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Synapse

OFFICIAL JOURNAL OF THE **ASSOCIATION OF CHARTERED PHYSIOTHERAPISTS IN NEUROLOGY**

INSIDE

Editorial

Dear members,

The aim of *Synapse* – the official journal of ACPIN – is to provide its readership (nationally and internationally), including wider multi-disciplinary teams, an international, peer-reviewed platform for the publication, dissemination, knowledge exchange and discussion of recent developments and current research in the field of neurological rehabilitation.

The journal accepts original, quantitative and qualitative research reports, theoretical papers, systematic literature reviews, scoping reviews, service evaluations, quality improvement programmes, clinical case reports and technical clinical notes.

Featured in this edition are three articles: from Professor Roberta B Shepherd, Dr Steven Ashford and Professor Merrill R. Landers.

If you are interested in submitting your work for publication in *Synapse*, please follow the guidelines for manuscript preparation presented on page 22 and send your work for inclusion in the peer-review process. I look forward to receiving high quality work for publication in *Synapse*.

Praveen Kumar

Dr Praveen Kumar
EDITOR

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Key aspects to *Synapse's* publication and dissemination strategy are :

1. To provide a platform for publication of high quality research studies.
2. To provide peer-review feedback for novice researchers.
3. To have special/ supplementary editions on specific topics/areas/student related projects.
4. To have a clearly defined editorial board.
5. To have a review board that includes both national and international reviewers. (This includes academics, researchers, clinicians, ACPIN members, non-ACPIN members/experts in the field of neurology/neurological rehabilitation, physical medicine and rehabilitation).

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Movement science as the basis of modern physiotherapy

Professor Roberta B Shepherd
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DHScSydneyhonoris causa, FACP, AO

The study of human movement includes neuroscience, biomechanics, anatomy and exercise physiology, knowledge of which is applied throughout musculoskeletal, neurological, cardiopulmonary, paediatric, and aged care physiotherapy. These areas of the scientific study of human movement provide the critical components of physiotherapy.

It is currently accepted that intensive exercise and physical activity have a profound effect on the brain and other bodily systems as seen in evidence of motor learning.

Over the last decades, since the 1970s and 1980s, there has been a move away from interventions based on theoretical concepts that originated in the first half of the 20th century and earlier, such as Neurodevelopmental Physiotherapy (NDT) and Proprioceptive Neuromuscular Facilitation (PNF). There has been little evidence of functional effectiveness of these therapies, and the methods used often depend on the learner being moved about by the therapist. Currently, physiotherapists, engineers, and movement and exercise scientists are developing up-to-date science-based interventions based on new knowledge of how bodily systems function (Jensen 2005, Carr & Shepherd 2010, Shepherd 2014). As scientific knowledge grows, we may have to upgrade or change our methods from time to time. As clinical research becomes more fine-tuned, we use evidence of effectiveness to develop *best practice* (see Nielsen *et al* 2015).

Physiotherapy's contribution to rehabilitation of motor performance involves intensive exercise and training of physical activity to increase muscle strength and extensibility, endurance, power, and motor control. But the overall aim is to improve task performance so that it is effective in achieving the person's specific goals in relevant environmental contexts. It is currently accepted that intensive exercise and physical activity have a profound effect on the brain and other bodily systems as seen in evidence of motor learning.

Basically, exercise and training should be both task-and context-specific so that the individual can learn to move independently and to achieve effectively their goals in different environments. But what does this actually mean?

We learn how to move effectively and achieve our goals by practising a meaningful action or task in relevant environments. This is so whether we are infants learning to stand up from the floor or from a seat, or as adults when we learn a new skill (eg tennis or swimming), and when we learn how to walk again after a stroke or a hip replacement.

Exercise may therefore only be effective in improving independent, functional performance when specific actions are practised in their natural contexts or environments. The dominant environmental context throughout all our actions is gravitational, hence the significance of balance training in different contexts. Investigations of sit-to-stand show that there may be little or no carryover from lower limb strength training to standing up from a seat without using the hands. Interestingly the muscles get stronger but sit-to-stand may not improve due to continuing instability as weight is shifted from buttocks to feet, and difficulty generating sufficient force to shift the body-mass forward over the feet. The evidence is therefore that there may be little or no carryover from simple exercises (such as single joint exercises) to improved functional performance if the action itself is not practised intensively. Note that when the therapist holds on to the patient the context is changed. Balance training is shown to be more effective when combined with repetitive practice of a variety of actions in standing – Bernstein's repetition without repetition – where repetitive attempts at the same task are accompanied by variable trajectories (Bernstein 1967).

Task- and context-specific exercise and training enable an action to be learned by affecting the neuromuscular system's basic plasticity ie training is specific to the action and the context (the environment, intention, goal). It involves meaningful tasks and not just random exercise. Task training exercises are practised as intensively as possible, to increase muscle strength, power and control both concentrically and eccentrically-repetitive sit-to-stand from different seat heights for example (Canning *et al* 2003, Chaovalit *et al* 2019). Recent research has demonstrated successful

training programmes that included task and environmental variability, repetitive practice and augmented feedback involving meaningful tasks (eg Rensink *et al* 2009). In another effective task-related training programme, the patients worked on a specific, self-driven and goal-directed activity in a position in which the weakened muscle(s) would normally function (Dean & Shepherd 1997).

Task-and context-specific training improves coordination of muscles, balance perception, and muscle extensibility and flexibility. It increases the control of synergistic muscle groups that contract in different actions concentrically, eccentrically, and isometrically (Safavynia *et al* 2011). A study in which emphasis was placed on repetitive and high-intensity walking training demonstrated improvements in walking competence in the first year following stroke (Cauraugh & Kim 2003). Playing electronic games in standing can increase postural stability and balance, as well as independence (Blennerhassett & Dite 2004, Morone *et al* 2014).

Finally, as Nielsen and colleagues commented in 2015, "Our understanding of the neural processes responsible for learning and memory has increased significantly in recent years and it is now established that the ability to change functionally and structurally is a fundamental essence of the nervous system. This creates a unique basis for a biological framework for neurorehabilitation…" as it does for rehabilitation of individuals with musculoskeletal problems since the neuromotor and musculoskeletal systems are intertwined. The significance of an understanding of biomechanics, motor learning and task- and context-specific exercise to the effectiveness of rehabilitation is critical in order to achieve optimal outcomes.

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Exercise may therefore only be effective in improving independent, functional performance when specific actions are practised in their natural contexts or environments.

Physiotherapy-related late onset clinical and grey matter plasticity changes in a patient with dysphagia due to long-standing pseudobulbar palsy – a longitudinal case study

Karin Gampp Lehmann[1]. Roland Wiest[2]. Eberhard Seifert[3]

Effective therapy methods for dysphagia due to long-standing pseudobulbar palsy, as in the current case study, have not been well investigated, with very little data available on the long-term effects of physical therapy (Langmore SE 2015, Speyer R 2010, Barikroo A 2017) or on the long-term need for physical therapy. The aim of this study is to show that long-term therapeutic success is possible in long-standing dysphagia due to pseudobulbar palsy.

… it has been recently demonstrated that grey matter plasticity in both perilesional and distant neural networks contributes to behavioural recovery of sensorimotor functions after stroke.

It is to be assumed that any chosen therapy has to influence facial oral structures as well as neuroplasticity to have a long-term effect on dysphagia due to long-standing pseudobulbar palsy (Robbins J 2008, Avivi-Arber L 2010).

As a base for best evidence practice the chosen therapy approach in this study was therefore based on actual principles of motor learning and training (Robbins J 2008, Shumway-Cook A and Woollacott M 2012, Burkhead LM 2007, Gampp Lehmann K 2015) as well as on new insights into the correlations and therapy of connective tissues, musculoskeletal system, muscle function and myofascial pain (Gampp Lehmann K and Sticher H 2015, Stecco 2015, Guarda-Nardini L 2012, Stecco C 2011, Stecco L 2009, Pavan PG 2014, Mauntel TC 2014).

Computer-assisted quantitative morphometry is increasingly used to assess longitudinal changes in gray matter density and cortical thickness that relates to synaptic sprouting and cortical reorganisation. Magnetic resonance imaging (MRI)-based morphometric studies suggest that changes in cortical thickness can be detected in human patients after post-inflammatory brain injury. We focused our analysis on the relationship between cortical thickness and recovery from dysphagia, since the latter represents a clinically relevant impairment and since rehabilitation based on evidence-based practice poses a novel window towards effective recovery.

In dysphagia, recovery of swallowing function after unilateral brain damage has been demonstrated by transcranial magnetic stimulation to be associated with increases of the cortical area map size of the unaffected hemisphere in the pharyngeal motor cortex (Hamdy *et al* 1998). As a consequence, longitudinal MRI may be capable to demonstrate cortical changes along the aberrant motor network via repetitive studies. For recovery of motor function after lesions in the primary motor cortex, it has been recently demonstrated that grey matter plasticity in both perilesional and distant neural networks contributes to behavioural recovery of sensorimotor functions after stroke (Abela *et al* 2015).

