Emotion recognition in Multiple Sclerosis

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ABSTRACT

The effect of multiple sclerosis (MS) on the ability to identify emotional expressions in faces was investigated, and possible associations with patients' characteristics were explored. 56 non-demented MS patients and 56 healthy subjects (HS) with similar demographic characteristics performed an emotion recognition task (ERT), the Benton Facial Recognition Test (BFRT), and answered the Hospital Anxiety and Depression Scale (HADS). Additionally, MS patients underwent a neurological examination and a comprehensive neuropsychological evaluation. The ERT consisted of 42 pictures of faces (depicting anger, disgust, fear, happiness, sadness, surprise and neutral expressions) from the NimStim set. An iViewX high-speed eye tracker was used to record eye movements during ERT. The fixation times were calculated for two regions of interest (i.e., eyes and rest of the face). No significant differences were found between MS and HC on ERT's behavioral and oculomotor measures. Bivariate and multiple regression analyses revealed significant associations between ERT's behavioral performance and demographic, clinical, psychopathological, and cognitive measures.

Key Words multiple sclerosis, emotion recognition, depression

1. INTRODUCTION

Multiple sclerosis (MS) is a chronic, inflammatory and neurodegenerative disease of the central nervous system. It is characterized by destruction of myelin sheaths and axonal loss (Frischer et al, 2009). MS is the most common cause of neurologic disability in young adults, affecting ~1/1000 people in industrialized countries (Hogancamp et al, 1997). Cognitive impairments (Langdon, 2011) and mood disorders (Silva et al, 2011), namely depression and anxiety, are relatively common in MS.

Recent studies have reported impairments in MS patients' ability to recognize emotions in facial expressions (Henry et al, 2009; Krause et al, 2009; Jehna et al, 2010; Phillips et al, 2011; Prochnow et al, 2011). However, there are also studies that have not found significant differences between MS patients and healthy individuals in decoding emotions from facial stimuli (Di Bitonto et al, 2011; Jenha et al, 2011a,b). These apparent inconsistencies in the literature may reflect differences in MS samples (e.g., degree of neurologic disability, psychopathological symptoms, and cognitive functioning).

This study aimed: 1) to explore the ability to recognize facial emotions in a cohort of MS patients without significant cognitive impairments, using a new set of stimuli, and 2) to explore possible associations with patients' demographic, clinical, psychopathological, and cognitive characteristics.

2. METHODS

2.1 Participants

The study included fifty-six patients diagnosed with MS (according to the McDonald Revised criteria; Polman et al, 2005) and recruited from the Neuroimmunology Outpatient Clinic from Hospital de Santo Antonio - Centro Hospitalar do Porto. The exclusion criteria were current or recent (i.e., within the previous 30 days) MS exacerbation, other CNS disorder or serious medical illness that could interfere with mood, and Mini-Mental State Examination (MMSE) <=26. Patients' mean time since clinical diagnosis was 9 years (SD=6.2); their mean age at onset was 29.93 years (SD=9.86); their mean Expanded Disability Status Scale (EDSS) score was 2.47 (SD=1.97); and their mean MMSE score was 29.29 (SD=0.90). The frequencies of MS clinical courses were: 48 (85.7%) relapsing-remitting, 3 (5.4%) secondary progressive, and 5 (8.9%) primary progressive.

The healthy control group (HC) included 56 individuals recruited in the community, without neurological or psychiatric disorders. All subjects provided informed written consent to participate in this study, as required by the Declaration of Helsinki.

2.2 Procedures

All participants performed the Emotion Recognition Test (ERT) and the Benton Facial Recognition Test, and completed the Hospital Anxiety and Depression Scale. The ERT consisted of labeling 42 pictures of faces depicting anger, disgust, fear, happiness, sadness, surprise and neutral expressions. For each emotion, 3 pictures of women and 3 pictures of men were selected from the NimStim set (Tottenham et al, 2009). The NimStim set is a large, contemporary, multiracial database of color pictures of professional actors enacting a variety of expressions. The selected pictures of European-Americans (n=40) and African-Americans (n=2) were presented in pseudorandomized order; and had $\geq$70% of the normative sample agreed with the intended expression (Tottenham et al, 2009). The interval between trials was 1500 ms, with a fixation cross, to make sure that subjects were looking at the center of the screen at the beginning of each picture presentation. The pictures were aligned so that the tip of the nose of the faces corresponded to the center of the screen. After 3 seconds of "free exploration" of the face, the response options (i.e., anger, disgust, fear, happiness, sadness, surprise and neutral) were added in a fixed order on the bottom of the screen and subjects were asked to choose among the 7 response options the one that better described the facial expression, by touching the desired response on the screen. There was no time limit for the response. The Presentation version 13.0 software and a TFT Monitor 19'' with touch screen (KTMT-1921-USB/B, Keytec) were used for stimuli presentation and behavioral response recording. The iView X™ Hi-Speed 1250 System, SensoMotoric Instruments, was used to record the eye movements during the first 3 seconds of each trial The behavioral responses were given by touch screen. The subject's score corresponded to the number of correct responses (i.e., emotional labeling of the picture). The fixation times were calculated for two regions of interest (ROI): eyes and rest of the face. Due to technical problems, oculomotor data were not collected during ERT performance of 3 MS patients.

