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Evidence-based summaries of the latest clinical neurology research

ABSTRACT & COMMENTARY

Neurologic Disease and Criminal Behavior – A Medicolegal Conundrum

By Matthew E. Fink, MD

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

SYNOPSIS: In a large, retrospective records review, patients with frontotemporal dementia, primary progressive aphasia, and Huntington's disease were found to have a high frequency of antisocial and/or criminal behavior.

SOURCE: Liljegren M, et al. Criminal behavior in frontotemporal dementia and Alzheimer disease. *JAMA Neurol* 2015;72:295-300.

Neurodegenerative diseases cause behavioral problems that result from impairments in judgment, executive behavior, emotional processing, sexual behavior, violence, and self-awareness. Many of these behaviors are deemed antisocial and have been associated, in some cases, with crimes, such as theft, traffic violations with or without alcohol use, violence, hypersexuality, and homicide. The Memory and Aging Center at the University of California, San Francisco, undertook a medical records review of 2397 patients evaluated at the center from 1999 until 2012, to identify all of those who were known to engage in acts that would violate the law or deviate from normal behaviors that could potentially lead to legal problems. The records were searched using a variety of keywords that identified such behavior. Only criminal behaviors that occurred during the patient's illness were included, and the behavior was considered to be the presenting symptom if this was specifically identified by the examining physician. The major diagnostic subgroups were then identified and associated with these behaviors: Alzheimer disease (AD), behavioral-variant frontotemporal dementia (bvFTD), semantic-variant primary progressive aphasia (svPPA), and Huntington's disease (HD).

Of 2397 patients, 204 (8.5%) had behaviors that could be interpreted as criminal. The major diagnostic groups were bvFTD (64), svPPA (24), AD (42), and HD (6). The diagnostic group with the highest percentage of

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patients with criminal behaviors was bvFTD (37.4%) followed by PPA (27.0%), while patients with AD were least likely to have committed crimes during their illness (7.7%; $P < 0.001$). Other disease categories were excluded because of their small numbers, as was mild cognitive impairment due to the lack of diagnostic specificity for this category. The odds ratio for criminal behavior in patients with bvFTD compared to those with AD was 7.2 ($P < 0.001$), and in patients with PPA compared to those with AD, it was 4.4 ($P < 0.001$). Criminal behavior was the first presentation in 14% of patients with bvFTD, 7.8% of patients with PPA, and 2% of patients with AD ($P < 0.001$). In addition, almost 20% of patients with bvFTD were reported to the police for criminal behavior compared to much lower numbers in the other categories. In addition, patients with bvFTD were significantly more likely to commit all types of crimes, and 6.4% of bvFTD patients exhibited some form of violence (roughly half verbal and half physical) at some time during their illness. Violent behavior was unusual in the other categories. In addition, men were significantly more likely than women to make sexual advances on others. There were no other differences between men and women. Although there was an absolutely small number of patients (6) identified with Huntington's disease, half were physically violent, and all of the patients were reported to the police for criminal behavior.

Thirty-one of the identified patients were deceased and autopsied. There was a 93% concordance between clinical and neuropathological diagnosis. One patient with a clinical diagnosis of bvFTD had a pathologic diagnosis of AD, and all of the patients with PPA had a spectrum of neuropathology that fit a pathologic diagnosis of frontotemporal lobar degeneration, as would be expected.

■ COMMENTARY

This study, while not breaking new ground, has been carefully and systematically performed, and confirms that certain neurodegenerative disease categories, particularly frontotemporal dementia and Huntington's disease, are often associated with antisocial and criminal behaviors, including violence. It also shows that such behavior, particularly violent behavior, is rare in patients with Alzheimer disease. The neuropathology of these disorders is notable in that the disorders that involve frontotemporal, orbitofrontal, and frontal subcortical circuits, with degeneration of frontal lobe structures, are the disorders most likely associated with antisocial and criminal behavior and are consistent with our understanding of these disorders, where there is loss of behavioral inhibition and emergence of impulsive behaviors.