Few reports have previously addressed late sequelae of cortical injuries related to dysphagia in patients with chronic encephalopathies (Mihai PG 2016, Galovic M 2013, Liu L 2017).

Patient and methods

The patient is a 52-year-old woman with long-standing dysphagia since age four weeks, suffering from long-standing impairment primarily of the left hemispheric oropharyngeal sensory and motor cortex with subsequent highly restricted tongue and jaw movements and severe drooling (*Figure 1*).

The patient was diagnosed with encephalitis at age four weeks. Pseudobulbar palsy, dysphagia and dysarthria were diagnosed at age five years. There was severely disrupted development of eating, drinking and communication with severely reduced oral movements. As a baby she was fully bottle-fed without being able to suck. She learned to eat by putting a spoon with puréed food on the back of her tongue. She underwent speech and language therapy

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and occupational therapy until age 15, after which no further therapy was applied. There is no detailed documentation of previous therapy approaches. So far eating and drinking has always been ingested orally. Finely cut moist food is swallowed without chewing by placing on the left side at the back of the tongue. Communication is via oral speech with significantly reduced intelligibility. The patient is married and has three healthy daughters.

At age 50, two years prior to commencement of physical therapy, the patient reported increasingly effortful swallowing, increasing dysphagia, painful tension in the left orofacial muscles as well as in the left craniomandibular articulation and in the left side of the pharynx. She reported she had to cough about five times during each meal, with a singular choking incident.

Clinical examination

The clinical examination before onset of physical therapy showed a high-vaulted hard palate, nearly Gothic. The active protrusion of the tongue was reduced to 3mm past the teeth. The limited voluntary tongue movements were initiated primarily with the left side of the tongue. No lateral tongue movement, no movement of the soft palate. No active forward or lateral movements of the jaw. During swallowing, an incomplete closure of the mouth and a prominent mentalis muscle due to hyperactivity was evident (*Figure 1*).

Oral sensation and sense of taste were tested by touch and by selective liquid application intraorally and were overall severely reduced. The bolus was only perceived on the left side of the cavity.

Mouth and lips were open in resting posture with constant drooling from the left side of the mouth (*Figure 1*). For the main clinical findings before therapy see *Table 1*.

Laryngoscopy

Laryngoscopy showed no abnormalities, vocal cords showed a regular movement with a small dorsal gap. Fiberoptic Endoscopic Evaluation of Swallowing (FEES) showed the liquid bolus was swallowed normally, but a decantation of the viscous bolus was observed (Langmore SE 2001). There were no signs of aspiration throughout the examination. There were no signs of pneumonia and no history of other related diseases or surgery. Because of the severely reduced oral movements and because of the increasing dysphagic symptoms we decided to use the Sydney Swallow Questionnaire (Wallace KL 2000) and a body mass index as best applicable clinical assessments. In this case the Sydney Swallow Questionnaire (SSQ) showed a score of 1274 (max dysphgia = 1700/ norm = 0). Her Body Mass Index (BMI) was 17 (norm 18.5 - 25).

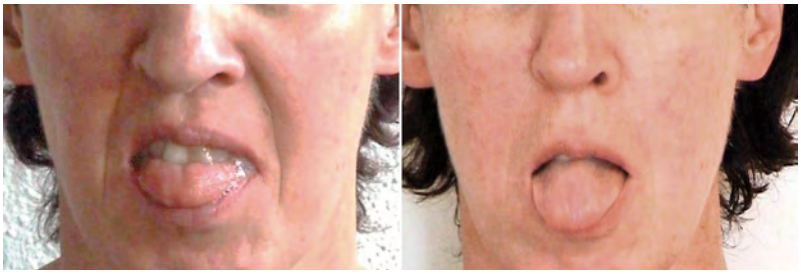


Figure 1 Lingual Mobility. Left, after four months of therapy: active protrusion of the tongue maximum 1.5cm past the teeth (tongue is still held by the teeth), drooling. Right, after ten months of therapy: active symmetrical, unrestricted protrusion of the tongue 3.5 cm past the teeth, no drooling.

MAIN INITIAL FINDINGS BEFORE ONSET OF PHYSIOTHERAPY	MAIN CHANGES WITHIN TWELVE MONTHS OF PHYSIOTHERAPY
Sydney Swallow Questionnaire score: 1,274 **Body mass index**: 17	**Sydney Swallow Questionnaire score**: 480 **Body mass index**: 23
TONGUE	TONGUE
Active protrusion of the tongue max. 3mm past the lower teeth whilst tongue is held by the teeth (*Figure 1*).	Active symmetrical, unrestricted protrusion of the tongue 3.5 cm past the lower teeth (*Figure 1*).
Absent lateral movement of the tongue to both sides.	Active lateral movement of the tip of the tongue 1 mm to the left.
Tongue body cannot be narrowed.	The tongue body narrows noticeably when attempting lateral movement to the left.
Reduced sense of taste and of food on the tongue.	Improved sense of taste and of food on the tongue.
The patient perceives tension across the entire left oropharyngeal region.	No tension across oropharyngeal region.
The patient has fear of suffocation because of choking incidents.	The patient no longer chokes during meals; no more fear of suffocation.
JAW	JAW
Mouth/lips open in resting posture.	Mouth/lips closed in resting posture, except when very fatigued.
Continuous drooling from the side of the mouth, which patient immediately wipes away.	No drooling from the side of the mouth, except when very fatigued (*Figure 1*).
Left lateral pterygoid muscle display increased tonicity and are shortened with associated pain.	Left lateral pterygoid muscle free of pain, normal tonicity.
Swallowing with incomplete jaw closure with strong activity of the dorsal part of the tongue.	Swallowing with jaw closure and strong activity of the dorsal part of the tongue.
Muscles of the floor of the mouth/oral cavity display increased tonicity and are shortened.	Muscles of the floor of the mouth/oral cavity display normal tonicity and length.
NECK AND TRUNK	NECK AND TRUNK
Limited active and passive upper cervical flexion and lateral flexion.	Unrestricted passive/active upper cervical flexion.
Hyoid movement lateral and cranial restricted.	Hyoid movement unrestricted.
The right trapezius, levator scapulae and sternocleidomastoid muscles display increased tonicity and are painful.	Shoulder muscles display normal tonicity and are pain free.
Limited neurodynamic mobility of the hypoglossus, accessory and mandibularis nerves on the right side.	Normal neurodynamic mobility of the hypoglossus, accessory and mandibularis nerves.
Restricted abdominal breathing, mainly chest breathing.	Unrestricted abdominal breathing.

Table 1 Main clinical findings and results

MRI acquisition and postprocessing

Both MRI studies at baseline and follow-up after twelve months were performed on a 3T Siemens Magnetom Trio TIM system (Siemens AG, Erlangen, Germany). High-resolution three-dimensional (3D) volume images were obtained using a multiplanar rapid gradient echo sequence (MP-RAGE, 176 sagittal slices, isovoxel resolution = 1.0 mm, FOV 256 × 256 mm, matrix size = 256 × 256, TR/TE/TI = 1,950/2.15/900 ms).

Automated image processing

The volumes of cerebro-spinal fluid (CSF), grey matter (GM) and white matter (WM) were estimated using the free software package FSL (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/, version 5.0 (Jenkinson M 2012), developed at the Oxford Centre for Functional MRI of the Brain (FMRIB). Surface-based morphometry was performed using the free software package FreeSurfer (https://surfer.nmr.mgh.harvard.edu, version 5.3.0) as developed previously by Dale *et al* (1999) and Fischl *et al* (2002).

Since the patient reported severe dysphagic symptoms, we focused our analysis on the dynamic changes in the atlas-based parcellations of the motor areas according to Destrieux *et al* (2010) compared to a normative databank of 322 healthy controls.

Therapy

The chosen therapy consisted of outpatient physical therapy specialised for dysphagia for 40 minutes once a week and an individual home programme. The therapeutic approach was based on the assumption that the clinical findings were induced by the initial illness as well as by long-standing unilateral use of the anatomical structures with subsequent secondary pain and increased tonicity of the left orofacial and pharyngeal structures (Pavan PG 2014, Avivi-Arber L 2010). Dysphagia could be recognised as a movement and coordination disorder. Therefore it requires profound knowledge of all relevant anatomical interrelations and of the required manual treatment approaches. The specific physical therapy applied for long-standing dysphagia as in this case was based on Facial-Oral Tract Therapy® (F.O.T.T. ®), which takes into account the relationship between facial and oropharyngeal functions and breathing and postural stability (Gampp Lehmann K 2015, Gampp Lehmann K and Sticher H 2015, Hansen TS 2010).

