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Neurology [ALERT®]

Evidence-based summaries of the latest clinical neurology research

ABSTRACT & COMMENTARY

Medication for Acute Low Back — A Randomized Clinical Trial

By Louise M. Klebanoff, MD

Assistant Professor of Clinical Neurology, Weill Cornell Medical College

Dr. Klebanoff reports no financial relationships relevant to this field of study.

SYNOPSIS: In a trial comparing naproxyn alone to combinations with cyclobenzaprine or oxycodone/acetaminophen in patients with acute low back pain, there was no difference in outcome after 1 week.

SOURCE: Friedman B, et al. Naproxyn with cyclobenzaprine, oxycodone/acetaminophen, or placebo for treating acute low back pain. A randomized clinical trial. *JAMA* 2015;314:1572-1580.

Acute, non-radicular, non-traumatic low back pain is a common medical condition accounting for 2.7 million (2.4%) emergency department visits annually. Patient are often treated with nonsteroidal anti-inflammatory agents, skeletal muscle relaxants, and/or opioid analgesics. There is minimal evidence-based support for any of these treatments. The authors conducted a randomized, double-blind, three-group clinical trial comparing naproxen and placebo with naproxen and cyclobenzaprine and naproxen and oxycodone/acetaminophen in patients with non-traumatic, non-radicular acute low back pain severe enough to cause functional impairment. The primary outcome was improvement on the Roland-Morris Disability Questionnaire (RMDQ), a 24-item questionnaire commonly used to measure acute low back pain and functional impairment. Subjects were interviewed by telephone at 7 days and 3 months following their emergency department visit.

The study took place over a 20-month period beginning in April 2012. A total of 323 patients were enrolled. The patients ranged from 21 to 64 years of age. The mean baseline scores on the RMQD ranged from 18.4 to 18.9 on the 24-point scale, indicating severe functional impairment. Patients were assigned to one of three groups. All patients received naproxen 500 mg to be taken every 12 hours. All patients

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were given 60 tablets of their assigned experimental medication, either 1) placebo, 2) cyclobenzaprine 5 mg, or 3) oxycodone/acetaminophen 5 mg/325 mg. The patients were instructed to take one or two tablets of their experimental medication every 8 hours as needed.

At 1-week follow-up, there was no significant difference between the three groups in terms of the primary outcome. The patients randomized to receive naproxen and placebo improved by a mean of 9.8% on the RMDQ, those randomized to receive naproxen and cyclobenzaprine improved by 10.1%, and those randomized to naproxen and oxycodone/acetaminophen improved by 11.1%. At the 1-week follow-up, regardless of study group, more than half of the patients continued to report low back pain severe enough to require pain medication. Patients randomized to oxycodone/acetaminophen were more likely than those randomized to placebo to report pain levels of mild or none. Adverse events were also more common in this group.

More than three-quarters of the study patients used naproxen daily, with two-thirds using it twice a day. There was significantly less compliance with the experimental medications, with only one-third of the study patients using the experimental medications more than once daily and nearly 40% using the experimental medication intermittently, only once, or not at all. At the 3-month follow-up, most patients had recovered. However, nearly one-fourth of patients in each study group still reported moderate or severe low back pain.

■ COMMENTARY

In this randomized, controlled study of treatment of acute, non-traumatic, non-radicular low back pain presenting to an emergency department, adding either cyclobenzaprine or oxycodone/acetaminophen to naproxen did not significantly improve pain or functional disability at 1 week or 3 months when compared to naproxen alone. By 3 months, most patients had recovered regardless of their randomly assigned treatment group. The study does not support the use of combination therapy for management of acute low back pain.

