Cervical spondylotic myelopathy is one of the most common spinal cord disorders in people older than 55 years. Chronic degenerative changes of the vertebral disc, the intraspinous ligaments, and the adjacent bony structures of the vertebrae are normal aging processes of the cervical spine. Dislocated disc material, thickened yellow ligaments, slowly growing osteophytes, and spinal instability can lead to stenosis of the cervical spinal canal with mechanical compression and dysfunction of the cervical spinal cord (cervical myelopathy).

Constant compression of the cervical spinal cord at the level of stenosis and repetitive microtrauma during neck movement may lead to structural tissue damage. Atrophy and neuronal loss in the gray matter and demyelination in the white matter have been demonstrated in biomechanical and autopsy studies. The diagnosis of a CSM is based on radiological and clinical findings. Typically, a degenerative cervical spinal stenosis with compression of the cervical spinal cord and a cervical myelopathy with neurological deficits are present. Cervical myelopathy is usually a slowly progressive process taking place over years with phases of acute clinical deterioration, phases of partial spontaneous recovery, and phases of chronically persistent deficits. Symptoms often develop insidiously and are characterized by neck stiffness, arm pain, numbness in the hands, and weakness of the hands and legs. It can finally lead to complete paralysis of all neurological functions below the level of stenosis.

To quantify the clinical impairment, the functional status in patients with CSM is usually assessed by the JOA scoring system.

**Cervical Spondylotic Myelopathy**

Morphological Imaging of CSM Using MRI

Clinically, CSM is usually visualized using MRI,
which offers an excellent visualization of the morphological aspects with high spatial resolution. The detection of stenosis, effacement of the subarachnoid space, spinal cord compression, and an intramedullary hyperintensity on T2-weighted images (the "myelopathy sign") are the essential findings.

However, the presence of these radiological features in patients with CSM does not always result in clinical symptoms (see Fig. 1B). Structural MRI defines the location and extent of cervical spine stenosis but may not reflect the complexity of this morphologically stable but clinically dynamic disease with variable courses even in asymptomatic patients. It is unclear how patients with cervical spine stenosis, obvious spinal cord compression, and MRI-documented myelopathy sign switch from a clinical inactive (asymptomatic) phase to one of symptomatic CSM.

Cervical spine stenosis and compression of the cervical cord are the primary causes of CSM. Thus, decompressive surgery appears to be the treatment of choice to improve the patients’ symptoms and to prevent further clinical deterioration. Standard microsurgical anterior decompression and cage fusion or posterior decompression with eventual instrumentation placement is routinely performed. Despite excellent neurosurgical results regarding the mechanical decompression of the cervical spinal cord, which can be visualized on postoperative MRI, patients’ outcomes are variable and unpredictable. Neither clinical symptoms nor postsurgical outcome correlates with the morphological aspects of CSM as assessed by structural MRI.

To date, our knowledge of what brings about recovery, even without decompressive surgery to resolve the cause of compression, is limited. Recently, there has been

![Fig. 1. Morphological and metabolic images in CSM in different clinical phases of the disease. A: Healthy control patient (JOA score of 17) without stenosis in MRI (A1). The PET scan shows a linear homogeneous FDG uptake (A2) along the complete cervical cord (normometabolism). B: Patient with incidental finding of radiological myelopathy. The T2-weighted MR image (B1) shows a stenosis with cord compression and an intramedullary hyperintensity (arrow). Clinically there were no symptoms of myelopathy (JOA score of 17). The corresponding FDG PET (B2) demonstrates a homogeneous glucose uptake (normometabolism) identical to healthy controls (A2). C–E: Three patients with a clinically acute onset of progressive myelopathy symptoms (JOA score < 12) within the last 6 months. The MR images (C1, D1, and E1) show, morphologically, the typical degenerative stenosis with cord compression and intramedullary hyperintensity (arrow). The corresponding 18F-FDG PET scans (C2, D2, and E2) reveal an increased “peak” uptake of glucose (local hypermetabolism) at the individual level of stenosis. F and G: Two patients with clinically chronic myelopathy and stable symptoms (JOA score < 12) for at least 12 months. The MR images (F1 and G1) show, morphologically, typical degenerative stenosis with cord compression and intramedullary hyperintensity (arrow). The corresponding FDG PET scans (F2 and G2) show a poststenotic decrease of glucose uptake (hypometabolism). There is no “peak” uptake at the individual level of the stenosis.]

