Frontostriatal deficit in Motor Neuron Disease/Amyotrophic Lateral Sclerosis (MND/ALS)

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Abstract

So far, cognitive derangements in MND/ALS have not been widely studied. Nevertheless, it seems that in subgroups of patients cognitive functions are impaired in different degree, so that often at least two sub-types of the syndrome are reported: Motor Neuron Disease/Amyotrophic Lateral Sclerosis/Dementia Syndrome (MND/ALS/DS) and Motor Neuron Disease/Amyotrophic Lateral Sclerosis/ Aphasia Syndrome (MND/ALS/AS) [1-4, 14]. A third subtype showing both symptoms of cognitive impairment may be identified in subgroups of patients and denominated Motor Neuron Disease/Amyotrophic Lateral Sclerosis/Dementia-Aphasia Syndrome (MND/ALS/DAS).
Frontostriatal system is reported as a network heavily damaged in MND/ALS/DS, MND/ALS/AS, MND/ALS/DAS [1-4, 13, 14]. The system is plausibly responsible of motor skills and verbs production, hence to become aware of a possible frontostriatal deficit in subgroup of MND/ALS patients might consent us to link at the brain level (motor) action and verbs and possibly ideomotor praxia and verbs.
We have used Goal-Oriented Perception Task (GOPT) and Action Fluency Task (AFT) in order to detect with some accuracy impairments related to gestaltic analysis directed toward a goal, and verb retrieval deficits possibly underlying executive system dysfunction that destabilizes the ability to mentally coordinate the information associated with a verb. These tests should consent to detect possible frontostriatal derangements [15].
We have tested 10 MND/ALS patients and 10 healthy subjects matched fore age, sex and laterality. AFT showed that 3 out of 6 patients are heavily impaired in this test (6.3 (mean) verbs generated vs 13.3 of the control group). GOPT detected a remarkable impairment in all patients: p=0.0021 (grammatical side), p=0.0002 (perceptual side).
Reported frontostriatal deficit in MND/ALS seems confirmed by this study, and probably it is more easily detected by GOPT than by AFT.

1.Introduction

Impaired activation in cortical regions including the dorsolateral prefrontal cortex (DLPFC; BAs 46 and 9), lateral premotor cortex (BA 8) and supplementary motor area (SMA, BA 6), medial prefrontal and premotor cortices (BA 8 and 9), and neuronal loss in the anterior cingulate gyrus (ACC) have been reported in MND/ALS/DS, MND/ALS/AS and MND/ALS/DAS patients, hence fronto-striatal circuits seems to be heavily involved in this disease [1-4, 13, 14]. The fronto-striatal *system* (dorsolateral prefrontal cortex (DLPFC), lateral orbito-frontal cortex (LOFC), anterior cingulate (ACC), supplementary motor area (SMA), and associated basal-ganglia structures (*Striatum*: ST)) is known to play a fundamental role in cognitive domain. The system plausibly controls our organizational adaptableness (decoding/encoding) to contextual clues and is involved in syntactic (motor/language) processing and in verbs naming and understanding.

It is known that derangements of the frontostriatal system underlie several psychiatric and/or neurodegenerative/neurodevelopmental syndromes: Obsessive compulsive disorder, Tourette's syndrome, attention deficit hyperactivity disorder, schizophrenia, autism, and most likely depression. The system is responsible for our correct responses (initiation, implementation, maintenance) to environmental stimuli [6]. Furthermore, cases of schizophrenic MND/ALS patients are reported in literature: as researchers point out, both disorders are central nervous system (CNS) disorders of unknown aetiology. Various neuromuscular alterations involving the alpha-motor neuron have been detected in subgroups of schizophrenics. It is possible that neuromuscular dysfunctions in schizophrenia may rouse MND/ALS onset in these subjects [10].
Frontostriatal circuits are deeply involved in motor programming (ideomotor praxia) and verbs production as well as in general language skills. Plausibly, ACC is a monitoring (endogenous stimuli) area, DLPFC a context unit both in action/language initiation/programming (exogenous stimuli) [9,11], while SMA is involved in motor planning, verbs production and syntactic elaboration: moreover a focal lesion in SMA will provoke, in a high percentage of cases, a severe and permanent form of agraphia. In addition, frontostriatal circuits are involved in motor imagery/ideomotor praxia. To assess frontostriatal deficits in MND/ALS patients through neurolinguistic tests would permit us to construct a bridge between actions and language, to link loss of actions to loss of verbs and syntactic impairments.