One concern in interpreting the study results is that the experimental medication was given on an as-needed basis; a large proportion of the study participants either did not take the experimental medication or did not take it regularly. It would be useful to see results from a similarly designed trial in which the experimental medications are given on a standing basis. In addition, considering the urban setting in which the study was performed, with an emergency department serving a socioeconomically depressed population with limited access to health care, the conclusions may not be applicable to a different patient population. Additional studies are needed to provide evidence for management of acute, non-traumatic, non-radicular low back pain, a common, disabling condition. ■

ABSTRACT & COMMENTARY

Clinical Features and Consequences of Inclusion Body Myositis

By Michael Rubin, MD

Professor of Clinical Neurology, Weill Cornell Medical College

Dr. Rubin reports no financial relationships relevant to this field of study.

SYNOPSIS: Inclusion body myositis, while poorly understood regarding cause, is clearly responsive to physical exercise, and patients should be encouraged to maintain robust physical activity.

SOURCE: Paltiel AD, et al. Demographic and clinical features of inclusion body myositis in North America. *Muscle Nerve* 2015;52;527-533.

Sporadic inclusion body myositis (IBM) is the most common primary myopathy in patients older than 40 years of age and the most common form of inflammatory myopathy in adults. With a prevalence estimated at up to nine cases per one million

adults, it has an insidious onset, a slowly progressive course, is often asymmetrical, and has a distally predominant weakness. Etiology and pathogenesis remain a mystery, and many questions remain unanswered. Those addressed by this study encompass the demographics of the IBM population in North America, the nature of their disability and its impact on their activities of daily living and quality of life, how they are diagnosed, and whether the natural history varies between diverse groups.

Under guidance from experts in the fields of medicine, economics, operations research, health care management policy, and registry design, a questionnaire was developed for use in this cross-sectional, self-reporting survey study. Patients diagnosed with IBM were sampled from two patient organizations, the Myositis Association (TMA) and the Muscular Dystrophy Association (MDA), and were sent electronic messages requesting that they voluntarily complete the survey. All records submitted by patients confirming the diagnosis of IBM were included. Informed consent was obtained from all participating patients, and submission of information was voluntary and anonymous. Statistical analysis included column statistics calculated with Microsoft Excel and fixed effects models fitted to the composite index, with all computations performed using Statistical Analysis System 9.3, and 95% confidence intervals and *P* values for pairwise comparisons generated.

Of 1400 emailed requests, 973 responses were obtained, of which 57 were considered duplicate. Men composed 66.9% of unique respondents, mean age was 70.4 years, and male:female ratio was 2:1. Presenting symptoms included weakness (69.9%), stair-climbing difficulties (59.6%), falling (56.8%), impaired use of arms and legs (53.4%), fatigue (32%), and dysphagia (23%), with diagnosis taking > 2 years in 45.9%, 1-2 years in 22.8%, 6-12 months in 14.3%, and < 6 months in 15.8%. Mean time to diagnosis from initial symptom was 4.7 years. Gait difficulties were reported in 94.3%, and included inability to climb stairs (56.8%), unsteadiness, or needing an assistive device or wheelchair. Two-thirds could not walk more than a block, and reported difficulties eating or swallowing. Activities of daily living were rarely reported as normal. Functional disability was directly related to advanced age, and degree of exercise, with more exercise being associated with higher functional index scores. Patients and clinicians are now better informed regarding prognosis, and IBM patients may now be instructed to "use it or lose it."

■ COMMENTARY

Absent a circulating autoantibody, sporadic inclusion body myositis (sIBM) has been considered an idiopathic inflammatory myopathy. However, recent reports of serum autoantibodies directed against a 44-kDa muscle protein in up to 72% of sIBM patients, compared to 5% of polymyositis or dermatomyositis patients, raises the possibility that autoimmunity may be central to its pathogenesis. Cytosolic 5'-nucleotidase 1A (cN-1A) — expressed in skeletal muscle, involved in energy balance control, metabolic regulation, and cell replication, and immuno-histochemically demonstrated to accumulate within rimmed vacuoles — has been identified as the target autoantigen. cN-1A autoantibodies are also found in Sjogren's syndrome and systemic lupus erythematosus, and thus their diagnostic utility for sIBM remains to be determined. ■

ABSTRACT & COMMENTARY

Neonatal MRI Can Predict Future Academic Difficulties for Children Born Preterm

By Matthew T. McCarthy, MD, and Barry E. Kosofsky, MD, PhD

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Dr. McCarthy and Dr. Kosofsky report no financial relationships relevant to this field of study.

