in recognition of anger and fear were included in a global disorder of the detection of subtle differences of mental states from eye cues, theory of mind deficit and dysexecutive function. Global cortico-sub-cortical disconnexion could thus be involved in the aetiology and physiopathology of such a deficit. The term "multiple disconnection syndrome" proposed for cognitive disorders, on the basis of functional, morphological and electrophysiological arguments (Calabrese, 2006), corresponds to a disconnection of widespread networks, in inter and intrahemispheric regions. In the same way, there are a wide range of neural systems involved in recognizing facial expressions of emotion, with frontal and temporal systems mainly involved (Sprengelmeyer et al., 1998; Ruffman, Henry, Livingstone & Phillips, 2008). Emotional deficits, and in particular deficit of facial emotions recognition, could be explained by such a "multiple disconnection syndrome". Indeed, recognition of facial emotions involves multimodal and multidimensional tasks, and requires the maintenance of more or less extensive neural networks. As localization of MS lesions is highly variable, it affects any region of the brain, and especially connections between different brain areas and global cortico-cortical connections (particularly the in frontal and temporal cortices). Longitudinal study would represent an important supplement of the current finding to assess the association between the evolution of global cognitive deterioration and deficit in emotional processing. Moreover, it seems important to assess jointly the evolution of global cognitive impairment, capacities of emotion recognition and neuroanatomical abnormalities, in order to determine precisely whether these emotion recognition difficulties are associated to cognitive disorders or to neuropathological changes.

In another hand, the present data show high level of depression and alexithymia scores in RRMS patients, which is in accordance with previous studies (Sà, 2007; Chahraoui, Pinoit, Viegas, Adnet, Bonin & Moreau, 2008). Mood and emotional disorders influenced the elevated incidence of facial emotional recognition, especially for anger recognition. However, although this impact of depression was independent to cognitive impairment, we cannot separate the specific effect of depression from alexithymia, since these two symptoms were significantly associated. These correlations underline that deficit in recognition of emotional facial expressions can be included in a global deficit of emotion processing.

The capacity of emotional facial expression recognition in MS seems to be influenced by cognitive and emotional factors. The unique presence of cognitive impairment or the unique presence of a depression or alexithyimic syndrome causes emotional expressions recognition difficulties. However, a subsequently analysis underlines that the presence of both cognitive impairment and mood disturbances increase the deficit of emotional expressions recognition, with a total score of emotion recognition significantly lower in MS patients presenting the two, than in MS patients with isolated cognitive impairment or isolated mood disorders. MS patients without cognitive impairment and without mood disorders were not impaired in emotional facial expressions recognition. Thus, deficit in emotional facial expression recognition in MS patients seems not to be aspecific disorder of this disease and of neuropathological process, but seems to be related to cognitive impairment and mood disorders, which are met frequently in MS.

(3) Limitations and future directions – A clear limitation of the present study was the absence of specific information relating to facial identification, although RRMS patients did not exhibit a deficit for recognition of neutral faces. However, it seems important to assess this capacity with a specific task of facial identification in RRMS patients, and also in RRMS patients with cognitive impairement, depression or alexithymia. Furthermore, an assessment of neuropathological change in MS patients must be performed in order to verify whether this deficit in emotion recognition could be integrated as a consequence of cortico-sub-cortical disconnexion. These assumptions have to be confirmed in further studies including neuropathological measures. Future researches should identify the possible link between underlying MS-related neuropathology with facial emotion recognition (by assessing of lesion load, global and regional atrophy), and information about interhemispheric transfert in patients, especially through the corpus callosum. Finally, we choosed a timed task of facial expression recognition, the time limit for submission of target alleged a more ecological aspect to the task. Nevertheless, it would be interesting to test the impact of the speed of processing emotional information by varying the time of presentation of targets.

References

Adolphs, R. (2002). Recognizing emotion from facial expressions: psychological and neurological mechanisms. *Behavioral and Cognitive Neuroscience Review*, 1 (1), 21-62.

Adolphs, R., Damasio, H., Tranel, D., & Damasio, A.R. (1996). Cortical systems for the recognition of emotion in facial expressions. *Journal of Neuroscience*, 16 (23), 7678-7687.

Adolphs, R., Tranel, D., Damasio, H., & Damasio, A.R. (1994). Impaired recognition of emotion in facial expressions following bilateral damage to the human amygdala. *Nature*, 372 (6507), 669-672.

Adolphs, R., Tranel, D., & Denburg, N. (2000). Impaired emotional declarative memory following unilateral amygdala damage. *Learning and Memory*, 7 (3), 180-186.