2.Material & Methods

2.1. Subjects

We have tested 10 MND/ALS patients and 10 healthy subjects matched fore age, sex, laterality. Preliminary memory tests results (working memory, short term memory and long term memory, visuo-spatial memory) ruled out that a possible organizational/language deficit depends upon these factors.

2.2. Tests

The Goal Oriented Perception Test (GOPT) is built on a modified version of Theory of Mind [5] and Luria's Thematic Figures [12]. Theory of Mind concerns what an individual can understand about others' intentions and Luria's Thematic Figures were used to assess whether a subject could understood a gestalt in its totality grasping the whole meaning. Patients with massive frontal lobe lesions, typically, could describe the figures in fragments without seeing the gestalt as a whole. Furthermore, they could not plan complex sequences of actions and/or execute goal-oriented actions. Not being capable of understanding others' goals may well be the other side of the coin, i.e. the perceptive one (executive/perceptive), hence frontostriatal circuits are plausibly greatly involved in this task.
The test is quite simple: the examiner shows a figure to the subjects and asks him to describe the figure saying: *now I want you to tell me what is going on in this figure. Feel free to describe it with all the particulars you want to. Tell me also what the people in the figure are doing.*
We have used the following picture, that is appropriate for the task we had in mind:

Fig. 1

GOPT is divided in two parts: a grammatical one and a perceptual one. Subjects' descriptions were audio-recorded with a micro-recorder Sony ® M-630V. Successively, the descriptions were written down and analyzed along 15 parameters for the grammatical side and 4 parameters for the perceptual one. The parameters used in Principal Component Analysis (PCA) for the grammatical side are: 1) Use of noun stereotypes; 2) use of verb stereotypes; 3) use of odd terms and/or neologisms; 4) errors of tense, mood, verbal aspect and/or incoherencies verbal aspect / Aktionsart; 5) omission of Function Words (FW); 6) agrammatical use of FW; 7) errors of syntactic agreement; 8) use of nominal verb forms; 9) errors affecting the syntactic hierarchic structure properly embedded and coherent with the given context; 10) verb argument structure and sub-categorization; 11) θ-roles[i] used incorrectly and linked to the wrong verb; 12) total or partial omission of θ-roles; 13) θ-roles mismatch; verb omission; 15) animacy effect.
The parameters used in PCA for the perceptual side are: 1) Proper interpretation of the figure; 2) figure described with particulars (also if fragmented); 3) non-fragmented description of the figure; 4) gestaltic interpretation of the figure for actors' goals (goal -oriented perception).
AFT is rather simple: the subject is instructed to nominate so many actions he can in one minute. If he/she doesn't understand the task, he/she is told to nominate all the verbs he/she can. Also in this case the subject's response is recorded and successively written down. If a verb is repeated it is deleted from the list, so that we can obtain merely a number of valid produced verbs.

3.Results

GOPT detected a remarkable impairment in all patients. They were heavily impaired, respect to the group of control, in both sides of GOPT: t-Test grammatical side $t = 4.26$, $p = 0.0021$; perceptual side: $t = 6.01$, $p = 0.0002$. AFT showed that 3 out of 10 patients are heavily impaired in this test (6.3 (mean) verbs generated vs 13.3 of the control group).
The following graphics are relative to GOPT (grammatical/perceptual) and AFT performances:

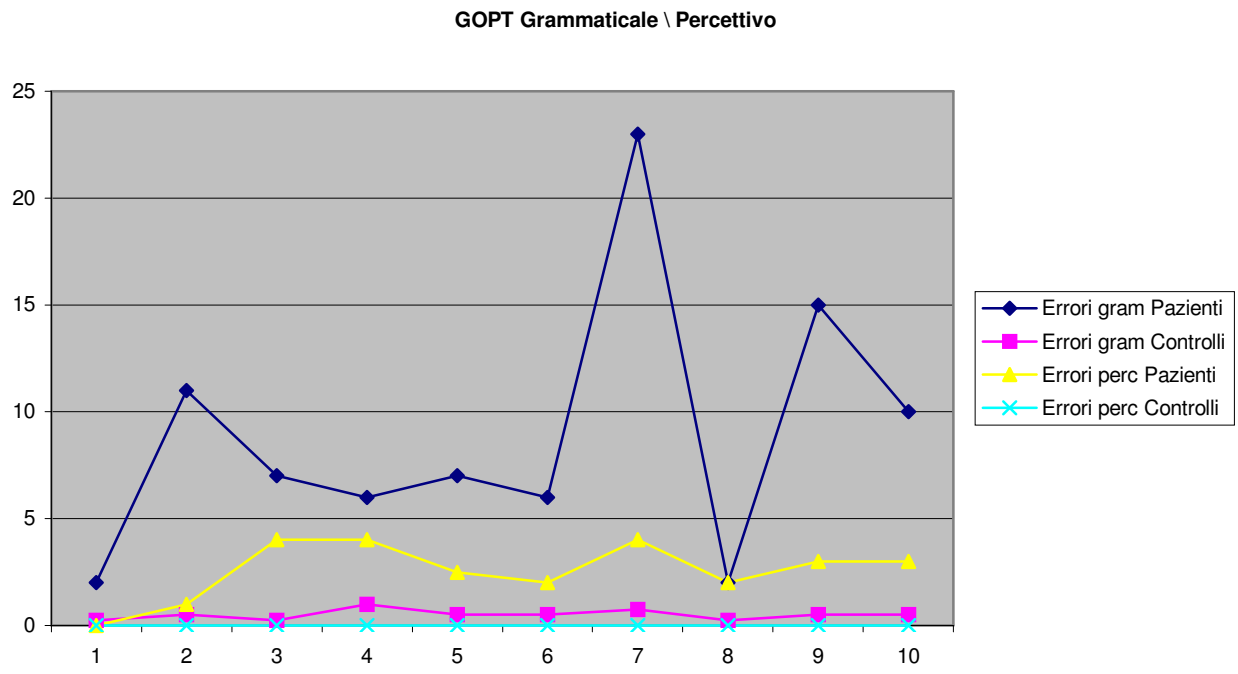

Grafico 1

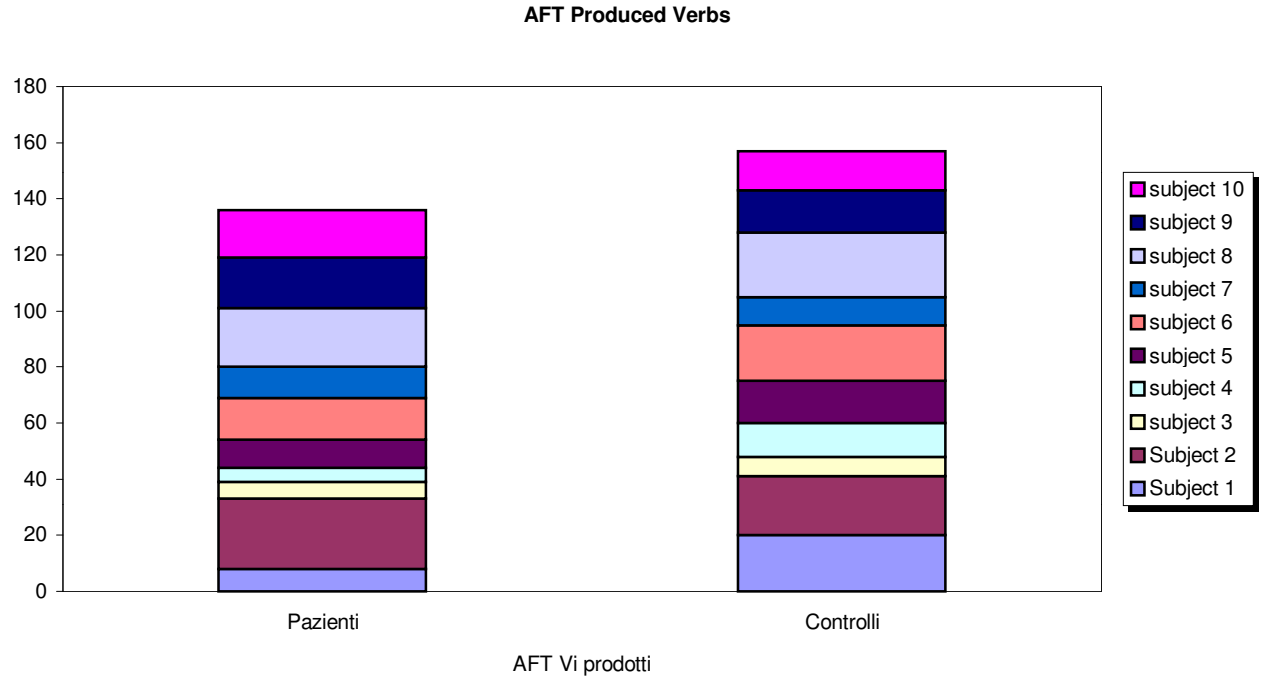

Grafico 2

4.Discussion

Frontostriatal deficits in MND/ALS are confirmed by this study. It is remarkable that the impairments are generally more easily detected by GOPT than by AFT, but perhaps this is due to the illness stadium in which the tests are administered. It should be noted that all patients have made more errors than controls in the GOPT grammatical and perceptual side, hence we don't deal with subgroup of patients – at least in this study – but with a general frontostriatal deficit affecting all the patients tested. Since MND/ALS is not usually considered as provoking cognitive impairments, this is an important finding that must be taken into account and confirmed by further studies. The confirmed frontostriatal derangement sheds a new light on the action/syntax parsing system, and links strictly action, language syntax, ideomotor praxia and goal-oriented activity, in the sense that when one of these three components are damaged is highly probable that also the others are not working properly unless a functional compensative strategy is at work.

Conclusions

Reported frontostriatal deficit in MND/ALS seems documented by this study, and probably it is more easily detected by GOPT than by AFT.

References

1. TH Bak & JR Hodges. **Noun-verb dissociation in three patients with motor neuron disease**. *Brain and Language* (Proceedings of the Academy of Aphasia Meeting, 1997), 60: 38-40 (1997).
2. TH Bak & JR Hodges. **Cognition, language and behaviour in motor neurone disease: evidence of frontotemporal dysfunction**. *Dementia and Geriatric Cognitive Disorders*, 10(S1): 29-32 (1999).
3. TH Bak & JR Hodges. **Motor neurone disease, dementia and aphasia: coincidence, co-occurrence or continuum?** *Journal of Neurology*, 248: 260-270 (2001).
4. TH Bak *et al.* **Selective impairment of verb processing associated with pathological changes in Brodmann areas 44 and 45 in the motor neurone disease-dementia-aphasia syndrome**. *Brain*, 124: 103-120 (2001).
