

From evaluation to treatment

Rehabilitation in progressive multiple sclerosis

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Probably half of the multiple sclerosis (MS) patients worldwide have progressive MS (PMS) and seek therapy beyond prevention of inflammatory bouts. Therapy plans in PMS have to focus on improvement of abilities in individual problem constellations. Standardized assessment methods in MS beyond the expanded disability status scale (EDSS) have been developed.

Recent studies show positive effects for activating therapies in immobile MS patients. Fair evidence exists for several nonpharmacological therapies. Some data indicate activation of neurotrophic factors and neuroplasticity during therapy. Few medication strategies including corticoid pulses are at hand for PMS. Combined pharmacological and multimodal symptomatic approaches promise increased efficacy. Complex inpatient therapy schemes may be of special value for severely affected patients.

Key words: progressive multiple sclerosis (PMS) assessment methods expanded disability status scale (EDSS) therapy concepts combined multimodal non-pharmacological therapies neuroplasticity



Introduction

Progressive multiple sclerosis (PMS) affects probably half of multiple sclerosis patients worldwide. Both secondary PMS and primary PMS typically start after the age of 40 years [1], and are subsumed under PMS in recent criteria (either “active” or “non-active”) [2].

The pathological bases of axonal loss and tissue atrophy may include diffuse or focal inflammation in meninges and parenchyma, mitochondrial deficiencies, oligodendrocyte dysfunction and microvascular changes [3]. Most *in-vivo* research is based on brain imaging data: magnetic resonance imaging (MRI) demonstrates brain atrophy. Spinal cord and gray matter atrophy are typical features of PMS. Optical coherence tomography shows retinal layer atrophy, which correlates with neurodegeneration [4].

Assessment

Several methods for the clinical assessment of PMS have evolved. With different neurological disabilities occurring with chronic disease, patient perspectives and quality of life are important assessment objectives [5]. From a patient perspective, a number of important disabling conditions characterise PMS: mobility/gait

problems (ataxia, spasticity), bladder dysfunction, fatigue, failing cognition, depression. All these bring increased rates of unemployment, social handicaps and increasing costs for society, persons with MS and their caregivers [6].

In a majority of cases PMS shows a spinal pattern of impairment – para- or tetraparesis, neurogenic bladder and impairment of gait. This pattern is reflected in the expanded disability status scale (EDSS [7]), with gait impairment as the main criterion from grade 4 onward; grade 6 equals loss of unaided walking. As the EDSS does not fully represent all important functional deficits, and has non-continuous steps, other standardised instruments are used. The EDSS scores walking “at all”, whereas assessing “walking distance in a given time” or “time needed for a given distance” (see table 1; [8]) yields more precise results.

An important additional burden with PMS stems from comorbidities, increasing the need for help and hospitalisations [9], and also aggravating MS disability. They deserve notice; urosepsis, aspiration pneumonia or infected ulcers may be lethal.

Table 1: Examples of PMS assessments.

Assessment domain	Tests
Neurological systems, mobility: Expanded disability status scale	EDSS
Walking: a) 2-minute-walking test, 6-minute walking test b) preset distance timed walk: 25 ft. timed walking test; timed-up-and-go	a) 2MWT, 6 MWT. b) 25FTWT; TUG
Hand function: 9-hole peg test	9-HPT
Bladder: infection; residual volume after voiding?	Urinalysis; sonography
Fatigue: fatigue scales (self-reported questionnaires, quantitative score results)	FSS; MFIS; MSFC; Weimus
Cognition: a) neuropsychological batteries; b) screening tests	a) MACFIMS; BRB; BICAMS b) SDMT, PASAT; MUSIC
Depression: a) psychiatric criteria (such as ICD, DSM); b) self-reported questionnaires (quantitative scores)	b) Beck Depression Inventory (BDI version II), Hamilton Anxiety and Depression Scale (HADS)
Personal functioning (everyday life, job, social etc.)	ICF assessment

Therapy rationale

Improvement of abilities is a key objective in PMS therapy. Thus it has to be symptom oriented and faces individual problem constellations. Few symptomatic therapies in PMS are evidence based, therefore. Unfortunately, most studies are small, often underpowered for statistics, and mix relapsing-remitting multiple sclerosis (RRMS) and primary or secondary PMS [10, 11]. Besides neurogenic pathology, secondary maladaptive functional patterns, psychosocial factors and loss of physical fitness (“deconditioning”) deserve attention. Several studies showed positive effects of activating therapies in immobile MS patients. Fair evidence exists for a number of nonpharmacological therapies [5, 10, 11], which are summarised in the table 2. A multidisciplinary team approach is preferable in PMS. PMS patients may be too handicapped for many single therapies. For these situations, inpatient treatment is advisable. After complex inpatient therapy, positive results with enduring effects have been demonstrated repeatedly [5, 10, 20, 21].

Table 2: Symptomatic therapies in PMS.

Nonpharmacological	Medication
Physical exercise, endurance/resistance training	Antispasticity muscle-relaxants
Physiotherapy	Anticholinergic bladder drugs
Occupational therapy	Antiepileptic channel blockers (neuropathic pain)
Speech/swallowing therapy	Antidepressive drugs
Behavioural therapy, psychology	Corticoid pulses
Educational programs	Botulinum toxin
Multimodal rehabilitation	THC/CBD (cannabinoid spray)
	Diaminopyridine

Medication

Few types of medication are available for PMS (see table 2) and side effects may be relevant. The benefits of disease-modifying drugs are limited as yet. Repetitive corticoid pulses may be beneficial in PMS, in terms of reduction of silent inflammation and of spasticity, for some time [12]. In PMS, pulses might be

administered intramuscularly, orally or intrathecally, as well as via intravenous infusion. Simultaneous combination with multimodal therapies is more effective [13].

Diaminopyridine (improving gait for about 25% of patients [14]), cannabinoid spray (THC/CBD) for spasticity (effective in about 50% [15]), and botulinum toxin for circumscribed muscle groups and the bladder were introduced more recently. Treating spasticity may also reduce pain. Drugs such as biotin promise axonal energy and structure restoration in PMS but still lack confirmation [16].

Lasting therapy effects

In a spasticity study with THC/CBD [15], antispastic effects were seen for several months after active treatment. Explanations for such prolonged functional improvements may be retraining, deblockade of physiological functioning, and even neuroplasticity [17]. Some data indicate activation of neurotrophic factors through physical exercise in MS [18, 19].

Other important issues of PMS therapy include information, counseling and education of patients and caregivers. Reduction of uncertainty, fear and depression may help improve quality of life and personal functioning [5]. A team approach combining medication strategies, multimodal symptomatic therapies, expert nursing and experienced neurologists in a time-synchronised effort seems most promising.

Key points

- Standardised assessment methods valuable
- Growing evidence for benefits of physical exercise
- Multidisciplinary therapy team approach superior to single measures
- Combined pharmacology + multimodal symptomatic approaches more effective
- Perspective for neuroplasticity, neurotrophic factor activation, functional reorganisation through therapy procedures

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References

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