The implications of these findings for our legal system are profound. Our legal system requires that a verdict of "guilt" requires that a person knows the nature of the act he or she is doing and knows that it is wrong, and in many patients with frontotemporal dementia, that definition will hold up. Many of these patients score normally in measurements of cognitive functions and memory, yet they develop severe behavioral disorders that can result in antisocial and/or criminal behavior. And in most cases, they will meet the definition of understanding "right from wrong." Therefore, it is important for neurologists to be aware of these problems, and to advocate for our patients when they find themselves involved in a legal problem due to antisocial behavior. The patient may meet the definition of understanding "right from wrong," but still have a neurological disorder that played a role in the genesis of their antisocial behavior or criminal behavior. ■

ABSTRACT & COMMENTARY

Relationship Between Brain MRI Biomarkers and Cognition

By Alon Seifan, MD, MS

Assistant Professor of Neurology, Weill Cornell Medical College, Memory Disorders Program

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

SYNOPSIS: In a prospective, longitudinal, cohort study of an asymptomatic, multi-ethnic Dallas community, brain MRI biomarkers measuring volume were associated with cognitive functions, as measured by the Montreal Cognitive Assessment.

SOURCE: Gupta M, et al. Association of 3.0-T brain magnetic resonance imaging biomarkers with cognitive function in the Dallas Heart Study. *JAMA Neurol* 2015;72:170-175. doi:10.1001/jamaneurol.2014.3418.

In persons presenting with neurological complaints, the clinical significance of MRI biomarkers is often obvious. Neurologists are expert at determining whether pathology explains a given symptom. In community-dwelling adults who don't seek neurological attention, however, the clinical significance of brain differences, including differences in white-matter disease distribution and cortical and subcortical atrophy, remains to be fully understood. Age-related brain changes are difficult to quantify using visual inspection alone. A significant proportion of asymptomatic adults harbor findings that might be considered pathologic in symptomatic individuals. In addition, individuals often harbor multiple simultaneous brain pathologies. These are critical research challenges because a better understanding of the clinical significance of readily available brain MRI biomarkers could help with earlier identification of individuals at risk for neurological disease. The study by Gupta et al takes a step forward by documenting cross-sectional associations between brain MRI biomarkers and cognitive outcomes in a younger, community-dwelling sample.

The Dallas Heart Study II was an extension of the initial Dallas Heart Study, a longitudinal, multi-ethnic, population-based cohort study of Dallas County residents. Between 2007 and 2009, a total of 2082 participants underwent brain MRI imaging and brief cognitive testing. For this study, non-English speakers and persons with known brain disease were excluded, leaving a final sample of 1645 subjects, which was 60% female, 48% African American, and 15% Hispanic, with a mean age of 50 years and an educational level of 13 years. Cognition was assessed using the Montreal Cognitive Assessment (MoCA). Brain volume was measured using 3.0-T MRI and quantified using the functional MRI of the brain software. The following volumes were quantified: white matter hyperintensity volume (WMH), total brain volume (TBV), gray matter volume (GMV), white matter volume (WMV), cerebrospinal fluid volume (CSFV), and hippocampal volume (HCV).

Results demonstrated a statistically significant (although low in magnitude) relationship between each MRI brain biomarker and total MoCA scores after adjusting for demographics (age, sex, years of education, self-reported race/ethnicity), with the exception of the association between white matter hyperintensity volume and MoCA score, which lost statistical significance after adjusting for demographics. Of the six MRI biomarkers, a combination of three (GMV, CSFV, and HCV) together formed the best predictive model related to total score on the MoCA. Years of education modified the association between cognition and each MRI biomarker except for WMH. Of all subdomains on the MoCA, the visuospatial/executive domain had the strongest correlation with brain volumes.

