



# Impaired Perception of Emotional Expression in Amyotrophic Lateral Sclerosis

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**Background and Purpose** The increasing recognition that deficits in social emotions occur in amyotrophic lateral sclerosis (ALS) is helping to explain the spectrum of neuropsychological dysfunctions, thus supporting the view of ALS as a multisystem disorder involving neuropsychological deficits as well as motor deficits. The aim of this study was to characterize the emotion perception abilities of Korean patients with ALS based on the recognition of facial expressions.

**Methods** Twenty-four patients with ALS and 24 age- and sex-matched healthy controls completed neuropsychological tests and facial emotion recognition tasks [ChaeLee Korean Facial Expressions of Emotions (ChaeLee-E)]. The ChaeLee-E test includes facial expressions for seven emotions: happiness, sadness, anger, disgust, fear, surprise, and neutral.

**Results** The ability to perceive facial emotions was significantly worse among ALS patients performed than among healthy controls [ $65.2 \pm 18.0\%$  vs.  $77.1 \pm 6.6\%$  (mean  $\pm$  SD),  $p=0.009$ ]. Eight of the 24 patients (33%) scored below the 5th percentile score of controls for recognizing facial emotions.

**Conclusions** Emotion perception deficits occur in Korean ALS patients, particularly regarding facial expressions of emotion. These findings expand the spectrum of cognitive and behavioral dysfunction associated with ALS into emotion processing dysfunction.

**Key Words** amyotrophic lateral sclerosis, emotion, emotion perception, facial expression, frontotemporal dementia.

## INTRODUCTION

A continuum between amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD) in connection with cognitive and behavioral changes has been proposed based on reported frontal or executive dysfunctions, which has been associated with prefrontal dysfunctions in a significant proportion of patients with ALS.<sup>1-5</sup> Besides the cognitive and behavioral changes in ALS, emotional and social cognition has recently become a focus of ALS research.<sup>6-9</sup> In a clinical situation, deficits in these abilities may develop early in the disease process and hinder diverse social activity decrease their quality of life, increase caregiver burden, and aggravate mood and behavioral disturbances.<sup>10-12</sup> Emotional and social cognition in ALS has paid relatively little attention, with few studies investigating deficits in these abilities in ALS, and the obtained results have also been inconsistent. However, several studies of emotion perception, processing, and memory have revealed that these functions might play a role in discriminating or classifying ALS with FTD from pure ALS.<sup>8</sup> In terms of the spectrum of neuropsychological dysfunction, investigations about emotion processing abilities, as well as cognitive or behavioral features, are important for understanding the

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heterogeneity of neuropsychological function in ALS and for managing these patients.<sup>1,4,7,11</sup>

This study was designed to examine emotion perception impairments regarding facial expressions in Korean ALS patients and to investigate how those impairments are related to neuropsychological and clinical factors.

## METHODS

### ALS patients

Twenty-four ALS patients were recruited consecutively from the Motor Neuron Disease Clinic in the Neurology Department of Hanyang University Hospital in Seoul, Korea between November 2013 and April 2014. All subjects fulfilled the revised El Escorial criteria for clinically probable, probable-laboratory-supported, or definite ALS.<sup>13</sup> Exclusion criteria included a history of other neurological conditions that could affect cognition (e.g., major stroke, traumatic brain injury, learning disability, or severe active epilepsy), alcohol dependence, severe active mental illness and the use of high-dose psychoactive medication, illiteracy, and serious motor or sensory deficits that hamper the administration of neuropsychological tests.<sup>3</sup> None of the ALS patients had received gastrostomies or noninvasive ventilation, and patients with severe respiratory failure [forced vital capacity (FVC) <40%] were also excluded.

The healthy control group consisted of 24 participants and included family members and friends of the ALS participants as well as visitors from the local community center. Exclusion criteria included the presence of any neuropsychiatric disorder, positive findings in a neurological examination, or a Mini Mental State Examination (MMSE) raw score of <26 (out of 30). None of the healthy controls were taking any medication that interfered with neuropsychiatric function.

