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# SUBJECTIVE COGNITIVE AND BEHAVIORAL SYMPTOMS IN ALS: TOWARD EARLIER DETECTION

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## INTRODUCTION

The identification of **subjective cognitive decline** (**SCD**) and **subjective behavioral changes** (**SBC**) has been overlooked in ALS, despite their potential as early markers of **mild cognitive impairment** (**MCI**) and **mild behavioral impairment** (**MBI**) seen in other neurodegenerative diseases. Detecting these in ALS is crucial for better understanding the progression, from subjective decline to mild impairment and, eventually, dementia.

## OBJECTIVES

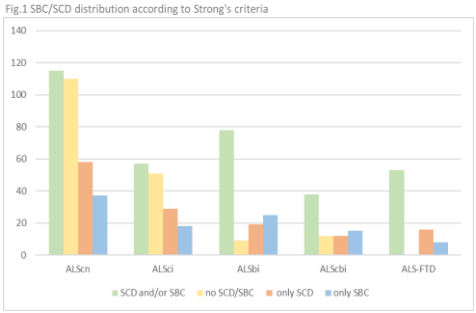
To describe the occurrence of **SCD** and **SBC** and their association with **neuropsychological profiles**.

## METHODS

The study included 523 people with ALS. SCD was identified when patients or caregivers reported declines in **memory**, **language**, **attention**, or **decision-making** abilities. SBC was defined as any spontaneously reported behavioral changes including **apathy**, **loss** of **empathy/sympathy**, **disinhibition**, **ritualistic behaviours**, and **appetite**. Mood alterations and emotional lability did not contribute to the SBC definition. Sleep disturbances, learning disorders, and premorbid psychiatric conditions were also collected (**Fig. 2**). Patients were categorized based on the presence of SCD/SBC (**Table 1**) and on **cognitive and/or behavioral impairments** (**ALSimp**), as defined by Strong criteria (**Fig. 1**).

| Table 1 | ALL PATIENTS | PRESENCE OF SCD AND/OR SBC | ONLY SCD | ONLY SBC | NO SCD-SBC |
|---|---|---|---|---|---|
| **No.** | 523 | 341 (65%) | 134 (25%) | 103 (20%) | 182 (35%) |
| **Clinical data** | | | | | |
| ALS / PLS/ | 487/36 | 316/25 | 125/9 | 93/10 | 171/11 |
| ALS spinal/ ALS bulbar | 361/126 | 230/86 | 92/33 | 70/23 | 131/40 |
| CN/ CI / BI / CBI / FTD | 225/108/87/50/53 | 115/57/78/38/53 | 58/29/19/12/16 | 37/18/25/15/8 | 110/51/9/12/0 |
| Disease duration (mths) | 22.5 (22.6) | 23.1 (22.6) | 23.1 (24) | 22.1 (21.5) | 21.5 (22.7) |
| ALSFRS-R total | 39.15 (5.8) | 39.16 (5.8) | 39.16 (5.8) | 39.09 (5.8) | 39.13 (5.8) |
| **Demographical data** | | | | | |
| male / female | 289/234 | 199/142 | 69/65 | 68/35 | 92/90 |
| Years of age | 61.9 (10.9) | 62.7 (10.7) | 64.1 (10.2) | 60.3 (11.7) | 60.4 (11.1) |
| Education (age) | 12.1 (13) | 12.0 (4.65) | 12.0 (4.72) | 11.7 (4.25) | 12.1 (3.89) |