The results suggest that clinically significant changes in brain volume can be detected in community-dwelling adults, even at younger ages. The small size of the association (1% of variance in cognition) can likely be explained by the fact that the MoCA (due to its brevity) is not the most nuanced of cognitive measures. The findings confirm a protective effect of education on cognition in the presence of pathology. The findings suggest that prior observations of clinically significant consequences of cortical atrophy in older individuals might also extend to younger individuals. Importantly, the study was done in a multi-ethnic population that was mostly non-Caucasian, allowing generalization of previous brain biomarker study results to a more diverse population.

Strengths of the study include the fact that it was population-based, it included several measures of brain anatomy, and it included individuals of diverse backgrounds. Population-based sampling minimizes selection bias and may allow for more generalizable conclusions. Using population-based approaches also captures samples with a high prevalence of vascular risk factors. Prior associations between MRI biomarkers and cognitive outcomes have yet to be replicated in more diverse populations. Studying several different MRI biomarkers at once, each of which represents a different type of potential underlying pathology, allows for speculation about the mechanisms by which brain anatomy might relate to cognition. For example, hippocampal volume may represent underling AD pathology, and white matter changes or ventricular size could represent cerebrovascular disease.

■ COMMENTARY

A few limitations are worth mentioning. The quantification method used in this study did not allow for region-of-interest based analysis. This precludes any conclusions to be drawn regarding specific brain structures. Also, although the authors performed some analyses to justify treating age and brain atrophy as co-linear, it is currently understood that the relationship between brain atrophy and age is not linear. Also, the study did not account for presence of neurodevelopmental disorders such as learning disability; that is critically important because up to 10% of adults may have atypical neuroanatomy related to neurodevelopment. In fact, a host of early life factors

besides education can influence the final attained brain size and cognition, including total brain size and hippocampal volume. Although the study used multiple MRI biomarkers, it could not account for the interrelatedness of each of these structures. Connectivity-based approaches are important because brain volumes are intricately interconnected.

The next wave of cognitive imaging biomarker studies should include an even more comprehensive set of imaging biomarkers, including functional, connectivity-based, and ligand-based methods. Future studies need to account for early life exposures, including childhood adversity, socioeconomic status, and nutritional deprivation. Also, future studies are required to extend these findings to populations in which vascular risk factors are not so prevalent. Addressing potential vascular components using functional imaging is important to explain some of the variance in cognition (cognition depends on blood flow not just brain structure). Future studies are still required to fully account for the full range of neurodiversity that exists both within and across cultures. To truly test brain-behavior associations, future studies will need to use more nuanced cognitive measures. In the meantime, the study by Gupta et al suggests that even in younger individuals without overt neurological presentations, brain volumes matter. ■

ABSTRACT & COMMENTARY

Does Traumatic Brain Injury Cause Sleep Disruption?

By Alan Z. Segal, MD

Associate Professor of Clinical Neurology, Weill Cornell Medical College

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

SYNOPSIS: In a well-designed animal model of traumatic brain injury, a sleep disorder was induced that resembles, in many ways, what is observed in spontaneous human narcolepsy.

SOURCE: Skopin MD, et al. Chronic decrease in wakefulness and disruption of sleep-wake behavior after experimental traumatic brain injury. *J Neurotrauma* 2015;32:289-296.

Traumatic brain injury (TBI) commonly produces difficulties with memory and multiple other aspects of cognition. TBI is also associated with mood disorders such as depression and anxiety, along with insomnia and excessive daytime sleepiness. Even in the absence of TBI, poor sleep can produce memory loss, impaired concentration, and depression. Therefore, it is likely that TBI and sleep disorders have complementary and synergistic effects.

TBI has been shown to decrease the density of orexin (hypocretin) neurons in the hypothalamus, though these data are limited to autopsy studies involving only a handful of patients. Such changes mimic those typically associated with the loss of orexin neurons seen in patients with narcolepsy. Clinically, both disorders are characterized by excessive daytime sleepiness, with poor nocturnal sleep efficiency and architecture.