Additionally, MS patients underwent a full neurological examination and a comprehensive neuropsychological evaluation (i.e., MMSE, Auditory Verbal Learning Test, Corsi-Block Test, Digit Span, Letter Word Fluency, Nine-Hole Peg Test, Sentence Repetition, and Wisconsin Card Sorting Test – Nelson's version) (for tests descriptions read: Strauss et al, 2006). During the neurological examination, the following data were collected: age at onset, disease duration, disease course, and degree of disability defined by EDSS (Kurtke, 1970). Due to logistic difficulties, only 48/56 MS patients underwent the comprehensive neuropsychological evaluation.

3. RESULTS

3.1 MS vs. HC

Table 1 shows that MS and HS were not significantly different on the demographic characteristics (i.e., gender, age, and education) and the visual perception abilities (i.e., BFRT). MS patients had higher depression scores on the HADS. However, the frequency of pathological anxiety (i.e., HADS – Anxiety =>11) and pathological depression (i.e., HADS – Depression =>11) were not statistically higher ($p>0.05$) for MS patients (respectively 21.4% and 8.9%) than HC subjects (respectively 8.9% and 5.4%). The groups' ERT – behavioral and ERT – oculomotor results are presented in Table 2. No significant differences were found.

Table 1. *MS and HC characteristics and test results.*

		MS	HC	*Chi-Square and Mann-Whitney*
Gender				
	Women	32 (57.1%)	31 (55.4%)	0.849
	Men	24 (42.9%)	25 (43.6%)	
Age		38.95 (10.34)	37.39 (10.57)	0.433
Education		13.21 (4.48)	13.77 (4.10)	0.497
BFRT		23.42 (2.11)	23.55 (2.33)	0.749
HADS				
	Anxiety	7.29 (4.31)	5.79 (3.35)	0.070
	Depression	4.48 (3.98)	2.91 (3.05)	0.018

Table 2. *ERT results*

	Behavioral			% fixation time in ROI – eyes		
	MS	HC	*Mann-Whitney*	MS	HC	*Mann-Whitney*
Anger	5.20 (1.15)	5.36 (0.94)	0.562	42.73 (22.13)	47.08 (20.54)	0.297
Disgust	5.61 (0.78)	5.70 (0.63)	0.720	37.30 (20.52)	41.18 (20.43)	0.265
Fear	4.21 (1.52)	4.45 (1.4)	0.458	42.72 (20)	44.52 (20.73)	0.658
Happiness	5.66 (0.84)	5.66 (0.66)	0.556	42.42 (21.36)	46.06 (22.01)	0.300
Neutral	4.84 (1.64)	5.02 (1.39)	0.585	45.19 (23.43)	49.09 (21.45)	0.347
Surprise	5.41 (1.02)	5.55 (0.71)	0.883	39.49 (21.64)	44.76 (21.33)	0.238
Sadness	4.66 (1.1)	4.93 (1.06)	0.182	46.35 (20.82)	46.44 (20.88)	0.686
Total	35.59 (5.29)	36.66 (4.11)	0.400	42.35 (20.47)	45.63 (20.11)	0.347

3.2 MS

MS patients' ERT – behavioral total score was significantly associated with age (r=-0.447), age at onset (r=-0.276), EDSS (r=-0.423), HADS – anxiety (r=-0.366), and HADS – depression (r=-0.348) scores. More accurate responses on the ERT were also related with better performance on every neuropsychological measure (Table 3). No significant associations were found with disease duration or with any of the

oculomotor measures (i.e., fixation time on the ROI – eyes, fixation time on the ROI – rest of the face, and percentage of fixation time on the ROI – eyes).

Multiple linear regression analyses were conducted with ERT – behavioral total score as the dependent variable. For the first analysis, the independent variables were: age, education, EDSS (<3 vs. =>3), MMSE, BFRT (<20 vs. =>20), HADS – anxiety (<11 vs. =>11), and HADS – depression (<11 vs. =>11). After applying the backward method and verifying the assumptions, the linear regression model was composed by the following variables: EDSS (β=-4.679; p<0.001), HADS – anxiety (β=-3.171; p=0.020), and HADS – depression (β=-4.226; p=0.033). These set of variables explained (R^2) 65% of the ERT – behavioral variance.