All subjects gave informed written consent, and the experimental procedure was approved by the Institutional Review Board of Hanyang University Hospital.

### Clinical measures

The clinical measures included demographic data [including age, sex, education, region of symptom onset, disease duration (duration from symptom onset to time of diagnosis)], ALS Functional Rating Scale-Revised (ALSFRS-R) score (range, 0–48; normal, 48) for the severity of ALS-related motor disability,<sup>14</sup> breathing capacity (predicted FVC percentage), and progression rate [(48-ALSFRS-R score)/(disease duration in months)].<sup>3,15</sup>

### Neuropsychological assessment

All participants were tested by applying the Korean version

of the MMSE (K-MMSE),<sup>16</sup> the Beck Depression Inventory (BDI),<sup>17</sup> and the Frontal Assessment Battery (FAB)<sup>18</sup> to examine their general neuropsychological function. A comprehensive neuropsychological assessment was performed only for ALS patients, using a previously published protocol.<sup>3</sup>

### Measures of emotional expression perception

The tests of emotional expression perception used materials derived from ChaeLee Korean Facial Expressions of Emotion (ChaeLee-E) images, which have been validated in previous studies involving Koreans.<sup>19</sup> The same facial emotion perception task was administered to all participants. Randomly selected images of facial expressions from ChaeLee-E were displayed on a screen. There were 126 images from each of 7 emotional expressions in 9 men and 9 women. Subjects were asked to select or provide an emotion label for each facial expression, with the images remaining on the screen during the entire experiment. Patients were allowed sufficient time to label each emotion. The subject selected one emotion from the following seven choices included in ChaeLee-E: happiness, sadness, anger, surprise, disgust, fear, or neutral. Immediately prior to testing, we ensured that the patients and healthy control subjects semantically understood the seven words.

The scores derived included an overall percentage of correctly perceived emotions, as well as the correct perception of each individual emotion. We also examined the distribution of scores obtained by ALS patients and healthy controls in the ChaeLee-E tests and the number of patients obtaining “impaired” scores (i.e., scores at or below the fifth percentile of the scores for controls) on measures of emotion perception.

### Statistical analysis

The demographic characteristics and scores on the ChaeLee-E tests were compared between ALS patients and control subjects using the Mann-Whitney U test or Fisher’s exact test. The association between measured profiles and the ChaeLee-E test scores of ALS patients was examined by both simple and multiple linear regression. The cutoff for significance was set at  $p < 0.05$ . Statistical analysis was carried out with SPSS (version 18, SPSS, Chicago, IL, USA).

## RESULTS

### Demographic and clinical characteristics of the participants

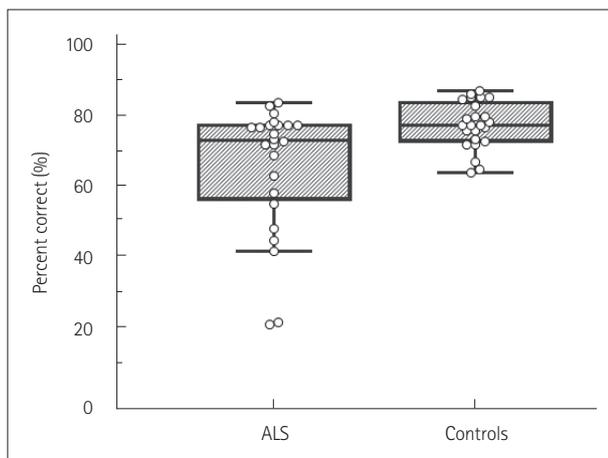
At the time of evaluation, the ALS patients and healthy controls did not differ in age [ $56.3 \pm 9.9$  years vs.  $51.0 \pm 11.1$  years (mean  $\pm$  SD),  $p = 0.170$ ], sex (50% males in both groups), or level of education ( $11.2 \pm 4.6$  years vs.  $13.1 \pm 2.8$  years,  $p = 0.171$ ) (Table 1). The K-MMSE and FAB scores were significantly

