Preliminary results after upper cervical chiropractic care in patients with chronic cerebro-spinal venous insufficiency and multiple sclerosis

Sandro Mandolesi*, Giuseppe Marceca**, Jon Moser***, Tarcisio Niglio*, Aldo d’Alessandro°°, Matteo Marco Ciccone°°, Annapaola Zito°°, Dimitri Mandolesi§, Alessandro d’Alessandro§§, Francesco Fedele*

*Department of Cardio-vascular and Respiratory Sciences, Sapienza University Rome, Italy
**Unit<=$ a persona Sapienza University, Rome, Italy
***Chiropractic Doctor, Philadelphia, USA
°Istituto Superiore di Sanità, Rome, Italy
°°Department of Neuroscience, Imaging and Clinical Sciences, “G. D’Annunzio” University, Chieti, Pescara, Italy
°°°Cardiovascular Diseases Section, Department of Emergency and Organ Transplant (DETO), University of Bari, Italy
§Medicina del lavoro Sapienza University Rome, Italy
§§Faculty of Medicine Foggia University, Foggia, Italy

The aim of the study is to evaluate the clinical and X-ray results of the Upper Cervical Chiropractic care through the specific adjustments (corrections) of C1-C2 on patients with chronic venous cerebral-spinal insufficiency (CCSVI) and multiple sclerosis (MS).

METHOD: We studied a sample of 77 patients before and after the Upper Cervical Chiropractic care, and we analyzed:
A) The change of the X-ray parameters; B) The clinical results using a new set of questions. The protocol of the C1-C2 upper Cervical Chiropractic treatment, specific for these patients, lasts four months.

RESULTS: We found an improvement in all kinds of subluxations after the treatment with respect to the pre-treatment X-ray evaluation, with a significant statistical difference. The differences between the clinical symptoms before and after the specific treatment of C1-C2 are statistically significant with p<0.001 according to the CHI-Square test revised by Yates.

CONCLUSIONS: The preliminary X-ray and clinical improvements of the Upper Cervical Chiropractic corrections on C1-C2 on these patients with CCSVI and MS encourage us to continue with our studies. We believe that the Upper Cervical correction on C1-C2 could be the main non-invasive treatment of the CCSVI mechanical type in patients with MS. Further studies are required to evaluate the correlation between the Upper Cervical Chiropractic correction on C1-C2 on the cerebral venous drainage and the cerebro-spinal fluid.

KEY WORDS: CCSVI, Multiple sclerosis, Upper Cervical Chiropractic care

Introduction

The CCSVI is a pathological condition characterized by alterations that affect the extra cranial veins, like the vertebral vein, the jugular internal vein and the azygous, the normal return of blood from the brain to the heart 1.
These conditions, that are reflux, stenosis and/or interruption of the flow and impaired postural regulation of the cerebral venous flow, have already been demonstrated in patients with MS, Meniere syndrome, neurodegenerative diseases of the central nervous system, and/or in healthy elderly people.

The CCSVI can be divided into three types according to the anomalous blood return and by means of our morphological hemodynamic map (MEM) able to detect structural and hemodynamic venous anomalies: Type 1 is characterized by block and/or stenosis and/or reflux of the internal jugular veins (IJV) and deep cerebral veins (DCVS); Type 2 by the block of blood flow in IJV and/or vertebral veins (VV) caused by external compression on the vein causing a narrowing of the vessel, and Type 3 is a mixed kind.

There are some anomalies involving the neck muscles that can determine a compression syndrome of the veins, also. The misalignment of the superior cervical vertebra, Atlas (C1) and Axis (C2), could compromise the normal drainage of the cerebral venous outflow.

The purpose of this preliminary study is to evaluate the clinical and X-ray results of the Upper Cervical Chiropractic correction on C1-C2, with specific correction of these vertebrae, on patients with CCSVI and MS.

**Method**

**Subjects**

According to the inclusion/exclusion criteria we chose 77 patients (46 female, 31 male, age 43±10 years) from the 100 visited from January to August 2011. All the patients chosen were affected by MS, diagnosed according to the revised McDonalds criteria, accepted by the Department of Cardiovascular and Respiratory Sciences of the “Umberto I” Policlinico, Sapienza University, Rome (Italy). Of the 77 patients, 46 had the relapsing-remitting clinical form of MS (RR), 18 with a progressive secondary form (PS), 13 with progressive primary (PP), and none with clinically isolated syndrome (CIS) (Table I).