Asthana, H.S., Mandal, M.K., Khurana, H., & Haque-Nizamie, S. (1998). Visuospatial and affect recognition deficit in depression. *Journal of Affective Disorders*, 48 (1), 57-62.

Bagby, R.M., Parker, J.D., & Taylor, G.J. (1994). The twenty-item Toronto Alexithymia Scale-I. Item selection and cross-validation of the factor structure. *Journal of Psychosomatic Research*, 38 (1), 23-32.

Barbizet, J., & Cany, E. (1968). Clinical and psychometric study of patient with memory distrurbances. *International Journal of Neurology*, 7, 44-53.

Beatty, W.W., Goodkin, D.E., Weir, W.S., Staton, R.D., Monson, N., & Beatty, P.A. (1989). Affective judgments by patients with Parkinson's disease or chronic progressive multiple sclerosis. *Bulletin of the Psychosomatic Society*, 27, 361-364.

Beatty, W.W., Orbelo, D.M., Sorocco, K.H., & Ross, E.D. (2003). Comprehension of affective prosody in multiple sclerosis. *Multiple Sclerosis Journal*, 9 (2), 148-153.

Beck, A.T., Ward, C.H., Mendelson, M., Mock, J., & Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry*, 4, 561-571.

Berneiser, J., Wendt, J., Dressel, A., Kessler, C., & Hamm, A. (Submitted). Impaired recognition of emotions in facial expressions in patients with multiple sclerosis. *Neuropsychologia* (submitted for publication), cited by Krause et al., 2009.

Bourke, C., Douglas, K., & Porter, R. (2010). Processing of facial emotion expression in major depression: a review. *Australian and New Zealand Journal of Psychiatry*, 44 (8), 681-696.

Buschke, H., & Fuld, P.A. (1974). Evaluating storage, retention, and retrieval in disordered memory and learning. *Neurology*, 24 (11), 1019-1025.

Calabrese, P. (2006). Neuropsychology of multiple sclerosis – An overview. *Journal of Neurolology*, 253 (Suppl. 1), I10-15.

Chahraoui, K., Pinoit, J.-M., Viegas, N., Adnet, J., Bonin, B., & Moreau, T. (2008). Alexithymia and links with depression and anxiety in multiple sclerosis / Alexithymie et liens avec la dépression et l'anxiété dans la sclérose en plaques. *Revue Neurologique (Paris)*, 164 (3), 242-245.

Chiaravalloti, N.D., & DeLuca, J. (2008). Cognitive impairment in multiple sclerosis. *Lancet Neurology*, 7 (12), 1139-1151.

DeLuca, J., Chelune, G.J., Tulsky, D.S., Lengenfelder, J., & Chiaravalloti, N.D. (2004). Is speed of processing or working memory the primary information processing deficit in multiple sclerosis? *Journal of Clinical and Experimental Neuropsychology*, 26 (4), 550-562.

Dubois, B., Slachevsky, A., Litvan, I., & Pillon, B. (2000). The FAB: a Frontal Assessment Battery at bedside. *Neurology*, 55 (11), 1621-1626.

Dujardin, K., Blairy, S., Defebvre, L., Duhem, S., Noel, Y., Hess, U., & Destee, A. (2004). Deficits in decoding emotional facial expressions in Parkinson's disease. *Neuropsychologia*, 42 (2), 239-250.

Dujardin, K., Blairy, S., Defebvre, L., Krystkowiak, P., Hess, U., Blond, S., & Destee, A. (2004). Subthalamic nucleus stimulation induces deficits in decoding emotional facial expressions in Parkinson's disease. *Journal of Neurology, Neurosurgery, and Psychiatry*, 75 (2), 202-208.

Dujardin, K., Sockeel, P., Cabaret, M., De Seze, J., & Vermersch, P. (2004). BCcogSEP: a French test battery evaluating cognitive functions in multiple sclerosis. *Revue Neurologique (Paris)*, 160 (1), 51-62.

Dutta, R., & Trapp, B.D. (2006). Pathology and definition of multiple sclerosis. *Revue du Praticien*, 56 (12), 1293-1298.

Ekman, P., & Friesen, W.V. (1976). *Pictures of facial affect*. Palo Alto, CA: Consulting Psychologists Press.

Godefroy, O., Rousseaux, M., Leys, D., Destee, A., Scheltens, P., & Pruvo, J.P. (1992). Frontal lobe dysfunction in unilateral lenticulostriate infarcts. Prominent role of cortical lesions. *Archives of Neurology*, 49 (12), 1285-1289.

Gronwall, D.M. (1977). Paced auditory serial-addition task: a measure of recovery from concussion. *Perceptual and Motor Skills*, 44 (2), 367-373.