A series of multiple linear regression analyses were conducted using the following independent variables: age, education, EDSS (<3 vs. =>3), HADS – anxiety (<11 vs. =>11), HADS – depression (<11 vs. =>11), and one neuropsychological measure. No variable selection method was used. After verifying the assumptions, the following neuropsychological measures remained independently related to ERT – behavioral total score: Nine-Hole Peg Test– right hand (β=-0.121; p=0.048), Nine-Hole Peg Test – left hand (β=-0.114; p=0.042), and Wisconsin Card Sorting Test – categories (β=0.859; p=0.034), and Wisconsin Card Sorting Test – perseverative errors (β=-0.320; p=0.034).

MS patients' fixation time on the ROI – eyes (r=-0.337), fixation time on the ROI – rest of the face (r=0.348), and percentage of time in the ROI – eyes during the "free exploration" phase of ERT (r=-0.370) were only significantly (p<0.05) associated with EDSS. No significant associations were found between oculomotor measures and age, age at onset, HADS – anxiety, HADS – depression, or with any of the neuropsychological evaluation measures (Table 3).

Table 3. *Correlations between MS patients' ERT and neuropsychological results*

	ERT	
	Behavioral	% fixation time in ROI – eyes
Mini Mental State Examination	0.350 *	0.123
Nine-Hole Peg Test		
Right	-0.389 *	-0.020
Left	-0.444 **	-0.022
Digit Span	0.434**	-0.160
Corsi-Block Test	0.427**	-0.178
Benton Facial Recognition Test	0.342*	0.118
Auditory Verbal Learning Test		
Immediate Recall	0.421 **	0.241
30' Recall	0.431**	0.259
Sentence Repetition	0.343	0.001
Letter Word Fluency	0.381*	0.018
Wisconsin Card Sorting Test		
Categories	0.422**	-0.160
Perseverative errors	-0.406*	0.184

* p<0.05 **p<0.01

4. CONCLUSIONS

MS patients without significant cognitive impairments showed a relatively preserved ability to label emotional expressions, as suggested by a lack of significant differences between MS patients and HC subjects on the number of correct responses. These negative results are consistent with previous reports (Jenha et al, 2011a; Di Bitonto et al, 2011). Nonetheless, recent fMRI studies have documented functional imaging differences in MS patients during emotion recognition, in the context of normal behavioral scores (Passamonti et al, 2009; Jenha et al, 2011b). These findings suggest that early stages of MS do not have a major effect on the ability to recognize emotions. However, subtle emotion processing differences are likely to occur.

Similar to recent reports, MS patients' recognition of emotions in facial expressions was negatively associated with higher disability index (Prochnow et al, 2011). The fixation time in the eye region of faces, essential for normal recognition of certain emotions (Adolphs et al., 2005), was also significantly associated with neurological disability. It is reasonable to speculate that patients in more advanced stages of MS, who have increasing lesion burden and atrophy, would have impaired emotion recognition of facial expressions (Benedict et al, 2004; Jehna et al, 2011a).

Consistent with findings from other patient populations, negative mood was associated with poorer emotion recognition of facial expressions (Gur et al, 2011). Level of anxiety and depression, and degree of neurological disability explained approximately 65% of the total behavioral score on the ERT.

Similar to previous reports (Henry et al, 2009; Jehna et al, 2010), accurate recognition of facial expressions was related to a series of neuropsychological tests, including measures of psychomotor speed and executive functions. These associations were not dependent of age, education, anxiety, depression, or degree of neurological disability.

Disease severity, level of cognitive functioning, and mood states are important confounders in the study of emotional recognition of faces in MS. Future research studies ought to account for these dimensions.

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5. REFERENCES

Adolphs, R., Gosselin, F., Buchanan, T.W., Tranel, D., Schyns, P., and Damasio, A.R. (2005), A mechanism for impaired fear recognition after amygdala damage, *Nature*, 433, pp. 68-72.

Benedict, R.H., Carone, D.A., and Bakshi R. (2004), Correlating brain atrophy with cognitive dysfunction, mood disturbances, and personality disorder in multiple sclerosis. *J. Neuroimaging*. 14(3 Suppl), pp. 36S-45S.

Di Bitonto, L., Longato, N., Jung, B., Fleury, M., Marcel, C., Collongues, N., de Seze, J., and Blanc, F. [Reduced emotional reactivity to negative stimuli in multiple sclerosis preliminary results.]. *Rev Neurol* (Paris). 2011 Sep 7. [Epub ahead of print].