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Cervical spondylotic myelopathy and FDG PET

discussion of an inflammatory response of the chroni-
cally compressed cord.3,4,42

Since morphological aspects of CSM visualized on
MRI have no predictive value regarding the spontaneous
clinical course and outcome after surgical decompres-
sion,15,18,25,34 18F-FDG PET scanning has been evaluated as
a tool to investigate the functional and metabolic changes
in CSM.

18F-FDG PET Imaging in Patients With CSM

Metabolic evaluation of spinal cord pathologies using
18F-FDG PET has been performed for more than 25 years,
especially in cases of neoplastic diseases8,10,16,24,26,27,29,32,40 but
also in a variety of cases involving benign inflammatory
intraspinal lesions such as infections,17 tophaceous gout,33
and neurosarcoïdosis.10,31 All in all of these space-occupying
and compressive lesions, 18F-FDG PET has been used to
differentiate between benign and malignant pathologies
or to monitor biological activity. For the most part, all
malignant entities like spinal metastasis and inflammatory
diseases like neurosarcoïdosis are characterized by
an increased glucose uptake. Furthermore, 18F-FDG PET
has also been evaluated in patients with radiation-induced
myelopathy. Increased glucose uptake has been observed
in the areas of demyelination, and, furthermore, the
glucose metabolism decreased correspondingly to clini-
cal problem, especially in our aging society. To assess the
metabolic aspects of compressive myelopathy, the glucose
metabolism of the cervical spinal cord has been evaluated
using 18F-FDG PET examinations.14,15,26,37,39 An overview
of the different patterns of physiological and pathological
-glucose utilization in 18F-FDG PET is illustrated in Fig. 1.

Physiological Glucose Uptake in Healthy Controls

Anatomical visualization and glucose utilization in
the uncompressed cervical spinal cord of healthy adults
has been described previously. The pattern of physiologi-
cal 18F-FDG uptake is characterized by a nearly homo-
genous linear glucose uptake along the entire cervical
spinal cord (Fig. 1A), with a slight decrease from the
cranio cervical to the cervicothoracic junction.8,9,14,15,22,28
A higher uptake at C-1 is observed in the majority of
individuals and seems to be related to a spillover from
the high glucose uptake of the lower brainstem.

Physiological Glucose Utilization in Asymptomatic
Patients With MRI-Documented Myelopathy Sign

Identical to healthy individuals without spinal canal
stenosis (Fig. 1A), asymptomatic patients with an inciden-
tal finding of cervical spinal canal stenosis, cord com-
pression, and MRI-documented myelopathy sign may ex-
hibit the same homogeneous linear glucose uptake in the
whole cervical spinal cord (Fig. 1B). Despite the cervical
cord compression, the patients’ metabolic status remains
unaffected and the patients show no clinical symptoms of
myelopathy.

Pathological Glucose Utilization in Symptomatic Patients
With CSM

The first studies using 18F-FDG PET in small inho-
mogeneous groups of patients suffering from symptomatic
compressive cervical myelopathy reported either a
global reduction or global increase of 18F-FDG uptake
across the entire spinal cord independent of the level of
stenosis.7,26,39 This is surprising since compressive my-
elopathy is morphologically a local phenomenon on MRI
and the neurological impairment, such as sensory and
motor deficits, is predominantly related to the segments
at and below the level of stenosis. Therefore, a local meta-
abolic reaction of the damaged cervical spinal cord at and/
or below the level of the cord compression should be ex-
pected instead of global changes in 18F-FDG uptake in the
entire cervical cord.