In all the subjects age, sex, duration of the disease, the pathological subtype of MS, and the degree of neurological impairment were considered through the Expanded Disability Status Scale (EDSS).

It is useful to remember that patients with EDSS=0 have a normal clinical neurological objectivity; patients with EDSS from 1 to 3 can be treated as outpatients, although they may have obvious mild or moderate neurological deficits in several areas (motor, sensory, cerebellar, visual, sphincteric), that don’t interfere with their autonomy; in patients with EDSS up to 6 the altered gait is predominant in the calculation of disability; the patients with EDSS up to 9 present a progressive loss of the functions of the four limbs (Table II).

In this study we evaluated the patients according to the EDSS scores of severity of the disease and grouped the scores as follows: “123 = mild”; “456 = medium”; and “789 = severe”.

The parameters of inclusion were: Patients of both sexes with a diagnosis of MS according to the McDonald criteria and the subsequent revisions; Patients with CCSVI type 1, 2 and 3; Age 18-60 years old; Course of the disease: relapsing-remitting (RR), secondary progressive (PS), progressive primary (PP), clinically isolated syndrome (CIS). Assessment of an objective neurological exam with an EDSS score up to 8; Duration of the illness: from 1 to 20 years for those with RR, SP, PP form Subjects who are not in a period of clinical relapse of the disease (at least 30 days since the last clinical recurrence) Subjects treated or not treated with immune-modulatory and immune-suppressive drugs. Acceptance of the informed consent.

The exclusion parameters were: A sharp relapse and/or treatment with steroids during the 30 days preceding the entrance to the study. Pre-existing medical conditions associated with cerebral illness. Abnormal kidney functions. Subjects who have had Behcet disease, Arnold Chiari syndrome, cerebral vasculitis, acquired and congenital cerebral deformities that cause hydrocephalus. All the patients with MS underwent an Eco-Color Doppler exam of the cerebrospinal venous return and an X-ray study of the cervical column for the C1-C2 vertebral misalignment.

**Table I - Baseline characteristic of study population.**

<table>
<thead>
<tr>
<th>CCSVI Positive</th>
<th>RR-MS</th>
<th>SP-MS</th>
<th>PP-MS</th>
<th>CIS</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>77</td>
<td>46</td>
<td>8</td>
<td>13</td>
<td>0</td>
<td>77</td>
</tr>
</tbody>
</table>

Patients’ sex
- (female + male) 46 + 31
- Patients’ age (mean years±SD) 43 ± 10

**Table II - Clinical variables according to types of CCSVI.**

<table>
<thead>
<tr>
<th>Cerebrovascular venous alterations</th>
<th>Type 1</th>
<th>Type 2</th>
<th>Type 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of MS patients</td>
<td>36</td>
<td>3</td>
<td>38</td>
</tr>
<tr>
<td>MS duration in years (mean ± SD)</td>
<td>13.7 ± 9.3</td>
<td>25.7 ± 9.6</td>
<td>15.3 ± 9.9</td>
</tr>
<tr>
<td>EDSS total score (mean ± S.D.)</td>
<td>4.6 ± 2.4</td>
<td>4.7 ± 3.9</td>
<td>4.5 ± 2.6</td>
</tr>
</tbody>
</table>
PROCEDURE OF THE X-RAY EXAM IN ORTHOSTATISM

We assessed our patients with high-frequency digital X-ray devices with a tilting bucky system in orthostatic position (Fig. 1).

We found and classified 9 possible X-ray misalignments of the C1-C2 vertebra: 1st right lateral misalignment, 2nd right anterior rotation, 3rd right posterior rotation, 4th left lateral misalignment, 5th left anterior rotation, 6th left posterior rotation, 7th superior tilt, 8th inferior tilt, 9th anterior intrusion (antero listesti).

The Principal misalignments of the C1-C2 vertebra are shown in (Figg. 2, 3).