Henry, J.D., Phillips, L.H., Beatty, W.W., McDonald, S., Longley, W.A., Joscelyne, A., & Rendell, P.G. (2009). Evidence for deficits in facial affect recognition and theory of mind in multiple sclerosis. *Journal of the International Neuropsychological Society*, 15 (2), 277-285.

Jehna, M., Neuper, C., Petrovic, K., Wallner-Blazek, M., Schmidt, R., Fuchs, S., & Enzinger, C. (2010). An exploratory study on emotion recognition in patients with a clinically isolated syndrome and multiple sclerosis. *Clinical Neurology and Neurosurgery*, 112 (6), 482-484.

Kesselring, J., & Klement, U. (2001). Cognitive and affective disturbances in multiple sclerosis. *Journal of Neurology*, 248 (3), 180-183.

Kohler, C.G., Turner, T.H., Bilker, W.B., Brensinger, C.M., Siegel, S.J., Kanes, S.J., & Gur, R.C. (2003). Facial emotion recognition in schizophrenia: intensity effects and error pattern. *American Journal of Psychiatry*, 160 (10), 1768-1774.

Kraemer, M., Herold, M., Uekermann, J., Kis, B., Daum, I., Wiltfang, J., & Abdel-Hamid, M. (2013). Perception of affective prosody in patients at an early stage of relapsing-remitting multiple sclerosis. *Journal of Neuropsychology*, 7 (1), 91-106.

Krause, M., Wendt, J., Dressel, A., Berneiser, J., Kessler, C., Hamm, A.O., & Lotze, M. (2009). Prefrontal function associated with impaired emotion recognition in patients with multiple sclerosis. *Behavioural Brain Research*, 205 (1), 280-285.

Kucharska-Pietura, K., & Masiak, M. (2004). The location of the deficits of emotional communication in dimensional models of schizophrenia. *Psychiatria Polska*, 38 (5), 809-818.

Kurtzke, J.F. (1983). Rating neurologic impairment in multiple sclerosis: an Expanded Disability Status Scale (EDSS). *Neurology*, 33 (11), 1444-1452.

Lane, R.D., Sechrest, L., Riedel, R., Shapiro, D.E., & Kaszniak, A.W. (2000). Pervasive emotion recognition deficit common to alexithymia and the repressive coping style. *Psychosomatic Medicine*, 62 (4), 492-501.

Lane, R.D., Sechrest, L., Reidel, R., Weldon, V., Kaszniak, A., & Schwartz, G.E. (1996). Impaired verbal and nonverbal emotion recognition in alexithymia. *Psychosomatic Medicine*, 58 (3), 203-210.

Loas, G., Otmani, O., Verrier, A., Fremaux, D., & Marchand, M.P. (1996). Factor analysis of the French version of the 20-Item Toronto Alexithymia Scale (TAS-20). *Psychopathology*, 29 (2), 139-144.

Luzzi, S., Piccirilli, M., & Provinciali, L. (2007). Perception of emotions on happy/sad chimeric faces in Alzheimer disease: relationship with cognitive functions. *Alzheimer Disease and Associated Disorders*, 21 (2), 130-135.

Mann, L.S., Wise, T.N., Trinidad, A., & Kohanski, R. (1994). Alexithymia, affect recognition, and the five-factor model of personality in normal subjects. *Psychological Reports*, 74 (2), 563-567.

McDonald, W.I., Compston, A., Edan, G., Goodkin, D., Hartung, H.P., Lublin, F.D., McFarland, H.F., Paty, D.W., Polman, C.H., Reingold, S.C., Sandberg-Wollheim, M., Sibley, W., Thompson, A., van den Noort, S., Weinshenker, B.Y., & Wolinsky, J.S. (2001). Recommended diagnostic criteria for multiple sclerosis: guidelines from the International Panel on the diagnosis of multiple sclerosis. *Annals of Neurology*, 50 (1), 121-127.

Parker, J.D., Taylor, G.J., & Bagby, R.M. (1993). Alexithymia and the recognition of facial expressions of emotion. *Psychotherapy and Psychosomatics*, 59 (3-4), 197-202.

Pedrosa Gil, F., Ridout, N., Kessler, H., Neuffer, M., Schoechlin, C., Traue, H.C., & Nickel, M. (2008). Facial emotion recognition and alexithymia in adults with somatoform disorders. *Depression and Anxiety*, 25 (11), E133-141.

Persad, S.M., & Polivy, J. (1993). Differences between depressed and nondepressed individuals in the recognition of and response to facial emotional cues. *Journal of Abnormal Psychology*, 102 (3), 358-368.