Subsequent studies in larger patients groups have
used more strict inclusion criteria, and the results suggest
that monosegmental local compressive myelopathy on
MRI corresponds to local—and not global—alterations in
the glucose metabolism of the cervical cord, with strict
relation to the individual level of stenosis (Fig. 1C–G).14,15,37
This may indicate that the alteration of glucose uptake is
restricted to the neural tissue at the level of stenosis and
distal to the mechanical compression and does not influ-
ence the entire cervical spinal cord.

Different patterns of pathological 18F-FDG uptake in
patients with CSM have been observed, and the pattern
may be specific for the different clinical phases of sym-
ptomatic CSM. The early myelopathy phase with acute
onset of clinical deterioration is characterized by a focal
hypermetabolism at the level of stenosis, while the late,
more chronic myelopathy phase with persistent deficits
exhibits a poststenotic hypometabolism.14,15,37

Glucose Hypermetabolism at the Level of Stenosis

Patients in the acute-onset phase of symptomatic
CSM and also patients with chronic-stable myelopathy
and new-onset symptoms exhibit a focally increased 18F-
FDG uptake at precisely the individual level of their ste-
nosis and cord compression (Fig. 1C–E).14,37

Decompressive surgery during the phase when hy-
permetabolism is present at the level of stenosis results
in a good clinical recovery and favorable outcome with
significant improvement of functional JOA scores.14 This
suggests that the hypermetabolism at the stenotic level
represents a condition with functionally damaged spinal
cord that is potentially reversible.

Poststenotic Glucose Hypometabolism

With ongoing symptomatic CSM, the disorder’s clin-
ic activity may slow down and convert to a chronic
phase of CSM. In this phase of myelopathy, the metabolic
pattern may change; the initial focally increased glucose
metabolism at the level of cervical cord compression van-
ishes and a poststenotic glucose hypometabolism occurs
(Fig. 1F and G).14,15 The observed metabolic impairment
Role of Compression-Induced Inflammation in CSM

Neuroinflammation has been suggested to play a key role in the pathophysiology of patients with CSM. Stirling and colleagues identified minocycline as a promising drug to reduce oligodendrocyte apoptosis in an animal model of acute cervical spinal cord injury.44 Nobel and coworkers demonstrated that the administration of matrix metalloproteinase–9 inhibitor reduces tissue damage in an animal model of acute cervical spinal cord injury.45 Despite several similarities between acute cervical spinal cord injury and CSM, CSM’s slow progressive conditions seem to be unique. Thus, Yu et al.46 examined molecular changes in postmortem human spinal cord tissue from patients with CSM. They demonstrated that an innate immune response may lead to neuronal and oligoden -droglial death, which was mediated by Fas and Fas ligands. After transforming this knowledge to an animal model of CSM, they furthermore have shown that blocking Fas by repeated injection of Fas ligand–neutralizing antibody improves locomotion in comparison with control animals.

On the basis of the experiences with other neuroinflammatory diseases (for example, multiple sclerosis), it is supposed that treatment with corticosteroids may suppress the influx of inflammatory cells and subsequently the epiphenomenon of hypermetabolism in the compressed cervical spinal cord. From findings in animal models it is known that increased 18F-FDG uptake occurs in inflammatory tissue,41 and both the invasion of inflammatory cells and the subsequently increasing 18F-FDG uptake can be successfully suppressed by administration of corticosteroids.6 Those findings provide a rationale for neuroprotective strategies in addition to treatment by the usual procedure of decompressive surgery. On the basis of these findings and other preclinical pharmacological treatment results, it has to be assumed then that antiinflammatory drugs like corticosteroids also may suppress the influx of inflammatory cells (for example, macrophages) as they do in other neuroinflammatory diseases (for example, multiple sclerosis).