Therapeutic interventions were as follows:

- **Myofascial release- and mobilisation-techniques** in conjunction with upper cervical flexion were applied in every therapy session for all oropharyngeal structures, especially for the jaw muscles, the connections of the hyoid bone, the neck and trunk and for the diaphragm. The aim was to achieve greater range of motion, new sensorimotor input and improved motor control which allows the patient to become differently aware of relevant structures, instead of practicing accustomed limited patterns (Gampp Lehmann K and Sticher H 2015, Mauntel TC 2014, Von Piekartz 2005, Ishida R and Palmer J 2002). This may promote enhanced motor control and bring about neuroplasticity (Langmore SE 2015, Mauntel TC 2014, Avivi-Arber L 2010). The trunk and diaphragm were included because of fascial connections between diaphragm, trunk and throat (Gampp Lehmann K and Sticher H 2015). As emphasised by Horak already in 1991, the musculoskeletal system is a critical element of control in motor coordination. Therefore major efforts must be placed on identifying and correcting constraints placed on movements by deficits in the musculoskeletal system (Horak, 1991). Research by Stecco *et al* (2015)shows the important correlations between the connective tissue and the functioning of muscles of the face.
- **Neurodynamic techniques (sliders)** for the hypoglossal, facial, mandibular and accessory nerves were applied in every therapy session to ensure free mobility of the relevant neural structures (Von Piekartz 2005).
- **Combined functional facial-oral activities** with increasing strength and complexity were practised at each therapy session. Instead of abstract exercises, task oriented functional activities of daily living ("try to lick your lip", "try to clean your teeth with your tongue", "try to breathe deeply with your mouth closed") were carried out using motor imaging techniques as a stimulus for initiating new movements and in accordance with current motor learning principles to enhance neural plasticity (Robbins J 2008, Shumway-Cook A and Woollacott M 2012, Burkhead LM 2007, Gampp Lehmann K 2015).
- **Deep thoraco-abdominal breathing** was encouraged and exercised repeatedly to improve the lung capacity and the swallowing- breathing- coordination (Robbins J 2008) (Gampp Lehmann K and Sticher H 2015, Martin-Harris B 2008) as well as to influence fascial connections between diaphragm, trunk and throat (Gampp Lehmann K and Sticher H 2015).

Over the whole therapy phase the patient had an **individual home programme** with functional active and passive facial-oral movements (for example passive and active protrusion and stretching of the tongue and

activities as described above) twice a day for ten minutes, carried out with adequate postural stability and upper cervical flexion (Gampp Lehmann K and Sticher H 2015). She was encouraged to perceive the position of her tongue during eating and daily activities and to exercise abdominal breathing.

At the patient's request, puréed food was not employed. Eating and drinking were always ingested orally. Finely cut moist food was swallowed without chewing by placing on the left side at the back of the tongue.

This intense physiotherapy phase lasted one year, after which no additional improvement was achieved. The patient did not take part in any other therapy or new activities, which suggests that the results were induced by the targeted physiotherapy.

Clinical findings, body mass index, Sydney Swallow Questionnaire score and changes in fMRI were evaluated before and after one year of therapy.

Results

The chosen physiotherapy approach over one year resulted in improved functions (*Figure1*, *Table1*). The Sydney Swallow Questionnaire score improved from 1274 to 480. Body mass index increased from 17 to 23. The patient's perception of food on the tongue and the sense of taste improved. The patient no longer drools except when very fatigued. She no longer chokes during meals. The patient reports that her drinking ability is better than before onset of therapy, and that the awareness of the right-hand side of her face and inside her mouth has improved to better than ever before. For the main results see *Table 1*.

Imaging findings

The initial MRI ahead of therapy indicated unilateral cortical atrophy along the inferior bank of the central sulcus and volume loss in the posterior insula and temporal operculum. The superior band of the precentral gyrus was relatively spared (including the hand notch and the paracentral lobule). The underlying white matter appeared with normal signal on T1 w images. The left lateral ventricle was enlarged and the subcortical white matter volume appeared reduced compared to the contralateral unaffected hemisphere. The visual analysis was complemented by automated cortical thickness analysis. While the visual analysis did not reveal any apparent changes after follow-up one year later, automated image analysis indicated significant cortical thickness changes (> 2 SD) in the precentral gyrus. While cortical thickness decreased further in the atrophic inferior bank of the precentral gyrus, these findings were opposed by a compensatory trend towards increase of thickness in the ipsilateral superior bank of the precentral gyrus and the motor cortex of the unaffected hemisphere (*Figures 2* and *3 overleaf*). Whole brain volume was in keeping with the stable visual analysis; grey and white matter volumes and the volumes within the cerebrospinal fluid (CSF) remained within age-related normal ranges (*Figure 4*).

While lesioned brain areas show progressive decrease in cortical thickness over time, we observed compensatory maintenance or increases of cortical thickness in the superior premotor areas, both ipsilateral and contralateral to the lesion.

Laryngoscopy and FEES have not been repeated because of financial reasons. Their results were expected to be of minor relevance.

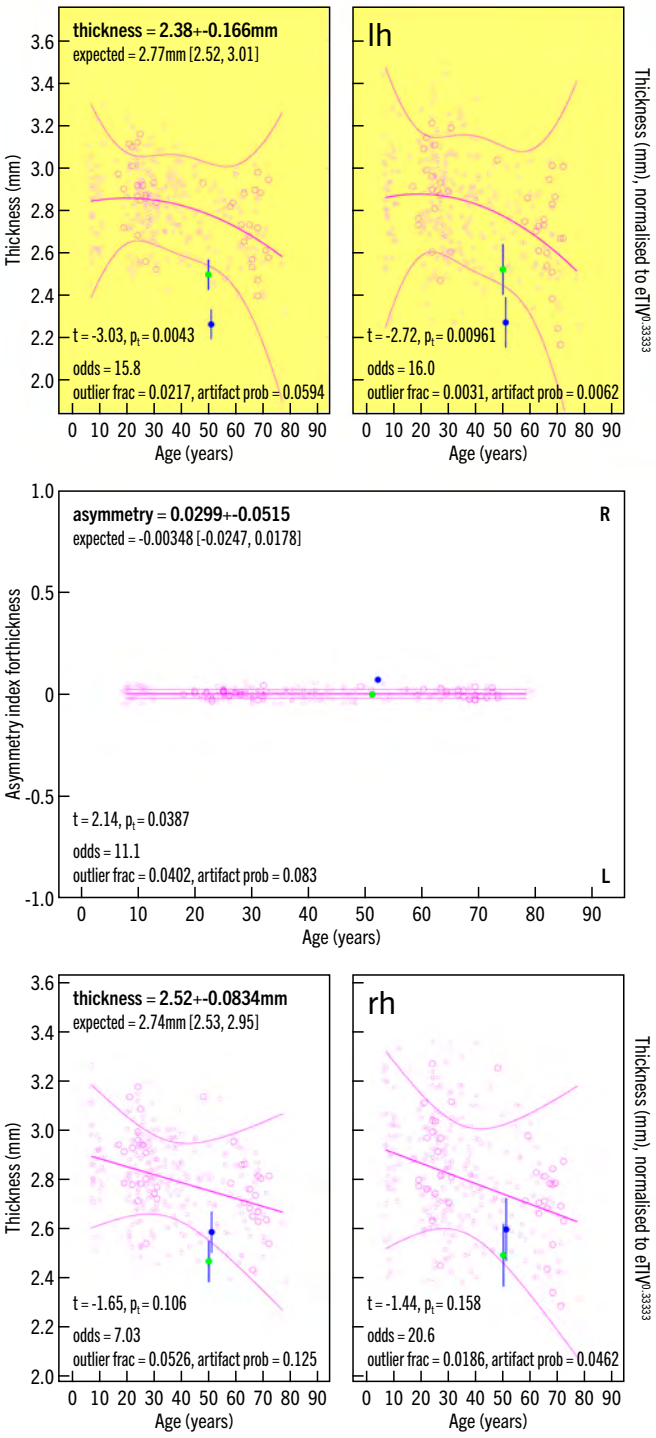
Follow-up occurred nine years after onset of physiotherapy to document the long-term need of therapy: After the initial intense physiotherapy phase of one year, the patient continued to have physiotherapy once every three weeks for thirty minutes and a continuing home programme which the patient performed after her needs with the aim to sustain the results, to avoid increasing tension in the relevant structures and to ensure further safety for eating and drinking (*Figure 5*). The status quo was primarily sustained over one year, after which the patient went on a four-months-travel without any therapy. She continued her home programme irregularly. On returning, she showed increased difficulties in eating, frequent coughing during meals and her Sydney Swallow Questionnaire (SSQ) score had changed from former 480 to 800 (max = 1700/ norm = 0). Her BMI had stayed on 23. The left orofacial and pharyngeal structures showed increased and painful tension. Subsequently she had intense physiotherapy (as described above) twice a week for thirty minutes over two month, after which her SSQ score went again down to 640. The patient was content with the score because she could eat again safely and without coughing. Since then, a regular therapy schedule once every three weeks for thirty minutes and an individual home programme has proved to be the ideal frequency to sustain safe eating and drinking and adequate physiological tension for the relevant structures as shown in *Table 1*. Actual SSQ score 598, actual BMI 22.