In the current report, the lateral fluid percussion (LFP) model of TBI is used. A craniotomy is performed, followed by indirect head trauma, generated by a pendulum striking a column of water. This is the most widely used TBI animal model and has been shown to correlate well with the behavioral and neuro-anatomic abnormalities observed in humans. LFP tends to create damage most prominently in the cortex, hippocampus, and corpus callosum. LFP in comparison to other models, such as direct cortical impact, is thought to most closely resemble the typical concussive injuries that occur, for example, during motor vehicle accidents or sports collisions.

In the current study, rats were subjected to LPF and compared with sham controls at intervals of 6, 19, and 29 days post-injury. Polysomnography was performed for 24-hour periods at each of these intervals with a dark phase from 8 p.m. to 8 a.m. and light phase from 8 a.m. to 8 p.m. Behavioral tests included those of spatial memory (using novel object recognition) as well as contextual and emotional memory (using a "fear-based" sequence of electric shocks and a water maze). These tests are thought to test both cortical as well as subcortical (limbic system) function and were all adversely affected among animals exposed to head trauma.

Results demonstrated that the overall sleep times (both rapid eye movement [REM] and non-REM) did not differ between the two groups, but TBI rats showed markedly disordered nocturnal sleep architecture with frequent bouts of awakening and showed increased intrusion of sleep into daytime alertness. This is a fairly typical pattern seen in narcoleptics. Sleep-onset REM, however, which is characteristic of narcolepsy, was not

increased in the experimental animals.

Perhaps most importantly, brain-injured rats showed an approximately 50% reduction ($P < 0.001$) in orexin-positive neurons in the lateral hypothalamus when compared with controls. In prior human studies using transcranial magnetic stimulation, TBI has been shown to produce decreased cortical excitation. This is thought to be a direct result of impaired orexin-mediated subcortical input and is similarly seen in patients with narcolepsy.

■ COMMENTARY

These results confirm that traumatic brain injury, as demonstrated in a well-recognized animal model, produces both excessive daytime sleepiness and nocturnal sleep disruption. Therefore, difficulties in memory and concentration seen in patients with TBI can be the result of dual and likely synergistic causes. Superimposed on any direct destructive effects of TBI are the known cognitive difficulties associated with poor sleep. Perhaps more importantly, TBI may be associated with a loss of hypothalamic orexin neurons producing the same impairments in cortical activation commonly seen in patients with narcolepsy.

Given these results, therapy for narcolepsy possibly may be extrapolated to patients with TBI. In narcoleptics, sleepiness may be treated with stimulants such as modafinil to maintain daytime alertness. However, narcolepsy is as much a product of impaired nocturnal sleep as it is a disorder of daytime sleepiness. Gamma-hydroxybutyrate (GHB), also known as sodium oxybate (trade name Xyrem), is a prominent GABA-agonist that promotes slow wave sleep and is a crucial element in the pharmacological armamentarium for narcolepsy. Given the overlapping patterns observed here, GHB might similarly benefit patients with TBI and bears further investigation. ■

ABSTRACT & COMMENTARY

Is Early MRI Warranted for Back Pain in the Elderly?

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: In an analysis of a large dataset from several large integrated health care systems of patients older than 65 years of age with new-onset low back pain, early spine imaging did not alter management or outcomes, but added considerable cost to their care.

SOURCE: Jarvik JG, et al. Association of early imaging for back pain with clinical outcomes in older adults. *JAMA* 2015;313:1143-1153.

Back pain is the third most common cause for doctor visits, affects 85% of adults at some point in their lives, costs the United States more than $100 billion annually, and forces almost 50% of sufferers to give up sex as a consequence. Yet, in most instances, episodes are self-limited, resolve without therapy, and, in 85%, remain without a specific cause ever being established. Can anything be done to at least reduce the *cost* of low back pain? Perhaps limiting early magnetic resonance imaging (MRI) of the lumbar spine in new-onset, low back pain in the elderly can be done. And if so, would this be harmful to the patient?