SYNOPSIS: Neonatal brain MRI can identify structural changes that predict future difficulties in school performance for children who are born preterm.

SOURCE: Ullman H, et al. Neonatal MRI is associated with future cognition and academic achievement in preterm children. *Brain* 2015;138(Pt 11):3251-3262.

With the number of children born prematurely continuing to grow, and with an increase in survival and decrease in medical complications in neonates born at earlier gestational ages, it is important to understand the long-term consequences of premature birth. It is well known that the more premature an infant, the higher the likelihood that the child will experience greater cognitive and academic difficulties relative to their peers born

at term. This discrepancy usually persists throughout school years. This is particularly true for mathematics, with 10-18% of preterm children experiencing significant mathematical impairment and as many as two-thirds experiencing mild mathematical impairment. Underachievement in mathematics can have a long-term impact on school completion, eventual employment, and overall emotional and mental well-being. Therefore, it is important to discover factors that will help predict poor academic performance for preterm newborns to identify children at risk as early as possible to ensure that proper surveillance and appropriate interventions are provided in a timely manner.

The authors of this study investigated whether structural features detected on magnetic resonance imaging (MRI) performed on a cohort of Australian children born

[This study highlights the potential for emerging neuroimaging analytic techniques to characterize patterns of brain injury in premature children to predict subsequent academic and cognitive difficulties.]

preterm (224 infants born < 30 weeks' gestational age and/or < 1250 g birth weight) and in healthy full-term controls (46 infants born ≥ 37 weeks' gestational age) were associated with later cognitive outcomes related to mathematics. Participants were enrolled in a prospective longitudinal cohort study in which an MRI was performed near term (40 weeks' gestational age ± 2 weeks) to establish correlations predictive of cognitive impairment subsequently evident in neuropsychologic testing performed at 5 and 7 years' corrected age.

Specifically, the authors were interested in looking at two automated MRI measures — a structural Jacobian map derived from deformation-based morphometry (DBM) and fractional anisotropy maps derived using diffusion tensor imaging (DTI). DBM is useful for identifying subtle differences in brain shape and regional volumetric differences, while DTI is sensitive in detecting the integrity of white matter tracts. To predict early mathematical ability, these investigators administered tests of working memory (Backward Digit Span Test) and early mathematics skills (Numbers Skills Scale at 5 years' corrected age and Math Computation task at 7 years' corrected age). For the statistical analysis, this research team used both a univariate analysis (general linear model) and a multivariate analysis (support vector regression) controlling for gestational age at birth, gestational age at time of MRI, and additional covariates related to prematurity (including small for gestational age, patent ductus arteriosus, bronchopulmonary dysplasia, postnatal steroids, confirmed sepsis, and other white matter injury based on review of the clinical MRI scans).

Based on the DBM Jacobian maps, the authors found that increased tissue volume in the left insula region was positively associated with higher scores on the Numbers Skills Scale at age 5 and increased tissue volume in the right putamen region was associated with higher scores on Math Computation at age 7. These findings were derived from a univariate analysis controlling for gestational age at birth and time of MRI as well as other clinical perinatal factors identified above. There was also a suggestion derived from the univariate analysis that increased volume in the left insula region was associated with increased working memory at age 7, but this did not reach statistical significance. For the DTI fractional anisotropy maps, there was a positive association with working memory at age 5 and Numbers Skills Scale at age 5 based on multivariate analysis controlling for gestational age at birth and time of MRI as well as other clinical perinatal factors identified above, but not for the univariate analysis. The authors then repeated these identical analyses in the control group and did not find significant associations for these structure/function relationships in the group of full-term children studied.