Discussion

A focused, year-long targeted physiotherapy programme led to relevant clinical improvement of a very long-standing dysphagia due to pseudobulbar palsy. The clinical results are supported by relevant changes in the MRI findings.

Recovery after focal brain damage may be paralleled by profound plastic changes in grey matter morphology, including perilesional synaptogenesis, axonal sprouting or

Recovery after focal brain damage may be paralleled by profound plastic changes in grey matter morphology, including perilesional synaptogenesis, axonal sprouting or reorganisation of cortical motor representations.



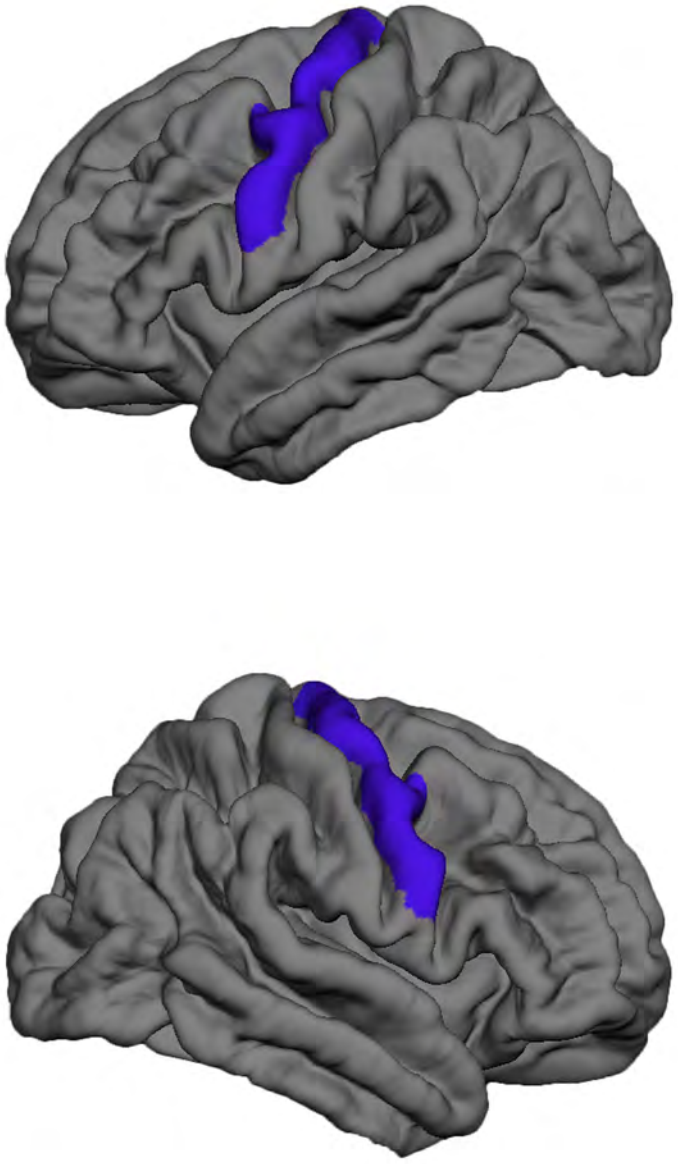
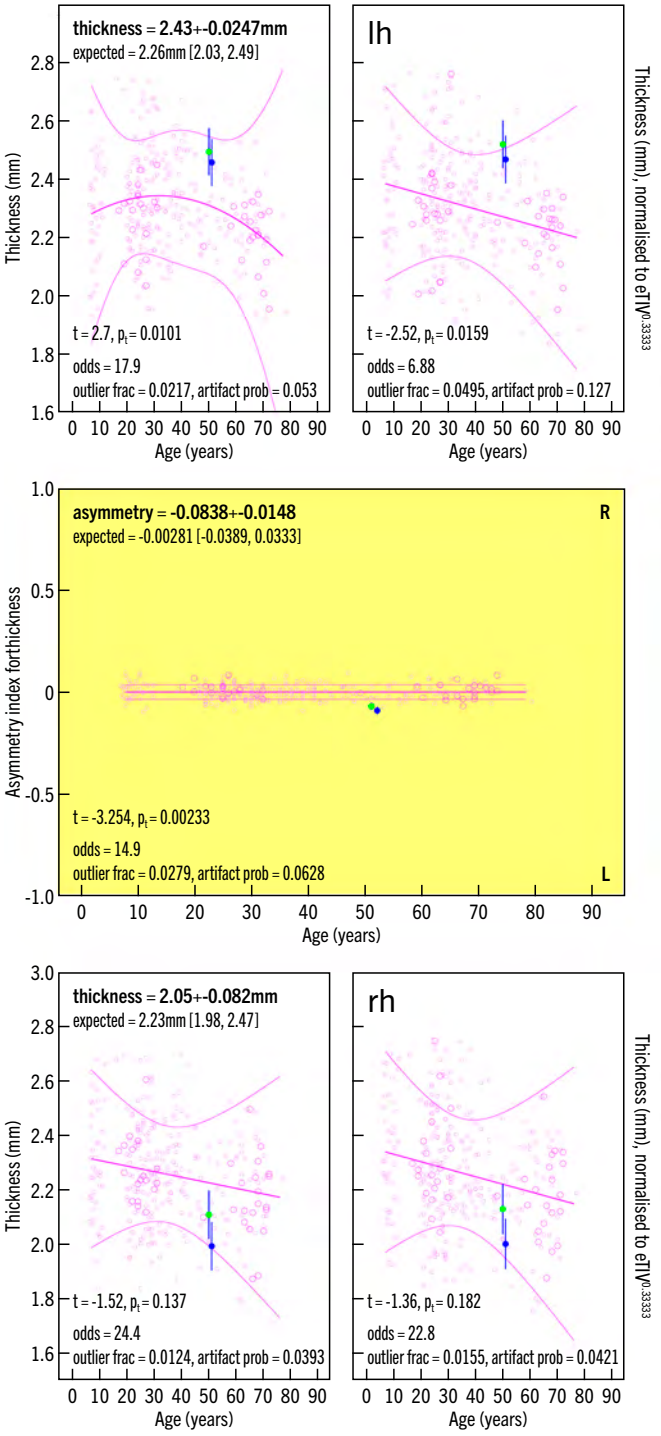


Figure 2 Longitudinal region-specific morphometric analysis (cortical thickness) in the precentral gyrus over a twelve- month follow-up period: the markers in green indicate the thickness ahead of therapy and the markers in blue the regional GM thickness in the precentral gyrus after therapy: left image = left precentral gyrus, right image = right precentral gyrus. Note the longitudinal decrease of the thickness in the left hemisphere, opposed by increased thickness in the right (unaffected) hemisphere. The middle row indicates the grade of asymmetry (relative to the contralateral reference region). Also shown is the Precentral gyrus (area of cortical thickness analysis).

reorganisation of cortical motor representations. In our case study, longitudinal regional cortical thickness changes were detected that may be a substrate of targeted physiotherapy, even years after the initial illness. Plasticity effects were clinically evident, despite progressive atrophy in the related hemisphere. However, this effect was counterbalanced by increased cortical thickness in the corresponding precentral cortex area of the contralateral hemisphere and