The four X-ray parameters of misalignment are:
- Parameter 1- right or left laterality.
- Parameter 2- (right or left) anterior or posterior rotation.
- Parameter 3- superior or inferior tilt.
- Parameter 4- anterior intrusion (antero listesti)

To assess Parameter 1 laterality, right or left, we used the Anterior Posterior Open Mouth (APOM) X-ray projection drawing a horizontal line through upper 1/2 to 1/3 of foramen magnum, bisecting the foramen magnum and drawing a vertical line, measuring distance from lateral mass and posterior arch junction from inferior side to vertical line, then measuring on both right and left side. Larger side is side of laterality (Fig. 4).

To assess Parameter 2 rotation, anterior or posterior, we used the base posterior X-ray projection putting a dot in the center of each transverse foramen, drawing a line across these two dots. This is the atlas line. We put a dot in the middle of nasal septum, bisecting the basilar process, then drew a line down to intersect the atlas line, thus measuring the angle on the side of laterality for anterior or posterior rotation (Fig. 5).
To assess Parameter 3 tilt, superior or inferior, we used the lateral X-ray projection drawing the atlas plane line from the middle of the anterior tubercle to the middle of the thinnest point of the posterior arch, then drew a horizontal line and measured the angle (Fig. 6).

To assess Parameter 4 intrusion anterior (antero-listesis), we used the lateral X-ray projection, drawing a line from the posterior foramen magnum to the posterior neural canal of axis. We will name this line A. We drew a line from the posterior of neural canal of posterior arch of atlas to the posterior foramen magnum. We will name this line B. Then we drew a line from the posterior of neural canal of atlas to posterior neural canal of axis. We will name this line C. Then we measured the distant from the point at which B and C meet at posterior neural canal at the posterior arch of atlas to line A at a perpendicular angle (Fig. 6).

In our sample we applied the specific Upper Cervical Chiropractic protocol on C1-C2 knee-chest “Palmer procedure” with clinical re-evaluations for four months (Fig. 7). After the first correction (adjustment of the subluxation) of C1-C2, every patient was subjected to a check-up visit once a week for the first 2 weeks. Subsequently, three Upper Cervical evaluations were carried out. At the end of the care, an X-ray exam was repeated to evidence the benefits of the correction of C1-C2 cervical vertebrae.

In order to evaluate the clinical effects on the patients, we used a new clinical questionnaire, completed before and after the correction. In order to quantify the specific symptoms of our patients with MS, we used a more detailed questionnaire than those for MSIS 29 e FSS, which are specific for the quality of life and chronic fatigue syndrome.

The questions analyzed five areas in which the specific symptoms are grouped: eyes; urinary and intestinal function; motor activities; perceptive and cognitive state (condition).

Every patient was given a score “C” for each symptom present before chiropractic treatment. After the Upper Cervical Chiropractic care each patient was given a new score for symptoms: “C” unchanged symptoms, “B” improved symptoms with a better clinical assessment, and “A” disappearance of symptoms.
ULTRASOUND ASSESSMENT OF THE CEREBRO-SPINAL VENOUS DRAINAGE

A non-invasive evaluation of the cerebral venous return was carried out on all the patients using the Eco-color Doppler exam in order to evaluate the influence of posture on the cerebral venous outflow. The subjects were studied in both supine and sitting positions (0° to 90°). Zamboni et al. proposed five venous criteria in order to identify the CCSVI which can be diagnosed in the presence of at least two of them: Criteria 1- Draining in the internal jugular vein (IJV) and/or vertebral veins (VVS) in supine and sitting position. The reflux is defined by a reverse flow with a duration of more than 0.88 seconds. Criteria 2- Reflux in the intra-cranial veins (internal cerebral vein, Rosenthal basal vein and Galeno cerebral vein). Criteria 3 - The presence of stenosis in the internal jugular vein using high definition B-mode ultrasound. It is possible to identify endoluminal anatomical defects, such as fixed valves and/or malformed valves, webs, septum associated with or without significant haemodynamic stenosis. Criteria 4- No detectable flow by Eco-Color Doppler in the internal jugular veins and/or vertebral veins. Criteria 5- Inversion of the postural control of the principal tract of the cerebral venous blood outflow. The difference between the area of the internal jugular vein in supine and sitting position (ΔCSA) is estimated at the middle level J2. The individualization of a negative ΔCSA indicates a loss of postural control of the predominant tract of venous drainage in the supine position. We also used additional hemodynamic models to identify the compression of the IJV and/or VV which are not detected in supine and/or sitting positions. This change causes a block in the blood flow which could be re-established by the expansion of the compressed vein through a change in the position of the neck and/or the maneuver of Valsalva. The compression can be identified at different levels of IJVs (J1, J2 and J3) or of VVs (V2 and V3).