**Table 1.** Characteristics of the amyotrophic lateral sclerosis (ALS) patients and healthy controls

	ALS (n=24)	Controls (n=24)	<i>p</i>
Age at evaluation, years	56.3±9.9	51.0±11.1	0.170
Male, <i>n</i> (%)	12 (50.0)	12 (50.0)	1
Education, years	11.2±4.6	13.1±2.8	0.171
K-MMSE score	26.9±2.7	28.8±1.2	0.002
FAB score	13.0±4.0	16.0±3.7	<0.001
BDI score	18.8±10.3	11.0±7.7	0.004
Age at symptom onset, years	55.1±9.8	-	-
Bulbar onset, <i>n</i> (%)	9 (37.5)	-	-
ALSFRS-R score	40.0±3.3	-	-
Disease duration, months	14.6±6.7	-	-
Progression rate	0.63±0.31	-	-

Data are mean±SD values except where indicated otherwise. Disease duration, time from symptom onset to evaluation, Progression rate, estimated from the decrease in ALSFRS-R score subsequent to symptom onset [(48-ALSFRS-R)/(disease duration in months)].

ALSFRS-R: ALS Functional Rating Scale-Revised, BDI: Beck Depression Inventory, FAB: Frontal Assessment Battery, K-MMSE: Korean version of the Mini Mental State Examination.

**Fig. 1.** Distribution of scores on the ChaeLee Korean Facial Expressions of Emotions test between amyotrophic lateral sclerosis (ALS) patients and healthy controls.

lower for patients than for controls (K-MMSE, 26.9±2.7 vs. 28.8±1.2,  $p=0.002$ ; FAB, 13.0±4.0 vs. 16.0±3.7,  $p<0.001$ ), and BDI scores were higher for patients than for controls (18.8±10.3 vs. 11.0±7.7,  $p=0.004$ ).

The ALS patients had been diagnosed 14.6±6.7 months prior to the commencement of this study (range, 4–45 months) and had relatively mild physical impairments (ALSFRS-R score=40.0±3.3).

## Emotion perception results

### Overall emotion perception

The analysis of overall emotions indicated that the percent-

**Table 2.** Percentage of correct responses for perceived facial emotions in ALS and healthy control subjects

Emotion	ALS (n=24)	Controls (n=24)	<i>p</i>
Happiness	94.0±12.0	96.8±7.1	0.331
Sadness	78.5±22.5	89.8±9.8	0.066
Fear	26.6±18.7	35.0±19.5	0.136
Anger	63.9±28.7	80.8±11.1	0.035
Disgust	43.5±25.9	59.7±16.7	0.035
Surprise	65.0±23.4	81.9±15.0	0.004
Neutral	85.2±28.6	95.4±9.6	0.204
Total	65.2±18.0	77.1±6.6	0.009

Data are mean±SD percentage values.

ALS: amyotrophic lateral sclerosis.

age of correct answers was significantly lower for patients (65.2±18.0%) than for controls (77.1±6.6%,  $p=0.009$ ). Eight of the 24 patients (33%) scored below the 5th percentile score of healthy controls in recognizing facial emotions ( $p=0.072$ , Fisher's exact test) (Fig. 1).

### Individual emotion perception

The analysis of individual emotions indicated significant differences between patients and controls in the percentages of correct answers for anger ( $p=0.035$ ), disgust ( $p=0.035$ ), and surprise ( $p=0.004$ ) emotions, but not for happiness ( $p=0.331$ ), sadness ( $p=0.066$ ), fear ( $p=0.136$ ), or neutral ( $p=0.204$ ) emotions (Table 2).

### Factors associated with emotion perception functioning

Simple and multiple linear regression analyses were performed to examine the associations between emotion perception and clinical factors. In simple regression, younger age at the time of evaluation ( $p=0.001$ ), higher education level ( $p=0.046$ ), higher K-MMSE score ( $p<0.001$ ), lower BDI score ( $p=0.001$ ), and higher FAB score ( $p<0.001$ ) were associated with better emotion perception, whereas sex, bulbar onset, ALSFRS-R score, and progression rate were not associated with the ability to perceive emotions. In the multivariable regression analysis, there were no associations between clinical factors and emotion perception with the exception of FAB score ( $\beta=3.329$ ,  $p=0.015$ ) (Table 3).