Phillips, L.H., Henry, J.D., Scott, C., Summers, F., Whyte, M., & Cook, M. (2011). Specific impairments of emotion perception in multiple sclerosis. *Neuropsychology*, 25 (1), 131-136.

Posamentier, M.T., & Abdi, H. (2003). Processing faces and facial expressions. *Neuropsychology Review*, 13 (3), 113-143.

Pöttgen, J., Dziobek, I., Reh, S., Heesen, C., & Gold, S.M. (2013). Impaired social cognition in multiple sclerosis. *Journal of Neurology, Neurosurgery, and Psychiatry*, 84 (5), 523-528.

Prochnow, D., Donell, J., Schäfer, R., Jörgens, S., Hartung, H.P., Franz, M., & Seitz, R.J. (2011). Alexithymia and impaired facial affect recognition in multiple sclerosis. *Journal of Neurology*, 258 (9), 1683-1688.

Rao, S.M., Leo, G.J., Bernardin, L., & Unverzagt, F. (1991). Cognitive dysfunction in multiple sclerosis. I. Frequency, patterns, and prediction. *Neurology*, 41 (5), 685-691.

Ridout, N., Thom, C., & Wallis, D.J. (2010). Emotion recognition and alexithymia in females with non-clinical disordered eating. *Eating Behaviors*, 11 (1), 1-5.

Ross, E.D., Thompson, R.D., & Yenkosky, J. (1997). Lateralization of affective prosody in brain and the callosal integration of hemispheric language functions. *Brain and Language*, 56 (1), 27-54.

Ruffman, T., Henry, J.D., Livingstone, V., & Phillips, L.H. (2008). A meta-analytic review of emotion recognition and aging: implications for neuropsychological models of aging. *Euroscience and Biobehavioral Reviews*, 32 (4), 863-881.

Sá, M.J. (2008). Psychological aspects of multiple sclerosis. *Clinical Neurology and Neurosurgery*, 110 (9), 868-877.

Sanchez, M.P., Nieto, A., Barroso, J., Martin, V., & Hernandez, M.A. (2008). Brain atrophy as a marker of cognitive impairment in mildly disabling relapsing-remitting multiple sclerosis. *European Journal of Neurology*, 15 (10), 1091-1099.

Sprengelmeyer, R., Rausch, M., Eysel, U.T., & Przuntek, H. (1998). Neural structures associated with recognition of facial expressions of basic emotions. *Proceedings of the Royal Society Biological Sciences*, 265 (1409), 1927-1931.

Sprengelmeyer, R., Young, A.W., Mahn, K., Schroeder, U., Woitalla, D., Buttner, T., Kuhn, W., & Przuntek, H. (2003). Facial expression recognition in people with medicated and unmedicated Parkinson's disease. *Neuropsychologia*, 41 (8), 1047-1057.

Surguladze, S.A., Young, A.W., Senior, C., Brebion, G., Travis, M.J., & Phillips, M.L. (2004). Recognition accuracy and response bias to happy and sad facial expressions in patients with major depression. *Neuropsychology*, 18 (2), 212-218.

Trapp, B.D., Peterson, J., Ransohoff, R.M., Rudick, R., Mork, S., & Bo, L. (1998). Axonal transection in the lesions of multiple sclerosis. *New England Journal of Medicine*, 338 (5), 278-285.

Trapp, B.D., Ransohoff, R., & Rudick, R. (1999). Axonal pathology in multiple sclerosis: relationship to neurologic disability. *Current Opinion in Neurology*, 12 (3), 295-302.

Vuilleumier, P., & Pourtois, G. (2007). Distributed and interactive brain mechanisms during emotion face perception: evidence from functional neuroimaging. *Neuropsychologia*, 45 (1), 174-194.

Yip, J.T., Lee, T.M., Ho, S.L., Tsang, K.L., & Li, L.S. (2003). Emotion recognition in patients with idiopathic Parkinson's disease. *Movement Disorders*, 18 (10), 1115-1122.

Zech, E., Luminet, O., Rimé, B., & Wagner, H.L. (1999). Alexithymia and its measurement. Confirmatory factor analyses of the twenty-item Toronto Alexithymia Scale and the Bermond-Vorst Alexithymia Questionnaire. *European Journal of Personality*, 13, 511-532.

Zonnevijlle-Bender, M.J., van Goozen, S.H., Cohen-Kettenis, P.T., van Elburg, A., & van Engeland, H. (2002). Do adolescent anorexia nervosa patients have deficits in emotional functioning? *European Child and Adolescent Psychiatry*, 11 (1), 38-42.