To compare outcomes among older patients with new-onset low back pain who underwent early MRI of the lumbar spine vs those who did not, a prospective observational cohort was recruited from three integrated health care systems, comprising Harvard Vanguard, Henry Ford Health System, and Kaiser Permanente Northern California, consisting of 5239 patients, 65 years of age or older, who, between March 2011 and March 2013, presented to their primary care physician with new-onset low back pain, defined as having had no visit for back pain in the prior 6 months. Early imaging was defined as undergoing lumbar spine radiographs, computed tomography (CT), or MRI within 6 weeks of this initial visit. Physical limitation due to back pain was the primary outcome measure, as assessed by the Roland-Morris Disability Questionnaire, whereas secondary outcome measures included noting the number of falls with injuries that occurred over the prior 3 weeks, rating average back and leg pain intensity over the prior week on a scale of 0-10, and completing the Brief Pain Inventory interference scale, the Patient Health Questionnaire, and the EuroQol health status measure. Statistical analysis comprised the McNemar tests for categorical variables, paired *t*-tests for continuous variables, and linear mixed-effects models to obtain adjusted differences between groups.

Among the 5239 participants, 386 were excluded from analysis due to premature withdrawal, unavailability of data, cancer visit, or lumbar spine surgery within the prior year; bone scan within 6 weeks; or death within a year. Of four patients who died of cancer within the year, two had early imaging and two did not. Among the 4853

remaining who underwent propensity score matching, 1174 had early radiographs, 349 had CT or MRI, 1353 served as matched controls, and 1977 were not in a matched set. None of the groups differed significantly on the primary outcome measure, the Roland-Morris disability questionnaire. Of patient-reported outcomes, only leg pain intensity was significantly lower at months 3, 6, and 12 among those who underwent early imaging compared to those who did not. However, this difference, only 0.5 points on the 0-10 point pain numerical rating scale, was clinically unimportant, given that 2-3 points represents a clinically important difference. In contrast, costs were 40% and 50% higher among the radiograph and CT/MRI groups, as measured by mean total relative value units (RVUs), translating into approximately $1380 and $1430, respectively, per patient. Cancer rates were comparable across all groups in the year following the study.

Clinical outcomes do not appear to be altered in elderly patients who undergo early imaging for new-onset low back pain, and, although not a randomized, double-blind, controlled study, circumspection with respect to early imaging may be advised in treating such patients.

■ COMMENTARY

Even brief exposure to a number of modifiable factors, both physical and psychosocial, can increase the risk of a new episode of low back pain.[1] Using a case-crossover design, 1639 patients were screened, of which 999 patients were included, with new onset low back pain, between October 2011 and November 2012, from 300 primary care clinics in Sydney, Australia. Moderate or vigorous physical activity, or being distracted during an activity or task, increased the risk of new onset LBP by an odds ratio of 2.7 and 25.0, respectively, with risk being highest between 7 a.m. and noon. Alcohol consumption and sexual activity were not associated with new onset low back pain. New approaches for the prevention of LBP should address these findings. ■

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ABSTRACT & COMMENTARY

Hypothermia after Acute Traumatic Brain Injury Revisited

By Halinder S. Mangat, MD

Assistant Professor of Clinical Neurology, Weill Cornell Medical College

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

SYNOPSIS: Hypothermia therapy is effective after severe traumatic brain injury for patients ages 50 years and younger. However, mortality was increased in patients treated with hypothermia who had diffuse injury with swelling on CT.

SOURCE: Suehiro E, et al. Diverse effects of hypothermia in patients with severe traumatic brain injury based on the computed tomography classification of the Traumatic Coma Data Bank. *J Neurotrauma* 2015;32:353-358.

The authors studied the effect of hypothermia after severe traumatic brain injury (TBI) in a secondary analysis of data collected from 2002-2008 in a prospective, randomized trial of 135 patients with severe TBI. They utilized CT classification of brain injury based on the Traumatic Coma Data Bank (TCDB) to identify subgroups that might derive benefit.[1] Although patients undergoing therapeutic hypothermia were targeted to 32º-34º C, patients in the fever-control group were cooled to 35.5º-37º C. Cooling was initiated within 2 hours after TBI and maintained for at least 72 hours. Sedation, analgesia, and paralytics were used for the temperature-control phase. Primary outcomes were the Glasgow Outcome Scale (GOS) and mortality at 6 months after injury.