## DISCUSSION

This study has demonstrated for the first time the presence of an emotion perception deficit in Korean ALS patients. The findings suggest that emotion perception deficits occur in approximately one-third (33%) of Korean ALS patients, and particularly affect the perception of emotional facial expres-

**Table 3.** Factors associated with emotion perception deficits identified in simple and multiple linear regression analyses of ALS patients

Variable	Simple linear regression			Multiple linear regression		
	$\beta$	SE	<i>p</i>	$\beta$	SE	<i>p</i>
Age at evaluation	-0.658	0.180	0.001*	0.063	0.417	0.882
Male	-1.620	4.283	0.707	5.879	5.755	0.324
Bulbar onset	9.012	7.532	0.244	0.418	5.650	0.942
Education, years	1.097	0.535	0.046*	-0.382	0.673	0.580
K-MMSE score	4.678	0.663	<0.001*	1.694	1.450	0.262
FAB score	2.295	0.403	<0.001*	3.329	1.206	0.015*
BDI score	-0.671	0.197	0.001*	-0.209	0.388	0.599
ALSFRS-R score	-0.828	1.143	0.476	-0.882	1.001	0.393
Progression rate	-4.581	12.217	0.711	2.739	11.342	0.813

Multiple linear regression analysis was performed using the enter method.

\*Significant results.

ALS: amyotrophic lateral sclerosis, ALSFRS-R: ALS Functional Rating Scale-Revised, BDI: Beck Depression Inventory, FAB: Frontal Assessment Battery, K-MMSE: Korean version of the Mini Mental State Examination.

sions. Perceptions of anger, disgust, and surprise emotions—but not those of happiness, sadness, fear, or neutral emotions—were significantly impaired in the ALS patients, and these impairment were associated with poor FAB scores. Compared with age- and sex-matched healthy control subjects, ALS patients had lower K-MMSE and FAB scores and higher BDI scores, indicating the presence of impairment in cognitive abilities and depressive symptoms in a typical group of patients with ALS. These findings expand the spectrum of narrow cognitive dysfunction into broader neuropsychological dysfunction, which includes depressive features and emotional cognition.

Previous studies on emotional perception including social and emotional cognition have showed inconsistent data, although most studies have found deficits in nondemented or FTD-combined ALS patients.<sup>8,9,20,21</sup> Interestingly, the present study showed that significant emotional perception deficits were found regardless of severity of cognitive dysfunction in the patients with ALS (Mann-Whitney U test,  $p=0.066$ ). However, the small number of ALS subjects in the present study may make it difficult to correctly interpret the results.

Of the facial expressions for basic emotions, the perceptions of anger, disgust, and surprise emotions were impaired in ALS patients compared with healthy controls. The neural substrate for perceiving these emotions is associated with the orbitofrontal region and amygdala,<sup>22</sup> although the findings have been inconsistent. Previous review has explained that negative emotions such as anger, disgust, and fear are commonly affected in FTD.<sup>22</sup> Another study of the perception of facial emotional expressions in frontal-variant FTD showing that the ability to recognize happiness, sadness, anger, and disgust emotions were significantly impaired compared with a control group, whereas the fear and surprise recognition abilities were not significantly affected.<sup>23</sup> These selective im-

pairments in recognizing facial expressions have not been consistently reportedly. The presence of emotion perception deficits in ALS is probably related to the degree of underlying dysfunction in the frontal and temporal lobes, since these structures are known to be crucial in the processing of social and emotional signals.<sup>8,24</sup> In the present study these emotion perception deficits were associated with FAB scores, which preferentially evaluate frontal functions, but not with K-MMSE scores, which preferentially evaluate the cognitive defects of Alzheimer's disease and are less sensitive to frontal executive function.<sup>25</sup> In addition, ALS-related clinical factors such as the ALSFRS-R score, progression rate, and bulbar onset were not associated with emotion perception deficits. Therefore, these findings support the idea that emotional cognition is associated with the functioning of frontal circuits rather than classical motor involvement in ALS, and that frontal dysfunction in ALS may be responsible for the emotion perception deficit.

