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Language impairments in Amyotrophic Lateral Sclerosis/Motor Neuron Disease (ALS/MND)

Abstract

We review 6 papers on Motor Neuron Disease (MND) and language impairments. ALS/MND (Amyotrophic Lateral Sclerosis/MND) is an wide-ranging term used to cover several derangements of the motor neurons. ALS/MND brings to progressive degeneration of the motor neurons. The motor neurons control the muscles that consent us to move and act.

Until some years ago, ALS/MND was thought not to affect language and higher-order cognitive functions, but at present it is acknowledged that about 3-5% of patients affected by ALS/MND show cognitive impairments. Up to date, it is not possible to establish whether this subgroup is affected by ALS/MND and Fronto-Temporal Dementia (FTD) or FTD/Aphasia syndrome or whether FTD/aphasia syndrome can be, in some cases, a consequence of ALS/MND. Furthermore, it is not clear whether MND/FTD syndrome brings to language breakdown or whether MND/Aphasia can be considered a self-standing syndrome. Lexical category-specific impairments affect more often than not verbs, while nouns appear to be by some means preserved. The verbs deficit is remarkable because it can place a new light on the link between actions, verbal and cognitive imagery, and ideomotor praxis. Language impairments detected in ALS/MND point largely to frontal and frontostriatal damages.

Actually functional neuroimaging studies show reduced frontal activation. Alterations in Broca's area, DorsoLateral PreFrontal Cortex (DLPFC) and fronto-striatal circuit have been all reported in ALS/MND: several functional studies link Broca's area to syntactic processing and DLPFC to verbs production as well as language Short Term Memory (STM). A basic issue is the link between action and verbs and, as a result, between action syntax and speech syntax. This connection would be involved in the origin of language: it would be evolved passing from action to speech syntax. According to our point of view, verbs are pivotal in this system. In short, when actions are missing, verbs, ideomotor praxis and their neurocorrelates would deteriorate.

A longitudinal study on the effect of massive motor derangement on the verb degeneration is at present carried out by our research group, so to date this is a working hypothesis waiting for further evidence.

Keywords: *ALS/MND, syntax, verbs, action, fronto-striatal circuit.*

Introduction

Motor Neuron Disease (MND) is an all embracing term used to cover a number of illnesses of the motor neurons. Amyotrophic Lateral Sclerosis (ALS), Progressive Muscular Atrophy (PMA), Progressive Bulbar Palsy (PBP), Primary Lateral Sclerosis (PLS) are MND subtypes. ALS/MND is characterized by progressive degeneration of the motor neurons in the brain, brainstem and spinal cord. The motor neurons control the muscles enabling us to move around, speak, breathe and swallow: with no nerves to activate them, muscles gradually weaken and waste. Symptoms may include muscle weakness and palsy, as well as impaired speaking, swallowing and breathing.

Until few years ago, MND/ALS was thought to spare cognitive functions. We review recent studies focused on language impairments in this syndrome and the possible consequences on higher-order cognitive functions. These researches show that about 3-5% of patients affected by MND/ALS have cognitive impairments. Up to date, it is not possible to establish whether this subgroup is affected by MND/ALS *and* Fronto-Temporal Dementia (FTD) or whether FTD can be, in some cases, a consequence of MND/ALS.

Grammatical category-specific impairments seem to affect mostly verbs, while nouns appear to be somehow preserved. The lack of verbs is striking, considered the nature of the syndrome: it sets out as a matter of great importance the link between actions and their verbal and cognitive imagery.

1. Materials and Methods

We have reviewed 6 papers – as far as we know, the entire literature on the topic: Bak & Hodges (1997), Cobble (1998), Bak & Hodges (1999), Neary et al. (2000), Bak & Hodges (2001), Bak et al. (2001).

The work by Bak & Hodges (1997) was carried out on 3 patients using a test of verb and noun naming and comprehension.

Cobble (1998) studied 9 patients: all subjects were given a range of tests examining various aspects of language function, i.e. naming ability, semantic processing, auditory comprehension of complex sentences, spelling and reading single words.

Bak et al. (2001) tested 6 patients with the Test of the Reception Of Grammar (TROG, Bishop 1989) and with a naming and comprehension test adapted from Berndt (1996): neuroimaging (CT and/or MRI) and functional (SPECT) studies were carried out in all patients, and in 4 cases post-mortem neuropathology as well.