■ COMMENTARY

The cognitive and academic struggles experienced by many preterm children compared to their full-term peers can have a significant impact on their educability, subsequent employment, and professional well-being. This study showed that specific structural findings identified using automated morphometric and DTI analyses of neonatal MRI were predictive of future school age math performance. There are several limitations to these findings, including the low number of healthy controls in the comparison group, variability in imaging protocols over the course of the study, and an inability to control for all factors that undoubtedly contribute to childhood cognitive functioning in general, and math skills in particular. While the results of this study do not lend themselves to any immediate clinical application, they do highlight the potential for emerging neuroimaging analytic techniques to help characterize patterns of brain injury in premature children that can help predict subsequent cognitive and academic difficulties. Ultimately, the hope is that further research in this area will allow for routine screening that will lead to early identification of children at risk for cognitive deficits and permit for additional services and accommodations to be initiated when indicated. ■

ABSTRACT & COMMENTARY

Selective Disruption of Thalamo-Cortical Connections in Patients with Disorders of Consciousness — a Possible Biomarker for Cognitive-Motor Dissociation

By Peter B. Forgacs, MD

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Dr. Forgacs reports no financial relationships relevant to this field of study.

SYNOPSIS: In this case-control, functional neuroimaging study, the authors developed a novel method to evaluate correlations between integrity of neural circuits involved in overt and covert motor behavior and apply the method to two patients: one with a dissociation of imaging-based vs bedside evidence of command following and one without.

SOURCE: Fernández-Espejo D, et al. A thalamocortical mechanism for the absence of overt motor behavior in covertly aware patients. *JAMA Neurol* 2015 Oct 19:1-9. doi: 0.1001/jamaneurol.2015.2614. [Epub ahead of print].

It is an increasingly well-described phenomenon that some severely brain-injured patients who appear to be in a vegetative or minimally conscious state at the bedside (collectively called disorders of consciousness [DOC]) may show evidence of preservation of higher cognitive capabilities detected by functional neuroimaging or electrophysiological methods. This syndrome of dissociation between clinically observable and covert motor behavior has gained widespread attention from clinicians, researchers, and the general public over the last 10 years, and recently has been named "cognitive motor dissociation" (CMD).[1] Several independent studies[2,3] involving large numbers of patients with DOC showed that approximately 10% of such patients may exhibit such dissociation between beside and functional neuroimaging findings. Fernandez-Espejo et al have taken an important step toward characterizing the different neural circuits that produce overt or covert motor behavior.

This case-control study involved 15 healthy volunteers and two patients with a history of severe brain injury and impaired consciousness. The authors used a mathematical modeling technique — dynamic causal modeling (DCM) — and applied it to functional magnetic resonance imaging (fMRI) signals to compare neural substrates of voluntary motor imagery and motor execution. In addition, diffusion tensor imaging (DTI) technique was also used in the patients to compare structural integrity of the neural fibers to those identified in DCM modeling. Their findings revealed that in healthy volunteers, motor execution was associated with excitatory coupling between the thalamus and primary motor cortex, but during a motor imagery task, coupling was not present. Furthermore, DTI analysis revealed selective disruption of these fibers in the one patient involved in the study with evidence of covert command following despite appearing to be in the vegetative state behaviorally. The other unconscious patient who had comparable injury and clinical history was able to exhibit goal-directed movements at the bedside, and had intact fibers between the thalamus and primary motor cortex as verified by the modeling and DTI fiber tracing.

■ COMMENTARY

This study addresses a very important but unresolved issue of assessing the underlying neuronal mechanism of the remarkable dissociation between lack of motor behavior with concordant preservation of high-level cognitive functions. It highlights the possible role of selective functional or structural loss of thalamo-cortical connections in cases of CMD, which frames the possibility of targeted restoration therapy in some cases of behaviorally unresponsive patients.