The association between the ability to perceive emotional expression and the presence of depression is inconsistent.<sup>7,26,27</sup> Some reports have explained that depression can impair the ability to recognize facial emotion expressions.<sup>26</sup> These explanations supporting a similar association between depression and emotion perception were based on findings obtained using a simple linear regression model. However, some studies have found no significant association between depression and emotion processing in ALS.<sup>7,27</sup> Also, in the present study we found no relationship between either function in the multiple linear regression model. While the results are currently inconsistent, it appears that an association between emotion perception ability and depression is necessary to explain a neurodegenerative condition such as ALS or a patients' adjustment, and so a more sophisticated explanation specific to ALS is needed.<sup>27</sup>

The present study has also revealed for the first time that emotion perception deficits are present in Korean ALS patients. Since ethnic and genetic differences influence emotion regulation, differences in genetic characteristics between Korean and non-Asian populations and the subsequent disparity of combined ALS and FTD<sup>1,3,28-30</sup> might affect impairments of emotional cognition, although no comparison has been performed. Despite some limitations regarding the presence of dementia in the present study population, previous studies of emotion perception found that negative perceptions of sadness, disgust, anger, and surprise emotions were impaired in ALS patients compared with healthy controls.<sup>8,9,20</sup> In addition, the perception deficits for individual emotions in our study were similar to the perception deficits for anger, disgust, and surprise emotions, but not for sadness, happiness, fear, or neutral emotions. Because neuroanatomical evaluations were not performed in this study, it is difficult to correlate the identified emotion perception deficits with specific brain structures. Although neural substrates implicated in emotion recognition have not been fully investigated, substrates such as the prefrontal cortex, insula, and amygdala are known to be associated with emotional recognition, and there is considerable overlap across different emotions.<sup>22</sup> The emotion perception deficits found in the present study could be associated with the insula, orbitofrontal cortex, amygdala, and superior temporal gyrus;<sup>22</sup> however, further neuroimaging studies are needed to identify the relationship between emotional deficits and their neural substrates. In the labeling tasks applied in this study, the label for fear was more ambiguous than the other labels, and it could easily be confused with surprise;<sup>31</sup> therefore, any metrics associated with the perceptions of fear and surprise need to be interpreted cautiously.

This study had some limitations that should be evaluated in further research. First, many instrumental tasks can be used to assess emotional and social cognition, other than perceptions of emotional facial expressions; therefore, further research utilizing tasks that have been validated in Asian and Korean patients are needed to comprehensively evaluate emotional and social cognition. Second, although this study is a small number of ALS subjects, analyses in which subjects are divided into nondemented and demented ALS groups using the consensus criteria<sup>5</sup> might differentiate subtle early symptoms from full-blown emotional cognition in the two groups. Third, the absence of neuroimaging results limited the ability to identify associations between emotion perception deficits and neural substrates. Crespi et al.<sup>32</sup> recently described a neural correlate of emotion recognition impairment in ALS patients using diffusion-tensor imaging, with their results suggesting that frontotemporal-limbic microstructural changes are present in socioemotional impairment in ALS.

Further neuroanatomical studies aimed at identifying and correlating microstructural changes are needed.

Our findings support the heterogeneity of neuropsychological involvement in ALS. The patients in the ALS group showed impairment in perception measures of emotional expression. Therefore, screening for these emotional deficits will help clinicians to understand the neuropsychological features of ALS. Further research into the perception impairment associated with specific individual emotions and the related neural substrates is needed to determine the changes in emotional functioning in this population and their implications for clinical management.<sup>27</sup>

#### Conflicts of Interest

The authors have no financial conflicts of interest.

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