A compression-induced inflammation of the cervical cord with infiltration of macrophages might be implicated in the acute onset of myelopathy symptoms and clinical deterioration. In the course of CSM, the initial clinical progression slows down, and symptoms may stabilize or even partially improve despite persisting stenosis and cervical cord compression. In patients with CSM in this phase of the disease, an inconspicuous 18F-FDG uptake is shown at the individual level of stenosis and cord compression, and a decrease of 18F-FDG uptake is present below the stenotic level (Fig. 1F and G). It is tempting to speculate that neuroinflammation is a self-limiting process and, in this late phase of myelopathy, the compression-induced inflammatory reactions are completed and a structural damage of the cervical cord tissue remains.

Clinical Outcome and Metabolic Changes After Antiinflammatory Corticosteroid Treatment

In a recent study (Floeth et al., unpublished data), we tested the hypothesis of an inflammatory component in CSM. We analyzed the glucose metabolism in 2 patients with symptomatic CSM who refused to undergo surgical decompression of the stenosis. Both patients were clinically in the acute-progressive phase of their myelopathy, and, accordingly, PET scanning showed increased 18F-FDG uptake at individual level of stenosis. A high dose of oral corticosteroid therapy (cumulative dose of 42 mg dexamethasone over 8 days) was administered, which led to a reduction of the increased 18F-FDG uptake in the spinal cord to normal levels (Fig. 2B). This immediate effect of corticosteroid administration on 18F-FDG uptake in the spinal cord appeared to be similar to that observed after surgical decompression (Fig. 2A). Both patients made a slight clinical improvement, but this partial clinical recovery only lasted for a few weeks, when myelopathy symptoms worsened. Second-line surgical decompression resulted (Fig. 2B) in a good and stable clinical improvement in both patients. These observations support the hypothesis that invasion of inflammatory cells (that is, macrophages), with their ability for clearance of cellular debris, and apoptotic cells contributes to the increased 18F-FDG uptake in an early hypermetabolic phase of cervical myelopathy, and steroid medication may be able to suppress this process of neuroinflammation (Fig. 2B).

Conclusions

The current literature suggests that metabolic imaging using FDG PET may play an important role in the management of patients with CSM. A hypermetabolism in the cervical spinal cord at the level of stenosis, as indicated by an increased 18F-FDG uptake, seems to be a marker for a potentially reversible phase of a compression-induced cervical myelopathy. The presence of this metabolic pattern appears to reflect the time frame when decompressive surgery can lead to substantial clinical improvement. Effective treatment of CSM must address the causative primary noxae of the cord compression within the stenosis, and there is no alternative to decompressive surgery (Fig. 2A). A substantial clinical improvement or even complete resolution of myelopathy symptoms can be achieved best within the initial acute progressive phase. The presence of temporary local hypermetabolism seen on 18F-FDG PET scans in this initial phase of myelopathy appears to reflect an acute inflammatory process, with a predominantly functional impairment of the neuronal tissue, and represents the phase of potentially reversible symptomatic CSM.

The focal hypermetabolism at the level of stenosis ap-
Cervical spondylotic myelopathy and FDG PET

pears to be caused by a compression-induced inflammatory response that involves intramedullary infiltration of glucose-consuming macrophages. This hypothesis could be substantiated in recent experimental studies and provides a rationale for antiinflammatory medical treatment, with, for example, corticosteroids. Initial therapeutic trials with corticosteroids in single patients with acute CSM induced a decrease of local FDG uptake and improved clinical symptoms, which confirmed this hypothesis.

Thus, suppression of the compression-induced neuroinflammation using corticosteroids can improve clinical activity in acute CSM. Steroid treatment, however, does not eliminate the cause of the disease, and the clinical effect is only temporary. Nevertheless, this time interval can be used to prepare the patient for surgery. The pretreatment of neuroinflammation with corticosteroids stabilizes or improves the clinical status and offers some time for decision making and preparation of the subsequent definitive treatment of the primary noxae of spinal cord compression by surgery.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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Address correspondence to: Sven O. Eicker, M.D., Department of Neurosurgery, University of Hamburg-Eppendorf, Martinistrasse 52, 20246 Hamburg, Germany. email: s.eicker@uke.de.