However, there are several weaknesses of the study. While their methods are validated in a single patient with CMD, the authors concluded that the findings of this study may be used as a possible biomarker for the absence of intentional movements in covertly aware patients. However, as the authors also agree, there may by significant individual structural and functional variations in localization of appropriate brain activity even in healthy volunteers; they could only identify suprathreshold activity using their DCM method in 60% (9 out of 15) of the healthy volunteers included in the study. These limitations may be even more pronounced and possibly restrict the generalization of their approach to severely brain-injured patients, who typically have significant structural damage and

possible functional reorganization of brain activity during recovery. In addition, while their findings may explain the presence of CMD in a subset of patients, there are many other possible injury patterns that can produce loss of motor outflow without disruption of fibers from the ventrolateral thalamus to the primary motor cortex. These include injury of motor efferents at the level of upper brainstem as in the complete locked-in state. Alternatively, paucity of movements may be a result of upper motor neuron dysfunction leading to highly increased muscle tone and development of severe contractures, which is often the case in the chronic stages of severe brain injuries. Lastly, while findings of this study explain the lack of voluntary motor control, they cannot account for several clinical features that are also absent in patients who are mistakenly thought to be in a vegetative state based on bedside examination, such as visual fixation, visual pursuit, or vocalization. As the authors noted, currently there are no reliable models that account for all the dysfunctions seen in patients with CMD.

In summary, this study frames a highly important question about the neurobiological mechanisms of CMD and highlights the importance of thalamo-cortical connections. The authors proposed a model — selective disruption of fibers to the primary motor cortex from the ventrolateral thalamus with preservation of central thalamic outflow to the frontoparietal areas.[4] They also propose that measurements of the selective integrity of these circuits may serve as a biomarker for CMD. However, while this paper involved two patients with DOC, previous studies using more conventional tools in a larger cohort of patients suggest that preservation of widespread cortical metabolism[5] and global thalamo-cortical functions as reflected in sleep-wake EEG organization[2] may be also used as a potential screening tool to identify preserved cognition.[6] Nevertheless, if further studies will identify more patients with similar functional imaging results, the results of this study may be used to select patients for targeted restoration therapy, such as deep brain stimulation. ■

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ABSTRACT & COMMENTARY

Postmortem Evidence of Limbic, Neocortical, and Basal Ganglia Deficits in Parkinson's Disease Dementia

By Claire Henchcliffe, MD

Associate Professor of Neurology and Neuroscience, Weill Cornell Medical College

Dr. Henchcliffe reports she is on the speakers bureau and advisory boards for Teva, IMPAX, and ACADIA and receives grant/research support from Biogen and Kaneka.

SYNOPSIS: Postmortem brain tissue from 15 individuals with Parkinson's disease dementia was analyzed by high-performance liquid chromatography and immunoassays, revealing widespread deficits in dopamine, serotonin, and noradrenaline innervation.

SOURCE: Buddhala C, et al. Dopaminergic, serotonergic, and noradrenergic deficits in Parkinson disease. *Ann Clin Transl Neurol* 2015;2:949-959.

Dementia in Parkinson's disease (PD) remains a major challenge to optimal management in the clinic, and has a profound impact on patient quality of life. Recent advances have highlighted widespread pathology associated with PD with dementia, but remaining gaps in understanding hamper efforts to provide better treatment. In this study, the authors have therefore investigated autopsy specimens obtained from 15 patients with PD and dementia, where the presence of dementia was defined either by clinical diagnosis or by the Clinical Dementia Rating scale. The deceased patients' median age at death was 79 (range 71-93) years, 12/15 were male, and their median disease duration was 14 (range 8-27) years. Medications reported included agents used to control motor symptoms (levodopa equivalents of 800 mg, range 0-1350 mg, daily), cognitive