Results showed that patients ≤ 50 years of age with evacuated mass lesions who underwent therapeutic hypothermia had a greater chance of having a favorable outcome than those who only had fever control (77.8% vs 33.3%), whereas patients with diffuse injury and swelling had higher mortality with therapeutic hypothermia.

■ COMMENTARY

The authors conducted a secondary analysis of a prospective trial utilizing the TCDB CT classification to study the benefits of hypothermia. The results are consistent with those from previous small studies.[2,3] Although the results in earlier studies were suggestive of these findings, in this study cohort, they are statistically significant. However, these are still preliminary data and the study was not adequately powered to make firm conclusions regarding treatment recommendations. The conclusions need to be fully validated in a larger prospective cohort. Although these data are encouraging,

this is by no means the first study showing encouraging benefits of hypothermia after TBI. The authors have also included patients with "moderate disability" as a good outcome, and this may not stand scrutiny in a larger cohort with a more rigid definition of "good outcomes." Age > 45 years was previously shown to be associated with poor outcome after hypothermia.[4] Although the current study enrolled patients up to 69 years of age, data are only reported for those ≤ 50 years or less. No reasons are provided for failure to report the data on older patients.

The finding that patients with evacuated mass lesions had significant benefit may be related to an ischemia-reperfusion type of brain injury that follows formation and evacuation of a mass lesion, including deformation of midline structures. Hypothermia has been shown to be effective in this type of brain injury as evidenced by benefit of hypothermia in patients after cardiac arrest. The mechanism of injury in diffuse brain injury with edema is characterized by axonal injury and, hence, the difference in effect in this subgroup.

In this study, comparison is made between the effects of hypothermia and fever control. The target temperature for the latter group was 35.5º-37º C. Therefore, this is not merely fever-control but may be classified as mild hypothermia when temperature of 35.5º C is reached (as on day 3). With this temperature target, adverse effects of cooling can be experienced due to the target temperature's proximity to the shivering threshold of 35.7º C.[5] The use of paralytics and how shivering was controlled are not detailed. The occurrence of shivering may contribute to significantly increased oxygen consumption and may affect brain metabolism. Studies are underway to explore this; shivering effects should be kept in mind for the planning of future trials.

The choice of temperature target may be important since more recent data suggest that there is no added benefit of therapeutic hypothermia as compared to fever control alone (36º C) in improving outcomes after cardiac arrest:

Neurology [ALERT®]

Stroke Alert

By Matthew E. Fink, MD

Endovascular Intracranial Clot Extraction Benefits Are Confirmed in Two More Clinical Trials

SOURCES: Saver J, et al, for the SWIFT PRIME Investigators. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *N Engl J Med* 2015; April 17 [Epub ahead of print] DOI:10.1056/NEJMoa1415061.

Jovin TD, et al for the REVASCAT Investigators. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med* 2015; April 17 [Epub ahead of print] DOI: 10.1056/NEJMoa1503780.

Furlan AJ. Editorial. Endovascular therapy for stroke – It's about time. *N Engl J Med* 2015; April 17 [Epub ahead of print] DOI: 10.1056/NEJMe1503217

On April 17, 2015, the *New England Journal of Medicine* published the results of two randomized clinical trials of endovascular stent-retriever clot extraction for ischemic stroke, simultaneous with their presentation at the European Stroke Conference. These two studies, added to those presented and published at the International Stroke Conference in February, bring the total number of studies to five that have shown dramatic benefits of this therapy in appropriately selected patients with acute ischemic stroke.