We carried out an Eco-Color Doppler exam asking each patient to perform the following dynamic tests: 4 movements of the neck (rotation to the right, rotation to the left, and front and posterior protrusion) to relieve the venous compression syndrome. The maneuver of Valsalva (moderate forced expiration with closed respiratory tract) shows the venous reflux. The Manconi respiratory test shows the presence of an obstacle to the venous draining and consists in the study of the ECD of the internal jugular vein registered at J2 level and of the subclavian veins at their armpit (axilla) origins, carried out during a nasal inspiration and expiration. If the reduction of the CSA in inspiration respect to the CSA in expiration is inferior to 30% and/or the speed of flow is more than double, the respirator test is positive.
positive. Its ROC curve is equal to 97%. The positivity of the test corresponds to a block of the discharge of the flow, and it is four times higher in the subjects with MS with respect to healthy subjects.

The CCSVI is identified on the basis of the above given hemodynamic venous parameters. We classified the people in our study by three different types of CCSVI: Type 1: characterize by block and/or stenosis and/or reflux of the IJVs and DCVs. Type 2: by the compression of the IJV and /or from the non-visibility of the VVS in the ECD. Type 3: from the block and/or stenosis of the IJVs and/or reflux of the IJV and DCVs and compression of the IJVs and/or the non-visible of the VVS in the ECD.

In April 2010, we presented at the Upper Cervical Evolution, in Charlotte, NC, USA, the Mandolesi Marceca theory on the Mechanical Postural Vascular Block (MPVB) in patients with CCSVI and MS. Successively, we reported the cerebro-spinal venous outflow studied with ECD on a morphological haemodynamic map (MEM) using different symbols to define the haemodynamic models and the structural vascular alterations, such as hypoplasia of the veins, veins with rigidity of the walls (noncompliant) septum, membrane, webs, annulus, twist and valve stiffness. We used the morphological and hemodynamic symbols of the Consensus Conference of the National Epidemiology Observatory CCSVI of February 2013.

Our data was analyzed using MEM-net software (www.mem-net.it), which includes the algorithm for the analysis of data (Fig. 9).

**Statistical Analysis**

All the data was analyzed using SPSS software in order to carry out a description of the numerical parametric variables. The statistical significance “between” and “within” the groups has been calculated on continuous variable by means of the variance analysis (ANOVA) in order to verify the equality of the averages.

The test $\chi^2$ corrected by Yates was used for the non-continuous variables (non-variable) by means of StatCalc and the Analysis programs of Epi-info. A value of $p<0.05$ was considered significant. Also were calculated the confidence intervals at 95%.

**Results**

Table I underlines the demographic characteristics at the base and subtypes of MS in showing that most of the patients had the recidivous-remittent form of the disease (46 pts).

Table II presents the clinical variables based on the three typologies of CCSVI. The average EDSS scores were similar in the patients belonging to the three groups of cerebrovascular venous alterations: 4.6 ± 2.4 in Type 1 (36 pts), 4.7 ± 3.9 in Type 2 (3pts) e 4.5 ± 2.6 in Type 3 (38 points).

Table III shows the scores of the questionnaire given to the patients with MS before and after the four months of Upper Cervical correction on C1-C2. In the Types 1 and 3 of chronic cerebrospinal venous insufficiency the scores produced were inferior to the initial values, after the correction on C1-C2, which suggests a subjective improvement of the general state of health.

We X-rayed 100 patients with MS and CCSVI (Table 2) and found a serious misalignment: in 31% with 4 parameters, 47% with 3 parameters, in 12% with 2 parameters, in 10% with 1 parameter and 0% with 0 parameter. We found the first parameter in 70%, the second parameter in 85%, the third parameter in 55%, the fourth parameter in 89% (Fig. 8).