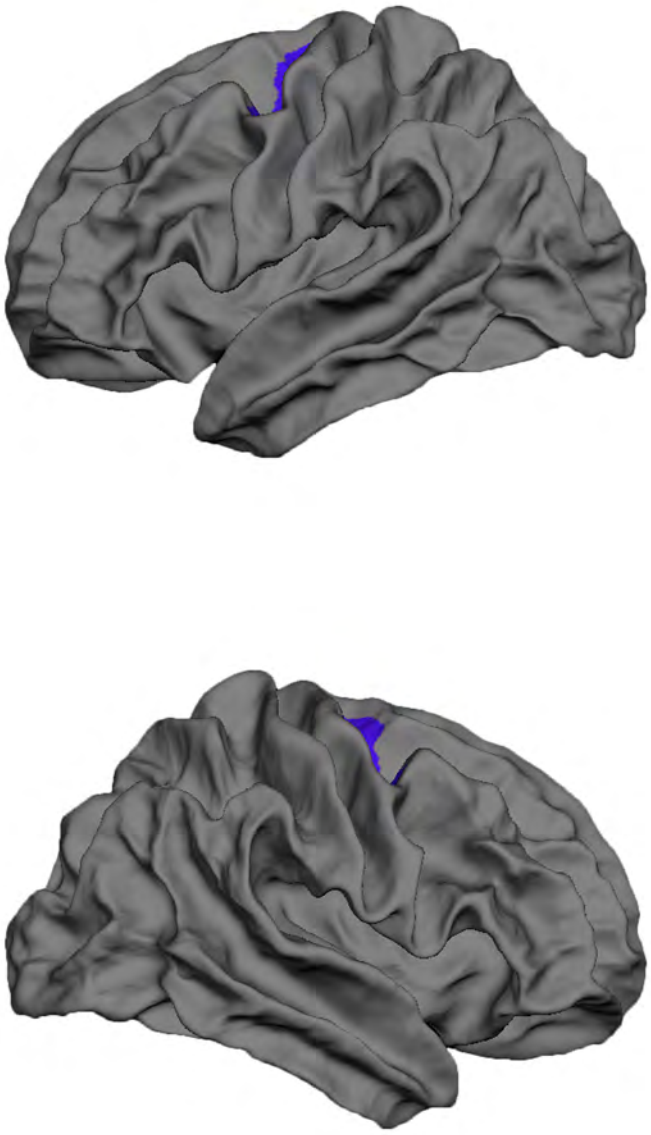


Figure 3 Longitudinal region-specific morphometric analysis (cortical thickness) in the left superior precentral sulcus over a twelve-month follow-up period (upper row): cortical thickness is significantly increased relative to the contralateral precentral sulcus and stable during the follow-up period (lower row). The middle row indicates the asymmetry towards the left superior precentral gyrus.

the superior bank of the ipsilateral motor cortex. The latter may be interpreted as late onset local reorganisation of sensorimotor representation within the bilateral motor network, gaining an improved yet not restored level of automatic motor behaviour.

Today's knowledge of sensory-motor training and motor learning suggests that a broad function-related, task-oriented and structural therapeutic approach with purposeful activities of daily living as described in the current case study may lead to determined improvements

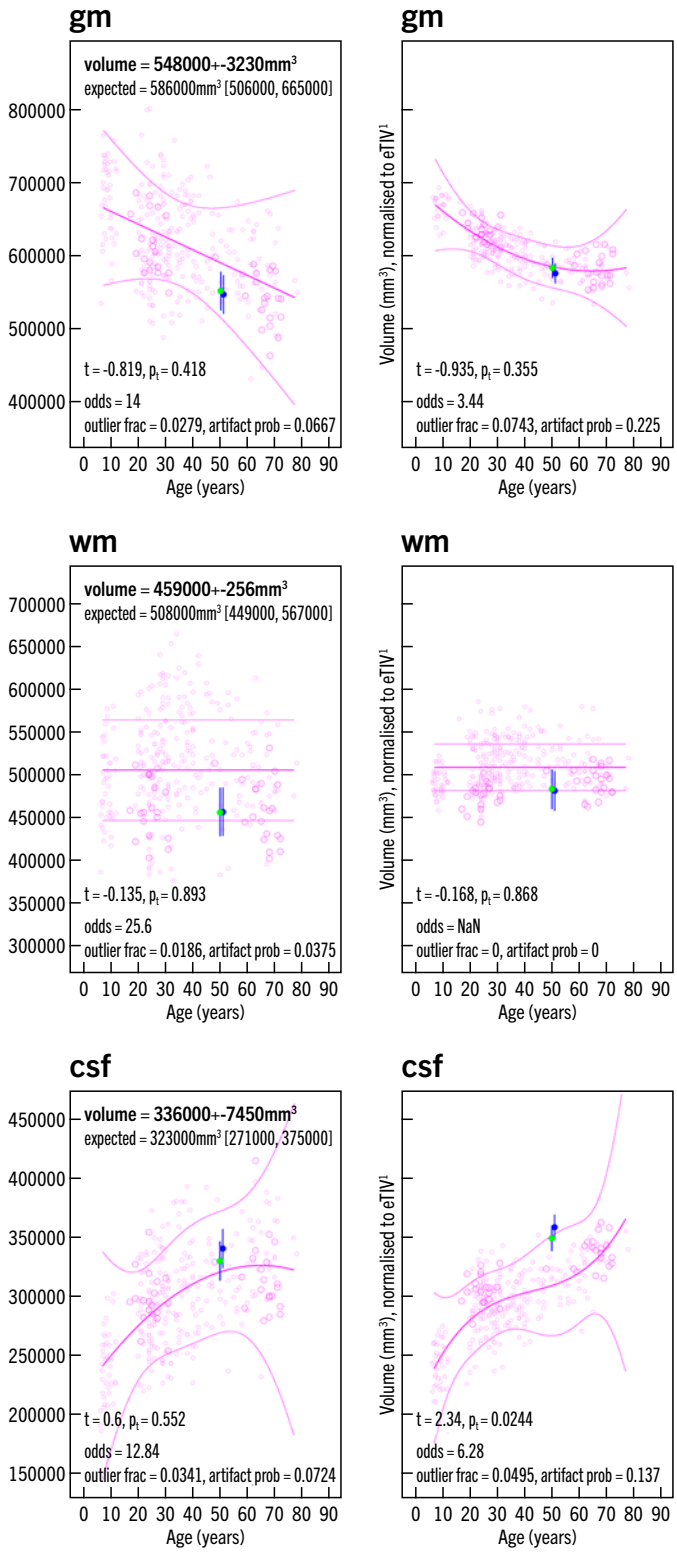


Figure 4 Whole brain gray matter (gm), white matter (wm) and CSF volume analysis indicates no significant differences between the hemispheres. The left row displays the absolute values, the right row after normalisation to the global brain volume. After normalisation, a trend towards increased CSF (p=0.02 was observed), GM and WM remained stable.

in patients' daily lives and induce neuroplasticity (Robbins J 2008, Shumway-Cook A and Woollacott M 2012).

As mentioned above, effective therapy methods for long-standing neurologically induced non-progressive dysphagia have not been well investigated, with very little data available on the long-term effects of therapy (Langmore SE 2015, Speyer R 2010, Barikroo A 2017).

Therapy for long-standing severe impairments may need a long-lasting continuation to sustain achieved results as confirmed in the current case study.

Apart from the improved wellbeing of the patients, the prevention of tube feeding contributes to saving costs, even compared to long-lasting therapy (Groher ME 1995, Haaks T 1999).

This individual case study may be informative to therapists dealing with patients with long-standing orofacial and pharyngeal impairments.

Further research into effective therapeutic approaches is necessary to ensure the best possible results in long-standing impairments.

Implications for rehabilitation and take home message

- In long-standing non-progressive dysphagia, all affected structures of the face, mouth, pharynx, postural stability and respiratory system must be therapeutically mobilised to restore tissue mobility as closely to physiological state as possible.
- Therapeutically restored tissue mobility allows the patient to become differently aware of relevant structures, instead of practicing accustomed limited patterns, allowing him to acquire enhanced motor control and to bring about neuroplasticity.
- Function-related physiotherapy in a patient with very long-standing dysphagia can lead to relevant clinical changes being accompanied by maintenance or increases of cortical thickness in the superior premotor areas, both ipsilateral and contralateral to the lesion.

Patient perspective

One year prior to commencement of therapy I had severe problems with swallowing. I was almost unable to eat and constantly suffered from a dry mouth which made food stick to my palate. There was a constant tension in the dorsal part of my palate as well as in my left cheek and throat. My present state has much improved: the tensions have decreased and I can eat safely again. Drinking seems to work even better than ever before. I am able to drink

from a normal glass without drooling. My wellbeing is therefore much better. The perception of food in my mouth and on my tongue has become more distinct even on my right side and I perceive the right side of my face and mouth better than ever before. I no longer drool except when very fatigued. Some people say that my intelligibility has improved.

The article has been written according to CARE case report guidelines (Gagnier JJ 2013).

Informed consent has been obtained from the patient.

