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The association of pathological laughing and crying and cognitive impairment in multiple sclerosis☆

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ABSTRACT

Background: Pathological laughing and crying (PLC) is common in multiple sclerosis (MS), defined as emotional expression that is exaggerated/incongruent with underlying mood. In other neurological disorders, PLC is associated with cognitive impairment (CI). Few studies have examined this relationship in MS.
Objective: To determine the association between PLC and CI in an MS population.
Methods: Retrospective chart review study of 153 MS subjects assessed in an outpatient clinic for CI. Data was collected on the minimal assessment of cognitive function in MS (MACFIMS), the Center for neurological study-lability scale (CNS-LS), a screening measure for PLC symptoms and the hospital anxiety and depression scale (HADS). Analyses of covariance compared performance on the MACFIMS between PLC (CNS-LS score ≥ 17, HADS-D ≤ 7) and non-PLC groups.
Results: MS subjects positive for PLC on the CNS-LS but without depression had lower scores on the controlled oral word association test, a measure of verbal fluency, and the California verbal learning test — 2 immediate recall score, a verbal memory measure.
Conclusions: This study demonstrates a connection between CI, specifically verbal fluency and verbal learning, and PLC in MS subjects. Further studies are warranted to explore the causative relationship between CI and PLC.

1. Introduction

Pathological laughing and crying (PLC), also referred to as pseudobulbar affect, is an emotional expression that is exaggerated and incongruent with underlying mood state [1]. PLC diagnosis requires patients on multiple occasions to display loss of emotional control expressed as repeated episodes of excessive laughter and/or crying in response to non-specific stimuli with lack of an associative, matching mood state [2,3]. People with PLC report impaired social and role functioning, reduced overall mental health and reduced overall quality of life [4]. PLC is known to occur in 10–29% of persons with multiple sclerosis (MS) [2,5]. PLC tends to occur during the later stages of MS, often more than 10 years after diagnosis, and is often associated with more physical disability [2,6].

PLC has been associated with cognitive deficits among populations with neurological disorders. Patients with amyotrophic lateral sclerosis (ALS) and PLC tend to show more errors on the Wisconsin card sort task, a measure of frontal lobe function [7]. Similarly, stroke patients with PLC have shown impairment on measures of selective attention and executive function, as demonstrated by the Stroop color–word test [8]. Cognitive impairment(CI) is also common in MS, with prevalence estimates ranging from 40–65% of MS patients commonly involving information-processing speed, working memory, and episodic memory, and less frequently, executive function and verbal fluency [9–11]. Yet, few studies to date have examined the relationship between PLC and CI in the MS population. Both PLC and CI are associated with poorer reported quality of life [12–14]. Thus it is imperative to gain a better understanding of the relationship between these symptoms in order to better address them and to enhance prognostic accuracy. Therefore, the aim of this retrospective study was to determine the association between PLC and CI in an MS cohort, using a screening test called the Center for Neurological Studies Lability Scale (CNS-LS) [4,15]. Although the CNS-LS has been validated among MS populations, and found to reliably identify people with PLC symptoms, critiques over the use of screening measures confounding PLC with other mood disorders have been raised

Abbreviations: BVMTR, brief visual memory test — revised; CI, cognitive impairment; CNS-LS, Center for; COWAT, neurological study - lability scale oral word association test; CVLT2, California verbal learning test 2nd edition; DKEFS, Delis–Kaplan executive function system; EDSS, expanded disability status scale; FSS, fatigue severity scale; HADS, hospital anxiety and depression scale; JLO, judgment of line orientation; MACFIMS, minimal assessment of cognitive function in MS; MS, multiple sclerosis; PASAT, paced auditory serial addition test; PLC, pathological laughing and crying; SDMT, symbol digit modalities test; PASAT, paced auditory serial addition test.

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[2,4,15]. In populations with ALS, CNS-LS score has previously been associated with depressive symptoms, however the effect of depressive symptoms accounted for only 6% of variance [15]. Thus this study also aimed to examine the association between PLC and CI while accounting for this issue.

2. Methods

This is a retrospective chart review study of an outpatient population assessed in the MS Cognitive Clinic in London (ON), Canada between February 2011 and May 2015, for cognitive complaints, brought to medical attention by the patient, family members or the referring clinician. Subjects were included if they had a confirmed diagnosis of MS according to 2010 McDonald criteria [16], were between the ages of 18 and 59, and had been assessed with minimal assessment of cognitive function in MS (MACFIMS) battery [10,17], the CNS-LS and the hospital anxiety and depression scale (HADS) [18]. Subjects were excluded if they had other psychiatric disorders such as bipolar disorder or schizophrenia, or reported significant marijuana use (daily).