5. Baron-Cohen, S. (1989b). **The autistic child's theory of mind: A case of specific developmental delay**. Journal of *Child Psychology and Psychiatry*, 30, 285–297.
6. J Bradshaw and D Sheppard, **The Neurodevelopmental Frontostriatal Disorders: Evolutionary Adaptiveness and Anomalous Lateralization**, *Brain and Language*, 73, 297-320, 2000.
7. M Cobble. **Language impairment in motor neurone disease**. *Journal of the Neurological Sciences,* 160(S1): 47–52 (1998).
8. CD Frith, SJ Blakemore and DM Wolpert, **Abnormalities in the awareness and control of action**, *Phil. Trans. R. Soc. Lond*., 355, 1771-1788, 2000 (2000b).
9. KY Haaland *et al.*, **Neural representations of skilled movement**, *Brain*, Vol. 123, No. 11, 2306-2313, 2000.
10. RH Howland, Schizophrenia and amyotrophic lateral sclerosis. Comprehensive Psychiatry 1990, 31-4:327-36.
11. E Koechlin *et al.*, **Dissociating the role of the medial and lateral anterior prefrontal cortex in human planning**, *Proceedings of The National Academy of Sciences of The United States of America*, Vol. 97, 7651-7656, 2000.
12. AR Luria, **The Working Brain**, Penguin, 1973.
13. S Maekawa *et al.* **Selective loss of inhibitory neurons in the cerebral cortex in motor neuron disease**. *Neuropathology and Applied Neurobiology*, 28: 149 (2002).
14. D Neary *et al.* **Cognitive change in motor neurone disease/amyotrophic lateral sclerosis (MND/ALS)** *Journal of the Neurological Sciences*, 180: 15-20 (2000).
15. AL Piatt **Action (verb naming) fluency as an executive function measure: convergent and divergent evidence of validity**. *Neuropsychologia*, 37: 1499-1503 (1999).

16. H Yamauchi *et al.* **Corpus callosum atrophy in amyotrophic lateral sclerosis**. *Journal of the Neurological Sciences*, 134: 189-196 (1995).

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[i] By θ-role we indicate, after Fillmore's Theory of Deep Case and Chomsky's Project ion Principle, the Agent, theme and Goal of an action. For instance, in the sentence *John was given a book by Mary* John has the θ-role goal, *book* the theme and Mary the Agent one.