Bak & Hodges (1999, 2001) and Neary et al. (2000) review a large amount of literature concerning FTD/MND.

2. Results

2.1. Neurolinguistic findings

Bak & Hodges (1997, 2001), Neary et al. (2000), Bak et al. (2001) highlight that language impairments observed in MND/ALS point mainly to frontal and frontostriatal breakdown.

Cobble (1998) states that most of the MND patients were performing close to the ceiling level, except for a subgroup of 3 patients who scored consistently lower than the rest of the group.

Syntax and verbs were consistently impaired in all patients examined, while nouns (single words) were relatively preserved. Bak and al. (2001), through TROG, found that syntax was impaired. Embedded sentences like ‘the book the pencil is on is red’ provoked errors. Five patients showed a massive impairment of sentence comprehension. The best result obtained by an MND patient (86% correct) was clearly below the worst result of the control group (91%), so that there was no overlap between both groups. The difference between the groups (patients/controls) was significant (Mann–Whitney *U* test, $P < 0.0001$). Two patients were still able to write for several weeks after the loss of their spoken language and their written language revealed numerous semantic paraphasias and syntactic violations. Comprehension and production of verbs were consistently more affected than those of nouns.

Bak & Hodges (1999) observe that in a small number of patients (with MND/ALS) a progressive aphasia may lead ultimately to mutism, and that, while the syndromes of MND/dementia and MND/aphasia constitute a comparatively small group, subtle but consistent cognitive alterations have also been observed – less pronounced – in the majority of nondemented MND patients. The behavior of nondemented patients, affecting mostly frontal-executive functions, resembles that of MND/dementia.

2.2. Neuromorphological findings

Post-mortem examination results (describing pathological changes in the frontal lobes) and functional neuroimaging data (showing abnormal pattern of frontal activation) give further support to the hypothesis linking MND to the fronto-temporal dementia (Neary et al., 2000).

Bak & Hodges (2001) state that post-mortem studies evidence pathological changes in the frontal lobes, and functional neuroimaging studies show reduced frontal activation. However, at the moment, it cannot be established whether MND/aphasia form separate disease entities or can be viewed as extreme forms of a cognitive deficit characteristic of MND/FTD in general.

Yamauchi et al. (1995) report that ALS/MND patients with cognitive decline or psychiatric symptoms had substantial atrophy of the anterior fourth of the corpus callosum (genu and rostrum), detected through MRI. Maekawa et al. (2002) explored whether selective loss of inhibitory (GABA(γ -aminobutyric acid)ergic) neurons occurs in MND: they found a significant reduction in proteins calbindin-D28K densities within lamina II of both area 4 and 9 in MND (however, post hoc comparisons of individual regions showed that these changes were only significant in area 9).

Bak et al. (2001) report that in addition to the typical involvement of motor and premotor cortex, particularly pronounced pathological changes were observed in the Brodmann areas 44 (Broca’s area) and 45.

3. Discussion

Dysfunctions in Broca’s area, bilateral Dorsolateral Prefrontal Cortex (DLPFC) and fronto-striatal circuit in ALS/MND – at least in subgroups of patients – shed new light on the observed language impairments. As we noted elsewhere, fronto-striatal circuit emerges as essential in verbs production and comprehension: No wonder that verbs result impaired in presence of massive fronto-striatal damages. There are several functional studies that link Broca’s area to syntactic processing, hence an impaired syntax is easily explainable along this line.

An intriguing matter is the link between action and verbs and, consequently, between action syntax and speech syntax. We stated elsewhere that there is a body of evidence of a total overlap between brain areas deputed to ideomotor praxia (goal-oriented preparatory motor

strategy) and those involved in language processing. From such a point of view, losing verbs means losing actions (Piatt 1999), and we can hypothesize vice versa that losing action may bring to losing verbs. This mechanism would be entailed in the evolutionary origin of language (Rizzolatti & Arbib 1998), namely language would be evolved passing from action to speech syntax, thus from putting object in series to putting words in series. Verbs are pivotal in such a system. In other words, when actions are missing, verbs – and the related brain areas – would degenerate.

This hypothesis deserves necessarily further studies: we are currently carrying on a study on the effect of massive motor derangement on the verb degeneration.

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