Frischer, J.M., Bramow, S., Dal-Bianco, A. et al (2009), The relation between inflammation and neurodegeneration in multiple sclerosis brains. *Brain*, 132, pp. 1175-1189.

Gur, R.C., Erwin, R.J., Gur, R.E., Zwil, A.S., Heimberg, C., and Kraemer, H.C. (1992). Facial emotion discrimination. II. Behavioral findings in depression. *Psychiatry Res.*, 42, pp. 241–51.

Henry, J. D., Phillips, L. H., Beatty, W. W., McDonald, S., Longley, W. A., Joscelyne, A., and Rendell, P. G. (2009), Evidence for deficits in facial affect recognition and theory of mind in multiple sclerosis, *J. Int. Neuropsych. Soc.*, 15, pp. 277–285.

Hogancamp, W.E., Rodriguez, M., and Weinshenker, B.G. (1997), The epidemiology of multiple sclerosis, *Mayo Clin. Proc.*, 72, pp. 871–878.

Jehna, M., Langkammers, C., Wallner-Blazck, M., Neuper, C., Loitfelder, M., Ropele, S., Fuchs, S., Khalil, M., Pluta-Fuerst, A., Fazekas, F., and Enzinger, C. (2011a), Cognitively preserved MS patients demonstrate functional differences in processing neutral and emotional faces, *Brain Imaging and Behavior*, Jun 9. [Epub ahead of print].

Jehna, M., Neuper, C., Ischebeck, A., Loitfelder, M., Ropele, S., Langkammer, C., Ebner, F., Fuchs, S., Schmidt, R., Fazekas, F., and Enzinger, C. (2011b), The functional correlates of face perception and recognition of emotional facial expressions as evidenced by fMRI, *Brain Res.*, 1393, pp. 73 – 83.

Jehna, M., Neuper, C., Petrovic, K., Wallner-Blazek, M., Schmidt, R., Fuchs, S., Fazekas, F., and Enzinger, C. (2010), An exploratory study on emotion recognition in patients with a clinically isolated syndrome and multiple sclerosis, *Clin. Neurol. Neurosurg.*, 112, pp. 482–484.

Krause, M., Wendt, J., Dressel, A., Berneiser, J., Kessler, C., Hamm, A. O., and Lotze, M. (2009), Prefrontal function associated with impaired emotion recognition in patients with multiple sclerosis, *Behav. Brain Res.*, 205, pp. 280–285.

Kurtke, J.F. (1970), Neurologic impairment in multiple sclerosis and disability status scale, *Acta Neurol. Scand.*, 46 (4), pp. 493-512.

Langdon, D.W. (2011), Cognition in multiple sclerosis, *Curr. Opin. Neurol.*, 24, pp. 244-249.

Passamonti, L., Cerasa, A., Liguori, M., Gioia, M.C., Valentino, P., Nisticò, R., Quattrone, A., and Fera, F. (2009), Neurobiological mechanisms underlying emotional processing in relapsing-remitting multiple sclerosis. *Brain*, 132, pp. 3380-3391.

Phillips, L. H., Scott, C., Henry, J. D., Summers, F., Whyte, M., and Cook, M. (2011), Specific Impairments of Emotion Perception in Multiple Sclerosis, *Neuropsychology*, 25, pp. 131–136.

Polman, C. H., Reingold, S., Edan, G. et al (2005), Diagnostic Criteria for Multiple Sclerosis: 2005 Revisions to the "McDonald Criteria*", Ann. Neurol.*, 58, pp. 840-846.

Prochnow, P., Donell, J., Schafer, R., Jorgens, S., Hartung, H.P., Franz, M., and Seitz, R. J. (2011), Alexithymia and impaired facial affect recognition in multiple sclerosis, *J. Neurol.*, 258 (9), pp.1683-1688.

Silva, A.M., Vilhena, E., Lopes, A., Santos, E., Gonçalves, M.A., Pinto, C., Moreira, I., Mendonça, D., and Cavaco, S. (2011). Depression and anxiety in a Portuguese MS population: associations with physical disability and severity of disease. *J Neurol Sci*., 306, pp. 66-70.

Strauss, E., Sherman, E.M.S., and Spreen, O. (2006), *A Compendium of Neuropsychological Tests: Administration, Norms, and Commentary*. Third Edition. New York: Oxford University Press.

Tottenham, N., Tanaka, J.W., Leon, A.C., McCarry, T., Nurse, M., Hare, T.A., Marcus, D.J., Westerlund, A., Casey, B.J., and Nelson, C. (2009), The NimStim set of facial expressions: Judgments from untrained research participants, *Psychiatry Res.*, 168, pp. 242–249.