dysfunction (acetylcholinesterase inhibitors in 8/15), mood (serotonin reuptake inhibitors in 10/15 and other antidepressant agents in 2/15), and psychosis, although corresponding clinical diagnoses were not reported. These late-stage patients had widespread alpha-synuclein pathology defined as Braak stage 6 (the most widespread pathology of stages that range from 1-6). Six healthy control brains were used for comparison, with slightly greater age at death of 84 (range 70-100) years, 2/6 males, and none were taking anti-PD, antidepressant, or acetylcholinesterase inhibitors. Multiple cortical and subcortical brain regions were analyzed by high-performance liquid chromatography or immunoassay to quantitatively measure dopamine, dopamine transporter (DAT), serotonin, serotonin transporter (SERT), norepinephrine, and vesicular acetylcholine transporter.

As expected, dopamine levels in PD were lower than control in the caudate (2.5% of control, $P = 0.001$), but of interest were also markedly decreased in the amygdala (27% of control, $P = 0.001$), and DAT levels were lower in PD with dementia vs controls in the caudate, hippocampus, amygdala, inferior parietal lobe, precuneus, and visual association cortex. Serotonin levels were decreased in PD with dementia vs controls in the caudate (31.6% of controls, $P = 0.003$), and in multiple cortical regions including the middle frontal gyrus (19.7% of controls, $P = 0.001$), inferior parietal cortex (16.8% of controls, $P = 0.001$), and visual association cortex (11.8%, $P = 0.003$). Reductions in SERT were observed in the same areas, once again with the most severe deficit present in the visual association cortex (9.9% of controls, $P = 0.001$). Norepinephrine levels were markedly reduced in all of these regions, most notably the inferior parietal lobe (4.2% of controls, $P = 0.001$), in addition to the anterior cingulate gyrus (3.9% of controls, $P = 0.002$). VAChT levels could only be measured in the caudate and hippocampus using assays in this study, and did not differ between PD and controls. In this small sample, neurochemical measures did not correlate with Mini-Mental Status Examination scores, Unified Parkinson's Disease Rating Scale motor scores, or Clinical Dementia Rating scale scores. Grouping PD study patients by pathology as alpha-synuclein alone vs alpha-synuclein plus beta-amyloid also did not reveal any correlation with neurotransmitter and transporter levels. Only two subjects had tau pathology, precluding any attempt to correlate this subset with neurotransmitter system disruption in this sample.

■ COMMENTARY

This study demonstrated at postmortem that, in addition to dopaminergic deficits, the serotonergic and noradrenergic systems are profoundly disrupted in PD with dementia when compared with normal controls. The finding of deficits in these neurotransmitter systems in neocortical and limbic, as well as basal ganglia regions, serves to emphasize that a reliance on treatment strategies that focus on dopamine supplementation alone are simply inadequate in late stages of disease, aligning well with current clinical strategies. Perhaps unexpectedly, although serotonin and SERT reductions were quite comparable across regions, dopamine and DAT differed.

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Stroke Alert

By Matthew E. Fink, MD

Carotid Occlusion Rarely Develops from Asymptomatic Carotid Artery Stenosis

SOURCE: Yang C, et al. Risk of stroke at the time of carotid occlusion. *JAMA Neurol* 2015; doi:10.1001/jamaneurol.2015.1843.

In recent years, there is increasing evidence that modern intensive medical therapy in most patients with asymptomatic carotid stenosis is effective in stroke prevention, and few patients seem to benefit from carotid endarterectomy or carotid stenting. However, in the United States, 90% of carotid interventions are for asymptomatic stenosis, compared to Denmark, where the rate is 0%. The investigators conducted a retrospective analysis of data collected from patients at the stroke prevention clinic of Victoria Hospital, Ontario, Canada, from 1990 until 1995 using annual surveillance carotid ultrasound, and then compared them to a similar group followed from 1995 through 2014.