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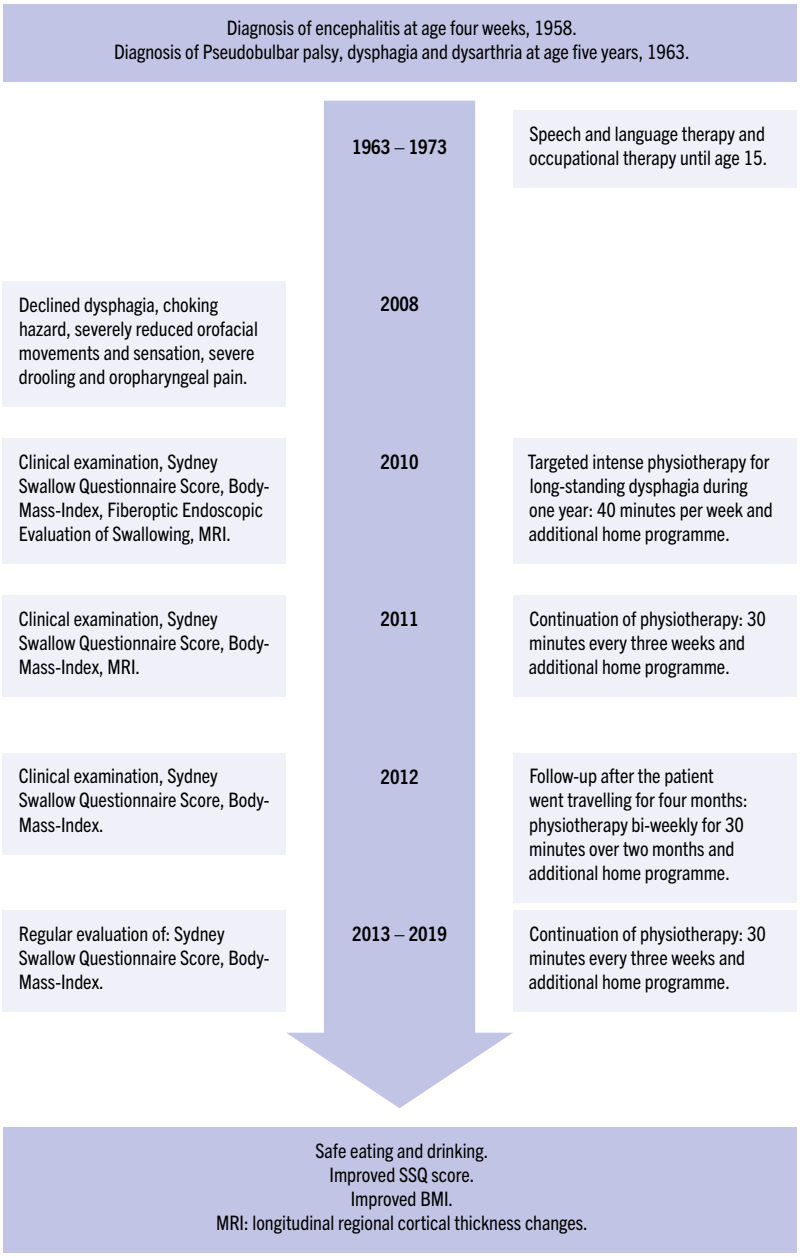

Figure 5 Timeline of the development of the current case.

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Modelling rehabilitation for those with spasticity following brain injury

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Spasticity may present a significant clinical problem in terms of limiting function at the level of activity performance by the individual, otherwise known as 'active function' (Sheean 2001).

Alternatively it may impact on carrying out care tasks by a caregiver or by the person themselves to a paretic limb, otherwise known as 'passive function' (Sheean 2001). Spasticity can also have further negative symptomatic implications at the level of body systems impairment such as pain.

Goal attainment scaling has been used as a method to set spasticity management related goals and evaluate outcome (Ashford and Turner-Stokes 2006, Ashford and Turner-Stokes 2009, Turner-Stokes, Baguley *et al.* 2010). Goals for treatment of spasticity are widely diverse, depending on the individual aspirations and priorities of the patient and/or their family. They may be directed at reducing impairment (eg preventing contractures and deformity), improving activities (such as personal care) or use of the limb for participatory activities (such as work, hobbies, recreation etc). In other words, goals may be directed at achieving change at any level of the World Health Organisation (WHO) International Classification of Function, Disability and Health (ICF), but most commonly in activity for both passive and active function.

Goal Attainment Scaling has now been used as the primary outcome measure in three large multi-centre studies of focal spasticity intervention in the upper limb, the BEST study (Ward AB, Wissel J *et al* 2014), Upper Limb International Spasticity II (Turner-Stokes, Fheodoroff *et al* 2013) and Upper Limb International Spasticity III (Turner-Stokes, Ashford *et al* 2016). Through these studies GAS was demonstrated to detect clinically important change in outcome for people with upper limb spasticity.

Goal setting and treatment planning in spasticity management

Alongside the systematic setting and evaluation of patient-directed goals, understanding what treatment is received and how it is best applied is essential to achieving the best outcomes. There is still limited understanding of the combined, complex intervention provided in the physical rehabilitation of those with spasticity. To deliver 'best practice' it is key that we examine which interventions are used and work best to begin to develop a clearer model of practice. In spasticity and associated contracture management, this issue becomes challenging when a combination of multiple physical and pharmacological interventions are often used and relate to the wider rehabilitation that individuals receive, not just the direct management of spasticity.

Understanding which treatments are used and are effective in practice for spasticity management is important to model, before further formal evaluation of those treatments can be undertaken. Categorisation of goals for focal spasticity intervention has identified consistent goal areas which may be associated with particular types of physical intervention (Ashford, Jacinto *et al* 2015). Achievement of spasticity treatment goals which are categorised to 'passive function' improvement, may be associated with stretch interventions such as serial casting, whereas for 'active function' improvements, practising functional tasks may be the key element. A previous Cochrane review identified 'low level' evidence for the effectiveness of outpatient rehabilitation in improving active function and impairments following botulinum toxin for upper limb spasticity in adults with chronic stroke (Demetrios, Khan *et al* 2013). In a further Cochrane review evaluating non-pharmacological interventions for spasticity in multiple sclerosis, there was also 'low level' evidence for physical activity programmes used in isolation or in combination with other interventions (pharmacological or non-pharmacological) in improving outcomes (Amatya,

Khan *et al* 2013). Further understanding of what interventions are relevant to what clinical presentations (or goal categories) is required before more formal evaluation of the treatment package can take place.

Through systematic evidence-based evaluation (Ashford, Slade *et al* 2008, Ashford and Turner-Stokes 2013, Ashford, Brown *et al* 2014), we have refined the approach to goal setting (Ashford, Jackson *et al* 2016, Turner-Stokes, Ashford *et al* 2016) alongside psychometrically-robust standardised measures to capture functional gain, the Arm Activity (ArmA) (Ashford, Slade *et al* 2013) and Leg Activity (LegA) (Ashford, Jackson *et al* 2016) measures. We have also developed standardised tools to record therapy interventions for both upper and lower limb spasticity: the Arm and Leg Therapy recording Schedules (the ULSTR and LegTS). This combination of goal setting, process and outcome measurement has been termed the Focal Spasticity Index (FSI), presented in the national guidelines (Royal College of Physicians, British Society of Rehabilitation Medicine *et al* 2018).

Six goal areas for arm spasticity rehabilitation were identified through this work.

Symptoms and impairment

- Reduction of spasticity-related *pain* (11%)
- *Prevention* of contractures and deformity (23%).
- Control of unwanted *involuntary movements* or spasms (11%).

Activities

- Making care for the affected arm easier ('*passive-function*' (Sheean 2001)) (35%).
- Using the affected limb ('*active-function*' (Sheean 2001)) (17%).
- Improved *mobility* (2%).

A prospective study confirmed the same findings (Turner-Stokes, Fheodoroff *et al* 2013). This framework has identified the primary goals for treatment in arm spasticity, with demonstration of the feasibility of structured goal setting leading to improved quality in the goals set. Improvements in practice have already been noted with recognition of the need to treat spasticity-related pain and addressing deficits as a result of shoulder spasticity (Turner-Stokes, Fhedoroff *et al* 2019).

We completed a further study in leg spasticity with similarly findings and two domains, each subdivided into three key goal areas. Following these insights, we have undertaken preliminary work developing these concepts to support treatment planning for rehabilitation in those with spasticity. The approach to date is called Direct-Rehab. In Direct-Rehab we aim to further develop a treatment selection menu for planning rehabilitation in individuals with spasticity. Direct-Rehab will enable more focused rehabilitation and care for those with spasticity and should result in provision of the most appropriate treatment in a timely and cost-effective manner.

… understanding what treatment is received and how it is best applied is essential to achieving the best outcomes.

Competing interests and sources of funding

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Evidence that exercise is neuroprotective in Parkinson's disease

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Parkinson's disease (PD) is the second most common neurodegenerative disease after Alzheimer's disease.[1] It is characterised by a long prodromal disease state (*Figure 1*) that gradually progresses to involve various brain regions until the cardinal motor signs become evident and a diagnosis is made.[2]

Currently, there is no medication or surgical intervention that prevents, slows, or halts this neuro-degenerative process in PD.

The previous notion that PD is caused by impairment of the nigrostriatal pathways is a facile view of PD pathophysiology. Work by Braak *et al* have demonstrated that multiple brain regions become progressively more involved as the disease progresses and the nigrostriatal pathways are not affected until midway through the disease process.[3] This expanded view of the neurodegenerative process helps explain the many symptoms, including non-motor features, of PD.[2] Currently, there is no medication or surgical intervention that prevents, slows, or halts this neurodegenerative process in PD.[2] Outside of finding a cure, identifying a neuroprotective treatment strategy that delays or slows the progression of the disease (*Figure 2*) is a top research priority. Some have called it the most critical gap in the field of PD research.[4] In this review, evidence that exercise is neuroprotective is presented.