Fig.1 SBC/SCD distribution according to Strong's criteria



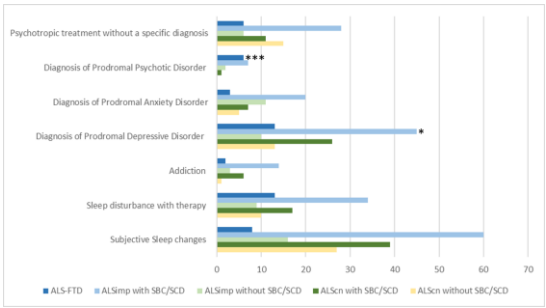

## RESULTS

According to Strong et al.'s criteria, 43% of patients showed a normal cognitive profile (ALScn), 48% were classified as ALSimp, and 9% met criteria for ALS-FTD. Interestingly, **25% of patients showed SCD, 20% SBC, and 20% exhibited both** (**Table 1**). The most common SCD issues were **memory and language impairments** (**Table 2**), while **irritability and apathy** were the most frequent SBC (**Table 3**). In relation to the Strong classification, 50% of ALScn patients and 70% of ALSimp patients were found to exhibit SBC/SCD. (**Fig. 3**). In the ALScn and ALSimp groups, the only differences between patients with and without SBC/SCD were **higher** levels of **depression** and **behavioral changes** (**Fig. 4**), including apathy, while demographic and cognitive performance were similar.

**Prodromal depressive disorders** were more common in ALSimp with SBC/SCD, while **prodromal psychotic disorders** were more prevalent in ALS-FTD (**Fig. 2**).

| Table 2 SCD | Reported by patients | Reported by caregivers | Table 3 SBC | Reported by patients | Reported by caregivers |
|---|---|---|---|---|---|
| Memory | 141 (27%) | 106 (20%) | Irritability | 35 (6%) | 122 (23%) |
| Language | 106 (20%) | 56 (10%) | Apathy | 17 (3%) | 86 (16%) |
| Attention | 58 (11%) | 33 (6%) | Obsession/ perseveration | 3 (.3%) | 10 (1%) |
| Calculation | 4 (.7%) | 3 (.5%) | Disinhibition | 3 (.5%) | 23 (4%) |
| Reading/writing | 1 (.1%) | 1 (.1%) | Psychosis | 2 (.3%) | 15 (2%) |
| Disorientation | 2 (.3%) | 33 (6%) | Loss of insight | - | 9 (1.7%) |
| Executive function | 4 (.7%) | - | | | |
| Apraxia | - | 1 (.1%) | | | |

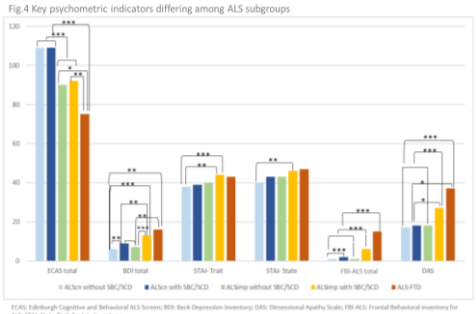
Fig. 2 Occurrence of mental health risk factors across ALS subgruops




## CONCLUSION

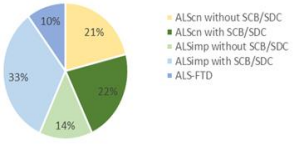
SBC and SCD were observed in **65%** of patients with ALS, with **22%** having isolated subjective symptoms but normal profile. Including SBC and SCD in diagnostic criteria allowed for the diagnosis of **MCI and/or MBI in 33%** of patients with **ALS,** indicating the need for ongoing monitoring. Behavioral changes and depressive mood are early indicators of extra-motor involvement. These findings underscore **the need to assess SCD and SBC as part of neuropsychological evaluations**, in order to enhance patient stratification and optimize care.

Fig.4 Key psychometric indicators differing among ALS subgroups




ECAS: Edinburgh Cognitive and Behavioral ALS Screen; BDI: Beck Depression Inventory; DAS: Dimensional Apathy Scale; FBI-ALS: Frontal Behavioral Inventory for ALS; STAI: State-Trait Anxiety Inventory

Fig. 3 Spectrum of cognitive and behavioral disorders in ALS (N = 523)




Spectrum of cognitive and behavioral disorders in ALS (N = 523) including mood alteration in SCB/SCD