Among 3681 patients followed with annual ultrasound, 316 (8.6%) were asymptomatic before a carotid occlusion occurred during the observation period. Most of the new occlusions (80%) occurred before 2002, when medical therapy was less intensive and the frequency of occlusion decreased in subsequent years. Only a single patient (0.3%) had a stroke at the time of carotid occlusion, and only three patients (0.9%) had ipsilateral stroke during follow-up. In reviewing survival analyses, neither severity of stenosis nor the presence of contralateral occlusion predicted the risk of stroke or TIA, fatal stroke, or death from other causes in > 3 years of follow-up from carotid occlusion. From this study, it appears that the risk of progression to carotid occlusion is well below the risk of carotid stenting or carotid endarterectomy, and intensive medical therapy appears to be preferred for the vast majority of patients with asymptomatic carotid artery stenosis. However, the CREST-2 trial, which is now underway and designed as a prospective, randomized trial, will be able to answer this question definitively. ■

Continued from page 31

Loss of DAT exceeded dopamine loss in the caudate, amygdala, hippocampus, inferior parietal lobule, precuneus, and visual association cortex. The authors suggested this may be due to levodopa administration increasing dopamine levels in neurons that possess dopa decarboxylase (but not DAT), thus masking endogenous loss, and further hypothesize that in cortical areas this could relate to cognitive side effects. Whether antipsychotic and antidepressant medications might have affected findings is not addressed and remains therefore unknown. This study also highlights the role of norepinephrine, reflecting loss of neurons in the locus ceruleus, and supports previous findings of decreased levels in frontal, cingulate, and entorhinal cortex as well as hippocampus. Of course, it would be interesting to examine correlation of such changes with clinical profiles and pathology, but, unfortunately, this was limited by the small number of cases. In the future, it would be extremely helpful for the clinician to have a study that correlates postmortem changes with neuroimaging findings. Nonetheless, this study serves to highlight the highly complex and extensive nature of dopamine, serotonin, and norepinephrine deficits in late-stage PD with dementia, and provides a stimulus for further development of non-dopaminergic treatments. ■

CME QUESTIONS

1. **For health adult patients presenting to the emergency department with acute, non-traumatic low back pain, which is the most appropriate treatment?**
   a. Oxycodone/acetaminophen
   b. Cyclobenzaprine
   c. Naproxen
   d. Naproxen and oxycodone/acetaminophen
   e. Naproxen and cyclobenzaprine

2. **Which of the following statements is true regarding inclusion body myositis?**
   a. Autoantibodies directed against a 44-kDa muscle protein have been reported in up to 72% of sIBM patients.
   b. Autoantibodies directed against a 44-kDa muscle protein have been reported in up to 72% of polymyositis patients.
   c. Autoantibodies directed against a 44-kDa muscle protein have been reported in up to 72% of dermatomyositis patients.
   d. None of the above

3. **Children born preterm are at increased risk of developing learning problems when they begin school.**
   a. True
   b. False

4. **Which statement regarding patients with depressed consciousness and cognitive-motor dissociation is correct?**
   a. Patients with brain injury and CMD have no evidence of conscious awareness.
   b. Patients in vegetative states have no conscious awareness.
   c. Functional MRI can identify patients with conscious awareness.
   d. Absence of any motor control implies a lack of conscious awareness.
   e. The bedside neurological examination can always recognize conscious awareness.

5. **In patient with Parkinson's disease with dementia, which of the following best describes changes in neurochemical transmitter systems?**
   a. Dopamine deficits are limited to the striatum while dopamine transporter expression is altered in a more widespread pattern.
   b. Expression levels of transporter proteins for dopamine and serotonin are inversely associated in cortical regions.
   c. Dopamine deficits in patients with both alpha-synuclein and beta-amyloid pathology is greater than in patients with alpha-synuclein pathology alone.
   d. Norepinephrine and serotonin levels are reduced in multiple cortical regions.

6. **Carotid endarterectomy or carotid artery stenting results in less morbidity and mortality than does medical therapy for asymptomatic carotid artery stenosis.**
   a. True
   b. False

[IN FUTURE ISSUES]

Update on Migraine Headaches