Table IV highlights the X-ray characteristics of the sample studied. The type of misalignments of C1-C2 identified by X-ray were left laterality, right laterality, left anterior rotation, right anterior rotation, left posterior rotation, right posterior rotation, superior tilt, lower tilt, and anterior listesis.

We found an improvement in all the subluxations of C1-C2 after the Upper Cervical care with respect to the evaluation before the correction/treatment, with significant statistical differences. Our results show that a misalignment of C1-C2 can compromise the normal cerebral venous outflow in patients suffering from MS. In fact, regarding the C1-C2 vertebra, we found a significant statistical difference in the X-ray characteristics pre and post Chiropractic Upper Cervical care (p<0.00001 for the left laterality; p<0.00001 for right laterality; p<0.0034 for the left front rotation; p<0.0174 for the right front rotation; p<0.00001 for the left posterior rotation; p<0.00001 for the right posterior rotation; p<0.0005 for the superior inclination; p<0.0032 for the lower tilt and p<0.00001 for the front sliding.

The anomalies identified in the X-ray examination improved in all the patients after four months of Upper Cervical care (Table IV). Moreover, the average score of the questionnaire given to the patients at the end of the therapy was inferior to that at the beginning showing the efficiency of the Upper Cervical Chiropractic care in producing clinical benefits. In fact, we found a reduc-

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**Table III - Results of clinical questionnaire administered to MS patients before and after four month treatment according to EDSS score.**

<table>
<thead>
<tr>
<th>EDSS (1-3)</th>
<th>Score Pre</th>
<th>Score Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1</td>
<td>18±3</td>
<td>8±2</td>
</tr>
<tr>
<td>Type 2</td>
<td>16±7</td>
<td>14±2</td>
</tr>
<tr>
<td>Type 3</td>
<td>20±3</td>
<td>16±3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>EDSS (4-6)</th>
<th>Score Pre</th>
<th>Score Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1</td>
<td>23±6</td>
<td>15±5</td>
</tr>
<tr>
<td>Type 2</td>
<td>21±11</td>
<td>15±13</td>
</tr>
<tr>
<td>Type 3</td>
<td>19±3</td>
<td>13±1</td>
</tr>
</tbody>
</table>

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The analysis was carried out on 27 patients with CCSVI and MS. Each patient had a score in accordance with the previous method shown. The differences in the clinical symptomatic assessment before and after Upper Cervical care are statistically significant with p<0.001 in accordance with the Chi-square corrected by Yates. We noticed in the patients studied that the different clinical areas changed in their function, presenting the following incidence percentages: perceptive (100%); motor (85%); urinary/intestinal function (85%); acoustic (67%); visual (48%), and cognitive (37%).

After the chiropractic Upper Cervical correction the same sample presented the following percentages of clinical improvement: The perceptive function was the most sensitive area (78%) followed by the cognitive (59.5%); acoustic (49.3%); urinary/intestinal (43.5%); visual (37.5%) and motor (35.3%) (Table V).

**Discussion**

CCSVI consists in the presence of reflux, stenosis and/or blocks in the flow in the extra-cranial veins which impair the cerebral venous outflow and cause an increase of the hydrostatic vascular pressure in the brain 14.

Several vascular studies support the association between MS and vascular cerebral alterations even though the underlying mechanism is unknown, and may imply a degeneration of the neurons, an increase in the deposits of iron and alterations in the permeability of the haemato-encephalic barrier 15,16.

The concept that insufficient cerebral venous drainage may have a fundamental role in the pathogenesis of MS has aroused great interest in the international scientific community for the possible benefits to be obtained from intravenous treatment with angioplasty with balloon 17.

However, there is evidence in literature that does not support this pathogenic role of the chronic cerebrospinal venous insufficiency but confirms the association between the two conditions 18-19.
On the basis of our experience, we considered three types of chronic cerebrospinal venous insufficiency according to the cause of the abnormal brain medullary venous drainage.

As mentioned in the introduction, Type 2 of CCSVI is characterized by an external compression on the veins causing a narrowing with a block of the blood flow. This identifies the CCSVI as being of the mechanical type.