SWIFT PRIME enrolled 196 patients at 39 centers who were randomized into a thrombectomy group with the stent-retriever plus intravenous TPA compared to intravenous TPA alone within 6 hours of symptom onset. The primary outcome measure was the global disability score as measured by the modified Rankin scale score. The rate of functional independence, a modified Rankin scale score of 0 to 2, was higher in the intervention group than in the control group (60% vs 35%, $P < 0.001$). There were no significant differences between the groups in 90-day mortality or in the rate of symptomatic intracranial hemorrhage (0% vs 3%, $P = 0.12$). This study was terminated early because of the dramatic benefits seen in the early enrollment.

REVASCAT enrolled 206 patients at four centers in Spain, who were randomized to stent-retriever clot extraction vs medical therapy, which could include alteplase, within 8 hours of symptom onset. Once again, using the modified Rankin score as a measurement of global disability at 90 days, there was a dramatic difference in the groups, with the interventional group attaining independence, a modified Rankin score of 0 to 2, in 43.7% vs 28.2% in the medical group. Again, there was no significant difference in the rate of symptomatic intracranial hemorrhage or in mortality between the two groups.

In an accompanying editorial by a pioneer in this field, Dr. Anthony Furlan, the reason for success in these trials was identified as: 1) careful patient selection with documentation of large vessel occlusion, 2) improvement in technology, particularly with the stent retriever device, and 3) rapid speed to enroll and treat patients as quickly as possible.

Endovascular stent retriever therapy for acute ischemic stroke should be considered part of the standard therapy available to neurologists for patients who arrive at their hospitals with acute ischemic stroke, and stroke teams need to focus on speed and efficiency to successfully accomplish these tasks. ■

both mortality and cognitive impairment.[6,7] However, the pathophysiology is not the same in cardiac arrest and TBI, and there may well be different results in patients with TBI. This underscores the importance of having a fever-control arm, in addition to a "no intervention" control arm, in future trials.

Although the evidence so far has suggested no benefit from hypothermia in patients suffering from severe TBI, these pilot data, along with data from subgroup analysis of previous trials, suggest a possible role for hypothermia in patients with surgical mass lesions. The design of future trials will be crucial to their success, to avoid adding to the existing list of negative Phase 3 trials in TBI. A widely accepted standard for classifying patients by imaging, as well as inclusion of patients ≤ 50 years of age, will help to clarify results. ■

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CME QUESTIONS

1. Which of the following statements is true regarding neurodegenerative disorders?
a. Frontotemporal dementia is never associated with violent behavior.
b. Alzheimer disease is often manifested by criminal behavior.
c. Huntington's disease is often associated with aggressive antisocial behavior.
d. Primary progressive aphasia is manifested by withdrawal and introverted behaviors.

2. Human cognition and intelligence are determined by the size of the human brain.
a. True
b. False

3. After experimental traumatic brain injury, the following derangements in sleep characteristics include which of the following?
a. Insomnia
b. Excessive daytime sleepiness
c. Nocturnal sleep disruption
d. Reduction in orexin-positive neurons
e. All of the above

4. Patients older than 65 years of age with new onset low back pain:
a. should have lumbar spine imaging as soon as possible.
b. do not necessarily need immediate MRI imaging of the lumbar spine.
c. should be put on strict bed rest for 3 days and then re-evaluated.
d. Both b and c

5. Which of the following statements is true regarding severe traumatic brain injury?
a. With severe TBI, the patient's age does not have any influence on outcome.
b. The presence of diffuse cerebral edema after TBI is a poor prognostic sign.
c. Cerebral ischemia and hypoxia occur in all patients with TBI.
d. There are effective medications that improve outcomes after TBI.

6. Which of the following statements is correct regarding successful intracranial endovascular therapy for stroke?
a. Patients must be treated rapidly after onset of symptoms.
b. Success is dependent on advanced technology.
c. Large vessel occlusion must be demonstrated by imaging.
d. Large infarct core is a contraindication to endovascular treatment.
e. All of the above

[IN FUTURE ISSUES]

Update on Epilepsy