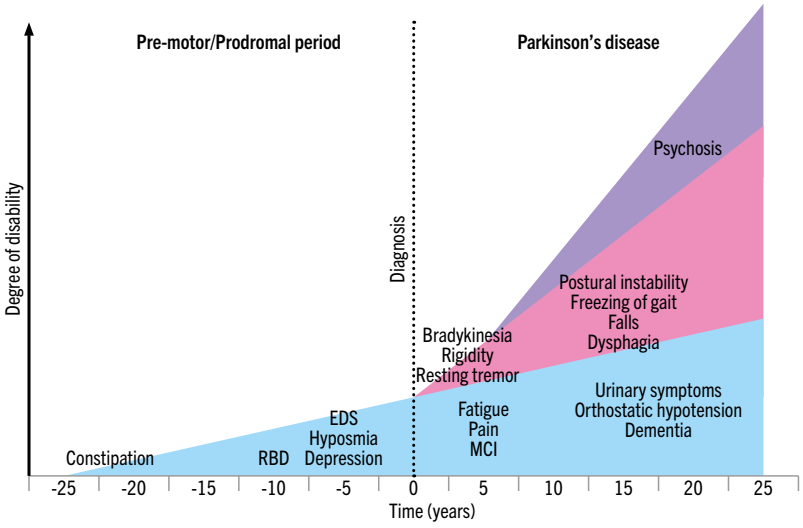

Figure 1 Illustration of the progression of Parkinson's disease (adapted from Kalia and Lang 2015[2]). Abbreviation key: REM sleep behavior disorder (RBD), excessive daytime somnolence (EDS), and mild cognitive impairment (MCI).

Biological plausibility of exercise neuroprotection

To confer neuroprotection against PD, it is imperative to understand the mechanisms that are involved in the development and progression of the pathology. Importantly, in order for exercise to be neuroprotective in PD, there must be face validity that it has a direct effect on some part of the pathological process. Currently, most of the early evidence for exercise-induced neuroprotection in PD suggests that it increases neurotrophins (eg brain derived neurotrophic factor (BDNF), glial derived neurotrophic factor (GDNF)) which is thought to enhance relevant neuroplasticity.[5,6] While the evidence in this area is indeed accumulating, it is important to note that there may also be other biological mechanisms contributing to exercise neuroprotection in PD.

The molecular hallmark of PD is the presence of Lewy bodies which consist of aggregations of misfolded α-synuclein, a natively unfolded molecular chaperone. It is not known what causes this protein to aggregate; however, it has been shown that these aggregations trigger mitochondrial respiratory dysfunction (type 1) which increases reactive oxygen species and oxidative stress.[7] Moreover, oxidative stress has been shown to influence α-synuclein aggregations. Thus, a vicious cycle ensues (*Figure 3*).[7] Cell death accumulates as a result of neurotoxicity directly from the α-synuclein aggregations and also from the reactive oxygen species and oxidative stress. In addition, a pro-inflammatory milieu and environmental toxins, which are complex 1 inhibitors, may also be contributing to this vicious cycle. From a theoretical perspective and based on associated research, aerobic exercise may interfere with several factors in this vicious cycle, including decreasing the inflammatory milieu, increasing antioxidant enzymes, and decreasing oxidative stress.

Of the PD pathological mechanisms,[8,9] it is biologically plausible that aerobic exercise exerts a potential neuroprotective effect either directly (ie oxidative stress/mitochondrial dysfunction, neuroinflammation, loss of neurotrophic factors) or indirectly (protein aggregation and misfolding) (*Table 1*). It is noteworthy that exercise-induced increases in neurotrophins (eg GDNF, BDNF), which are well-established in the literature, may have a positive effect on neuroinflammation, excitotoxicity, and apoptosis. Taken together, it is biologically plausible that aerobic exercise, both directly and indirectly, may have a disease modifying effect in PD.

Lines of evidence for exercise neuroprotection in PD

Rodent research

Evidence that aerobic exercise is neuroprotective in PD comes from several sources, including rodent PD models. While an exhaustive review of all of the rodent literature is not appropriate for this review, it should be noted that there have been many studies that have demonstrated robust neuroprotection in mice[10-19] and rat[16,20-27] models of PD before and after neurotoxic induction. There have been only a couple of studies showing a less robust neuroprotective effect.[28,29] Collectively, these rodent studies have demonstrated a decrease in rodent parkinsonian symptoms and a mitigation of underlying disease processes, including many that have demonstrated near complete amelioration of parkinsonian pathology and behavioral impairment. While robust neuroprotective or neurorestorative effects are unlikely in human PD, these rodent models offer evidence for exercise-induced neuroprotection and also elucidate potential neurobiological mechanisms (primarily neurotrophin upregulation and improved inflammatory milieu) related to exercise and PD.[30]

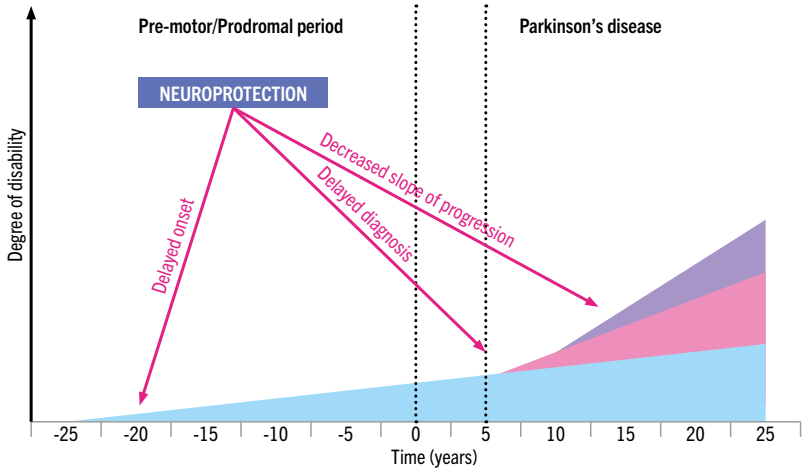

Figure 2 Conceptualisation of neuroprotection in Parkinson's disease.

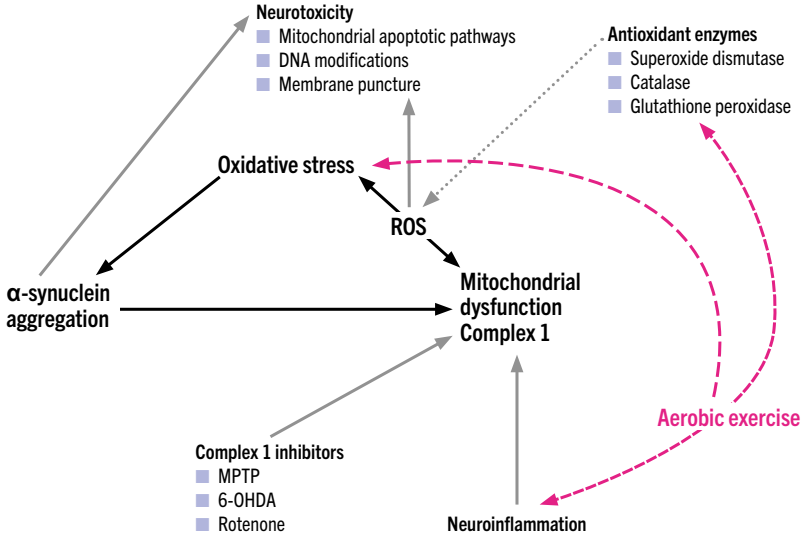

Figure 3 A theoretical model of the disease process in Parkinson's disease. Dotted lines indicate targets for neuroprotection. Red dotted lines indicate areas where exercise may exert a neuroprotective effect.

PD neuropathologic mechanism	Targets for neuroprotection
Oxidative stress and mitochondrial dysfunction	Inhibitors of dopamine metabolism (eg MAO inhibitors, dopamine receptor agonists) Electron transport enhancers (eg CoQ10) Other oxidents (eg vitamin E, uric acid) Anti-oxidant enzyme promotors Inhibitors of α-synuclein aggregation Therapeutic agents that reduce α-synuclein protein levels Enhancers of parkin function and UCH-L1 function Enhancers of proteosomal or lysosomal pathways
Protein aggregation and misfolding	Anti-inflammatory agents (eg NSAID, statins, minocycline) NMDA receptor antagonists Calcium channel antagonists Anti-apoptotic agents
Neuroinflammation	Neurotrophic factors (eg GDNF, BDNF, neurturin
Excitotoxicity	
Apoptosis and cell death pathways	
Loss of neurotrophic factors	

Table 1 Possible targets for neuroprotection (adapted from Yacoubian and Standaert[8] and Sarkar *et al*[9]).