In two patients with MS a syndrome of compression of the IJV, caused by the homohyoidean muscle, has recently been documented. The resection of the homohyoidean muscle restored the flow in the IJV supporting the hypothesis that muscular compression could have been one of the causes responsible for the unsuccessful clinical results of the angioplasty venous.

We think that it is possible that other muscles are involved in said venous compression. For example, the scalene muscle may compress the terminal tract of J1 of the internal jugular vein, while the sterno cleido-mastoid muscle may compress the J3 segment of the internal jugular vein.

We presume that all these compressions could be caused by the misalignment of the all cervical vertebrae which determines an asymmetric traction on the muscles and on the aponeurosis, with a compressive effect on the veins in the neck.

This block of the flow, tied to the compression of the vertebra and/or jugular veins, could be one of multi-factorial causes of clinical aggravation in the patients with MS and CCSVI. In fact, these patients often refer to a trauma to the head, neck or sacrum in the past.

Elster proposed a hypothesis of a correlation between MS and the misalignment of the superior cervical. She carried out a study on the misalignment of the C1-C2 cervical and hypothesized a link with MS and Parkinson's disease.

We used a new questionnaire which allowed us to identify the symptoms most frequently present in our study sample and which functional alterations are most sensitive to chiropractic Upper Cervical care.

In our study sample, the most present and sensitive symptom to the treatment was the "perceptive" function.

Conclusions

In subjects with MS and CCSVI given the high percentage of the venous syndrome compression of the IJV—about 48% it is essential for its specific identification to carry out an Eco-color Doppler of the veins in the neck in order to advise the patient of the most appropriate treatment.

Our study suggests that a misalignment of the Atlas and/or Axis vertebra has an impact on the health of patients suffering from MS and CCSVI.

The chiropractic Upper Cervical adjustment on C1-C2 could be a non-invasive primary treatment of the "mechanical" type of CCSVI in patients with MS.

Further studies are necessary to evaluate the correlation of the effect of the chiropractic Upper Cervical treatment on C1-C2 on the draining of the extra-cranium veins and on the cerebral spinal fluid.

Riassunto

SCOPO: Lo scopo dello studio è quello di valutare i risultati clinici e radiografici della cura chiropratica Upper Cervical attraverso le correzioni di C1-C2 su pazienti con insufficienza venosa cronica cerebro-spinale (ccsvi) e sclerosi multipla (sm).

METODO: Abbiamo studiato un campione di 77 pazienti prima e dopo il trattamento chiropratico. Il protocollo del trattamento Chiropratico specifico per C1-C2 è durato quattro mesi. Da un punto di vista emodinamico abbiamo diviso i pazienti in 3 tipi: Tipo 1 - puramente vascolare con anomalie endovenose; Tipo 2 - "meccanico" con sindrome compressiva venosa; Tipo 3 - misto.

RISULTATI: I risultati clinici dimostrano gli effetti positivi del trattamento chiropratico Upper Cervical su C1-C2. Nei tipi 1 e 3 di CCSVI è stato ottenuto un punteggio medio dei questionari clinici ridotto dopo il trattamento specifico di C1-C2 rispetto al punteggio precedente. Abbiamo trovato un miglioramento radiografico in tutti i tipi di sussultazioni dopo il trattamento rispetto alla valutazione pre-trattamento, con una differenza statisticamente significativa. Le differenze tra i sintomi clinici prima e dopo il trattamento specifico di C1-C2 sono statisticamente significative con p <0,001 secondo il test Chi-quadrato rivisto da Yates.

CONCLUSIONI: I dati radiografici e i miglioramenti clinici dopo correzioni Upper Cervical chiropratica su C1-C2 su questi pazienti con CCSVI e SM ci incoraggiano a continuare i nostri studi. Noi crediamo che la correzione di C1-C2 potrebbe essere il trattamento non invasivo principale della CCSVI di tipo meccanico nei pazienti con SM. Ulteriori studi sono necessari per valutare la correlazione tra la correzione chiropratica di C1-C2 sul drenaggio venoso cerebrale e il liquido cerebro-spinale.


23. Eduardo S: Compression of the internal jugular vein by the transverse process of the atlas as the cause of cerebellar hemorrhage after supratentorial craniotomy. Surgical Neurology, 1999; 51(5) 500-505.