2.1. Measures

The CNS-LS [4] is a seven-item self-report measure examining symptoms of PLC over the last week. Sample items include, "I find that even when I try to control my laughter, I am often unable to do so" and "I find that I am easily overcome by laughter". Participants respond on a scale from 1 (Applies never) to 5 (Applies most of the time) for a maximum score of 35, and a minimum score of 7. It has been validated for use among MS patients; a score of 17 or greater has shown sensitivity and specificity for the presence of PLC [4]. The MACFIMS battery was developed by consensus of a committee to evaluate the common cognitive domains affected in MS patients and found to be both valid and reliable in the MS population [10,17]. This battery consists of the following neuropsychological tests: 1) judgment of line orientation (JLO) [19]: a measure of visual/spatial perception; 2) controlled oral word association test (COWAT) [20]: a measure of generative verbal fluency; 3) California verbal learning test 2nd edition (CVLT2) [21]: a measure of auditory/verbal episodic memory; 4) brief visual memory test – revised (BVMTR) [22]: a measure of visual/spatial memory; 5) Rao's version of the paced auditory serial addition test (PASAT) [23,24]: a measure of speed and working memory in the auditory domain; 6) Rao's (verbal) symbol digit modalities test (SDMT) [23,25]: a measure of processing speed; and 7) DKEFS sorting test [26]: a measure of higher executive function. In addition, in this clinic, the Stroop color–word test, a measure of selective attention validated in the MS population, was also administered [27]. As recommended by the MACFIMS consensus statement, measures of mood symptoms are also administered, specifically the HADS. The HADS is a sensitive and specific measure of major depression and general anxiety validated in MS, with a score of 8 or above on either the depression scale (HADS-D) or anxiety scale (HADS-A) indication of the presence of that symptom [18]. In addition to these measures, charts were reviewed for demographic information including age, sex, years since MS diagnosis and expanded disability status scale (EDSS) score [28].

2.2. Statistical analysis

To examine the relationship between scores on the CNS-LS and MS characteristics or demographics, Pearson's correlations and chi-square tests were run for continuous and categorical variables respectively. Participants were then separated into PLC and non-PLC groups to examine group differences in demographic variables as well as MACFIMS performance through a series of t-tests and chi-square tests. Tests were run twice using two sets of criteria for PLC group membership. Firstly, anyone scoring 17 or higher on the CNS-LS was included in the PLC group in accordance with established test norms among the MS population [4]. Comparisons between PLC (CNS-LS score ≥ 17) and non-PLC groups on cognitive test performance used analyses of covariance (ANCOVA) to compare performance on the MACFIMS controlling for potential confounding variables. p values were not adjusted for multiple comparisons as the goal of analysis was largely exploratory. In the second analysis, more stringent criteria for inclusion in the PLC group were used to control for incongruity between expressed and experienced emotions consistent with the suggestions of Feinstein et al. [2]. Validation studies in an MS population indicate a score of 8 on the HADS depression scale is an efficient screen for clinical depression [18], thus to ensure the PLC group performance on cognitive tests was not influenced by depression symptoms, people were included in the PLC group for the second set of analyses if they both scored 17+ on the CNS-LS and scored below 8 on the HADS depression scale. Comparisons between PLC (CNS-LS score ≥ 17 and HADS-D ≤ 7) and non-PLC groups on cognitive test performance used analyses of covariance (ANCOVA) controlling for years of education, HADS depression score, and HADS anxiety score.

3. Results

In total, 153 subjects were identified and included in the study (Table 1). The majority of the sample were female (n = 119, 77.8%) and Caucasian (137, 89.5%) with an average age of 45.6 (±8.1) years, and 13.8 (±2.0) years of education. Regarding MS characteristics, the majority 113 (73.9%) had a relapsing–remitting MS course. Median expanded disability status scale (EDSS) score was 3.0 (0–8), participants had MS for an average of 11.3 (±7.9) years; 84 (54.9%) of the sample was on a disease modifying therapy to treat their MS.

CNS-LS was found to be significantly correlated with years of education ($r(153) = -0.26$, $p = 0.001$). CNS-LS scores were also found to be significantly correlated with the HADS depression subscale ($r(149) = 0.39$, $p < 0.001$) and anxiety subscale ($r(149) = -0.36$, $p < 0.001$). No other significant relationships were found between CNS-LS scores and demographics or MS characteristics. CNS-LS scores were negatively correlated with performance on the COWAT ($r(151) = -0.22$, $p = 0.003$), BVMTR immediate recall (IR), ($r(152) = -0.13$, $p = 0.049$ BVMTR delayed recall (DR) ($r(152) = -0.17$, $p = 0.016$), PASAT 3.0 ($r(152) = -0.14$, $p = 0.041$), DKEFS card sort ($r(152) = -0.17$, $p < 0.05$), DKEFS card sort description, ($r(152) = -0.19$, $p = 0.01$), and Stroop score ($r(148) = -0.21$, $p = 0.006$).

Table 1
Demographics of the study sample.

Demographics	
Age (years)	
Mean ± SD	45.6 ± 8.1
Range	21.0–58.0
Gender # (%)	
Female	119.0 (77.8%)
Ethnicity # (%)	
Caucasian	137.0 (89.5%)
Other	16.0 (10.5%)
Education (years)	
Mean ± SD	13.8 ± 2.0
Range	8.0–22.0
MS course # (%)	
Relapsing–remitting	113.0 (73.9%)
Secondary progressive	32.0 (20.9%)
Primary progressive	8.0 (2.5%)
EDSS*	
Median	3.0
Range	0.0–8.0
Disease duration	
Mean ± SD	11.3 ± 7.9
Range	0–35
Disease modifying therapy # (%)	
Yes	84.0 (54.9%)

* Expanded disability status scale.