Epidemiological research

Epidemiological evidence suggests that exercise, when performed in the pre-clinical phase, can lower the risk of developing PD. In a recent systematic review and meta-analysis of only prospective studies,[31-37] Fang *et al*[38] reported that higher levels of total physical activity in the pre-clinical phase, particularly moderate to vigorous activity, was associated with a reduced risk of PD. These studies were mostly very large cohorts (over half a million adults collectively) that were followed over time to determine who would eventually develop PD. It is interesting to note that the beneficial effect of exercise was observed among males and males/females together but not among the females in a subgroup analysis. However, in another meta-analysis by Xu *et al* they found that moderate to vigorous physical activity at ages 35-39 or in the last ten years was associated with a future 40% lower risk for PD in both males and females.[35] Taken together, these two meta-analyses suggest that exercise/physical activity prior to PD diagnosis may be neuroprotective. However, one limitation of these epidemiological studies is the potential for reverse causality which would mean that lower physical activity or exercise participation levels prior to diagnosis might be a prodromal PD symptom. The argument against this is that Xu *et al*[35] did not find an association between lower physical activity levels and a higher risk for PD. Additionally, analyses of repeatedly measured activity levels showed that decreased physical activity in PD does not typically appear until 2-4 years before diagnosis.[31]

Specifically, those who participated in more moderate physical activity in the pre-clinical disease state were older at PD diagnosis, which is consistent with the notion that exercise is neuroprotective.

Exercise and physiotherapy outcomes

There is considerable evidence that exercise and physiotherapy are beneficial for people with PD. In a systematic review and meta-analysis, the authors concluded that exercise was beneficial for physical functioning, health-related quality of life, strength, balance, and gait speed for people with PD.[39] In a more recent systematic review, the authors concluded that exercise improves aerobic capacities, muscle strength, walking, posture and balance parameters.[40] These findings support other systematic reviews and meta-analyses that have found similar benefit as a result of physiotherapy for people with PD.[41,42] Other systematic reviews have found that treadmill training improves gait[43] and aerobic and strength training programmes are effective at improving many physical function dimensions in people with PD.[40] Taken together, these systematic reviews offer compelling evidence supporting the effectiveness of physiotherapy programmes and general exercise programmes for people diagnosed with PD. Moreover, in a more recent randomised control trial (RCT) comparing high intensity exercise to low intensity (usual care), results demonstrated that high intensity exercise drove more improvements across more outcome domains than the low intensity group.[44] This is consistent with results from a systematic review and meta-analysis on high intensity exercise which concluded that it is safe, feasible, and beneficial.[45] Importantly, in that RCT, evidence that exercise may affect the underlying PD course was also reported.[44] Specifically, BDNF improved for both exercise groups and there was a positive association between improvement in outcomes and higher levels of potentially neuroprotective anti-inflammatory conditions. This is believed to be the first human PD trial that has reported evidence supporting the biological evidence of exercise neuroprotection in PD.

Pre-diagnosis exercise habits

A recent study demonstrated that self-report moderate physical activity from the 3rd to 5th decades of life was associated with age at PD diagnosis.[46] Specifically, those who participated in more moderate physical activity in the pre-clinical disease state were older at PD diagnosis, which is consistent with the notion that exercise is neuroprotective. These results also demonstrated that every hour increase in weekly moderate physical activity was associated with a PD diagnosis a little over a quarter of a year later. That is, four more hours of exercise per week would have delayed the PD diagnosis by just over one year. While this relationship only explained 14.6% of the variance in age at PD diagnosis, it does provide supportive evidence that is consistent with the aforementioned epidemiological studies.

Discussion

The evidence that exercise produces many multi-system benefits for all adults is not disputed. Moreover, these multi-system benefits are beneficial to all people, including those with PD. Speelman *et al*[47] concluded that exercise has the following possible PD-specific benefits: prevention of cardiovascular complications, arrest of osteoporosis, prevention of depression, improved sleep, decreased constipation, decreased fatigue, improved motor performance, improved drug efficacy, and optimisation of the dopaminergic system. If those were the only benefits of exercise for people with PD it would be compelling enough to advocate for exercise as a first line therapy for people with PD. However, the current thesis of this review is that aerobic exercise provides something over and above these benefits. That is, it affects the underlying disease course. While each of the aforementioned lines of evidence in isolation are not sufficiently strong enough for causal inference

of neuroprotection in PD, the validity for causal inference is enhanced by the considerable number of studies supporting the construct, the consistency of results across different designs, the strength of the associations, and the biological plausibility. Thus, it is proposed that there is currently sufficient data to conclude that aerobic exercise affects the underlying disease process in such a way that it is neuroprotective in PD. Moreover, the evidence is compelling enough that aerobic exercise should indeed be a first line therapy in PD. It should be initiated early and preferably in the very early phases while it is still early enough in the neurodegenerative process to meaningfully intervene. This means that there is a need to better identify those who are at the highest risk. Moreover, it is proposed that aerobic exercise should be performed regularly to optimise the neuroprotective benefit which is consistent with the evidence.[48] Lastly, since PD is a progressive disease, exercise should be recalibrated by a physiotherapist on a regular basis to ensure that it addresses appropriately impaired systems and that the parameters are sufficiently tailored to enhance neuroprotective mechanisms.

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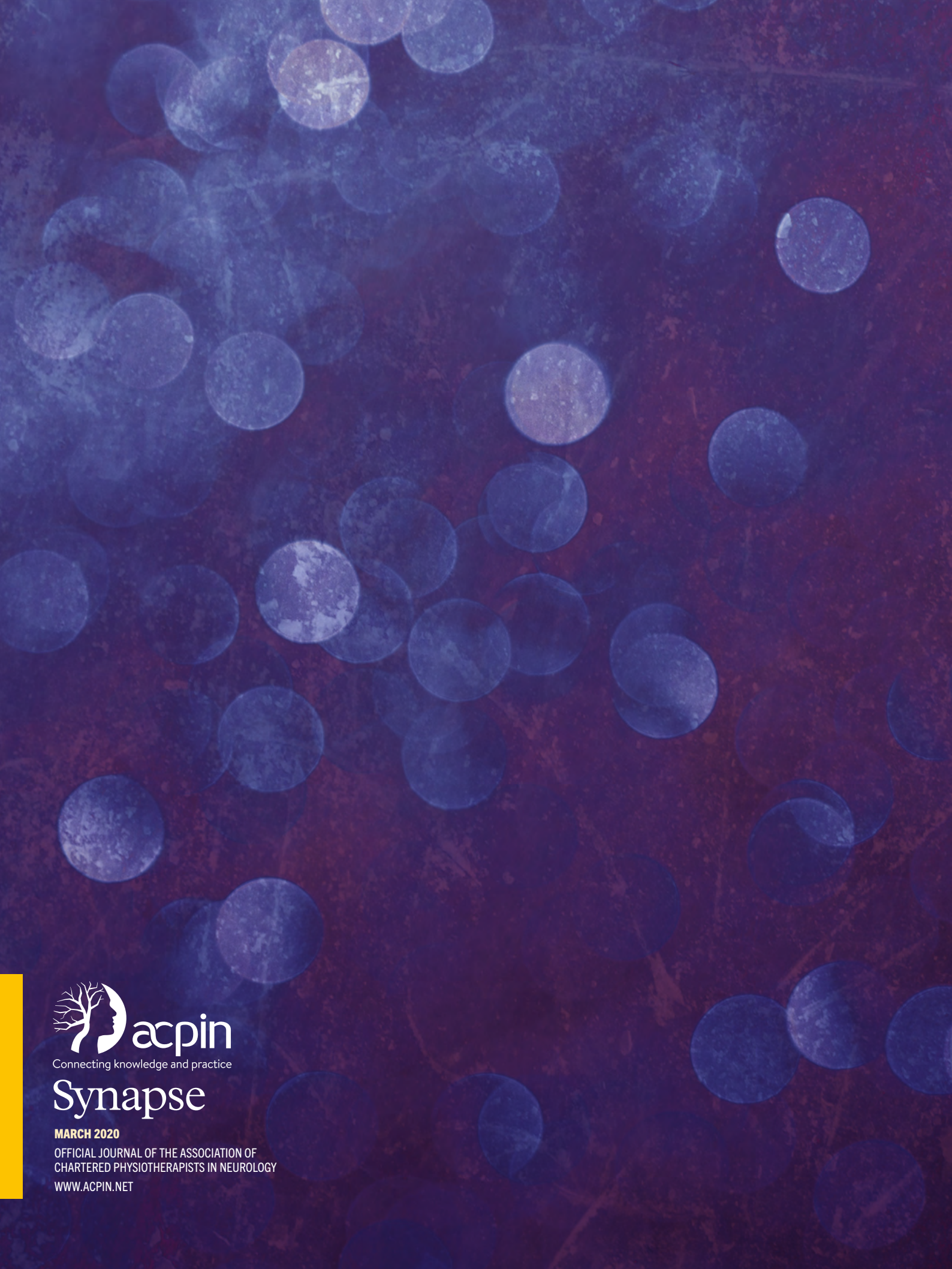

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