2013 SNM Highlights Lecture: Neuroscience

From the Newsline Editor: The Highlights Lecture, presented at the closing session of each SNMMI Annual Meeting, was originated and presented for more than 33 y by Henry N. Wagner, Jr., MD. Beginning in 2010, the duties of summarizing selected significant presentations at the meeting were divided annually among 4 distinguished nuclear and molecular medicine subject matter experts. The 2013 Highlights Lectures were delivered on June 12 at the SNMMI Annual Meeting in Vancouver, British Columbia. The first presentation is included here, and the remaining 3 will appear in the October and November issues of Newsline. Peter Herscovitch, MD, cochair of the Scientific Program Committee, introduced Satoshi Minoshima, MD, PhD, who spoke on highlights from the neurosciences. Note that in the following presentation summary, numerals in brackets represent abstract numbers as published in The Journal of Nuclear Medicine *(2013;55[suppl 2]).*

This is the 60th anniversary of this society's Annual Meeting, and it has been about 30 years since Henry N. Wagner, Jr., MD, and his colleagues obtained the first molecular image of the dopamine system in the human brain. I started nuclear medicine training 27 years ago, and one of the high points of the Annual Meeting then and in many other years was the opportunity to hear Dr. Wagner summarize—all by himself—the outstanding scientific highlights from the wide array of presentations and posters. He inspired so many of us.

This year's Kuhl–Lassen Award from the SNMMI Brain Imaging Council went to Hank F. Kung, PhD, who presented on his extensive and influential research in development of neuroimaging tracers for molecular imaging. Dr. Kung developed both dopamine imaging and amyloid imaging tracers. One, ^{18}F-florbetapir, has been approved by the U.S. Food and Drug Administration, and we saw many presentations using this radiotracer in this meeting. He has made extraordinary contributions to molecular neuroscience and molecular neuroimaging practice

Brain Imaging Council Young Investigator awards went to David Owen et al. from Imperial College London (UK) for "Determination of ^{11}C-PBR28 binding potential in vivo: A first human TSPO occupancy study" [81] (first-place award); Peter Werner et al. from University Hospital Leipzig (Germany) for "Feasibility of combined ^{15}O-H_2O PET/MRI in patients with acute stroke" [87] (second place); and Jussi Hirvonen et al. from the University of Turku (Finland) for "Decreased cannabinoid CB1 receptor binding in tobacco smokers examined with PET" [85] (third place). It is encouraging to see these investigators active and engaged in molecular neuroscience and also to see that SNMMI remains an international meeting that brings together the scientific interests of individuals around the world.

Neurodegenerative Diseases

Neurodegenerative disorders are and will continue to be major health care topics. Centers for Disease Control mortality figures and other data indicate that rates of both Alzheimer and Parkinson disease (AD and PD, respectively) are on the rise, and these and related diseases are the foci of much research interest in the United States and many other countries.

One area of continued research is in imaging of abnormal τ protein deposition in AD. Villemagne et al. from Austin Health (Melbourne, Australia), the University of Melbourne (Australia), and Tohoku University and School of Medicine (Sendai, Japan) reported on "In vivo τ imaging in AD" [304]. They compared ^{18}F-THK523 PET imaging in healthy individuals and those with AD and found highly region-specific τ deposition in the AD patients (Fig. 1). An interesting observation was that the τ uptake correlated with neuropsychological aspects of the disease much more closely than did amyloid uptake. So here we see that 2 imaging biomarkers can play significant and differentiating roles in the progression and pathophysiology of AD. This is an important observation, and this tracer is being further developed. Okamura et al. from Tohoku University School of Medicine (Sendai, Japan), University of Melbourne (Australia), and Austin Health (Melbourne) also reported on "PET τ imaging in AD using novel ^{18}F-labeled 2-phenylquinoline derivatives" [305]. Their improved version of the tracer, ^{18}F-TKH-5105, clearly showed increased uptake in the cortex in patients with AD compared with healthy controls, cortical uptake that was comparable to that with ^{11}C-Pittsburgh compound (^{11}C-PiB) in AD (Fig. 2).

Satoshi Minoshima, MD, PhD

Many researchers are now looking at the implications of the fact that imaging has been shown to detect changes in individuals many years before the clinical onset of AD. Characterizing and identifying the earliest stages of the disease are promising approaches for research in treatment and prevention. Lowe et al. from the Mayo Clinic (Rochester, MN) reported on "FDG changes in PiB-positive, cognitively normal subjects" [467]. They found hypometab-

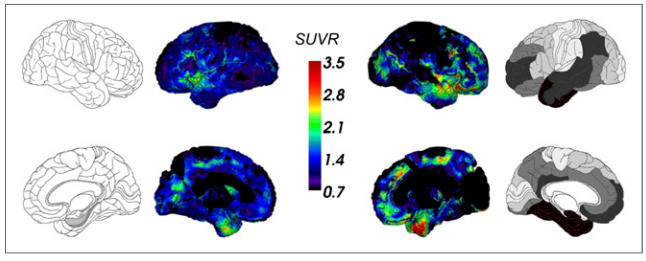

FIGURE 1. Regional distribution of paired helical filament τ proteins mapped (columns 1 and 4) and as imaged with ^{18}F-THK523 PET (columns 2 and 3) in healthy controls (left block of 4) and individuals with AD (right block of 4).

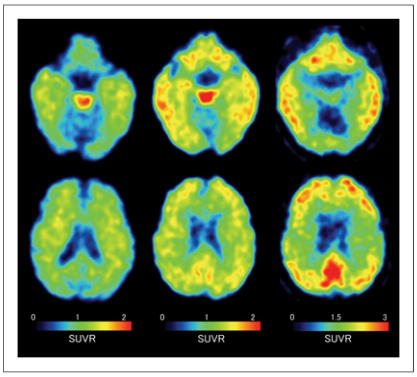

FIGURE 2. In vivo τ imaging using ^{18}F-THK-5105 PET in AD. Left column: ^{18}F-THK-5105 PET in controls; middle column: ^{18}F-THK-5105 PET in AD; right column: ^{11}C-PiB in AD.

olism in areas specific to AD in cognitively normal, PiB-positive subjects—one of the clues that evidence of AD begins very early before cognitive impairment and that alterations in function characterize these early images (Fig. 3).

Ament et al. from University Medical Center at the Johannes Gutenberg University (Mainz, Germany) reported on the "Relationship between Apoε4 and cerebral glucose metabolism in young and old healthy subjects" [86]. Apoε4 is a known genetic risk factor for AD. The group compared images in a group of old and young Apoε4-positive individuals with those from a group of old and young Apoε4-negative participants. Apoε4-positive and cognitively normal individuals showed decreased ^{18}F-FDG uptake in in some parts of the brain (Fig. 4). However, some younger individuals showed not only this decrease but an increase in FDG uptake in other parts of the brain, suggesting that in the beginning of the disease there may be compensation, upregulating some neuronal function. This is an interesting observation and requires additional research.

Amyloid deposition is also known to occur in Down syndrome, even in the early stages. Seibyl et al. from the Institute for Neurodegenerative Disorders (New Haven, CT), Banner Health (Sun City, AZ), Piramal Imaging (Berlin, Germany), and Bayer Healthcare (Berlin, Germany) reported on "Age-dependent ^{18}F-florbetaben brain PET uptake in adults with Down syndrome" [468]. Their images, comparing amyloid deposition in healthy volunteers and in individuals with Down syndrome at different ages, suggest that serial investigations in Down syndrome may provide additional information about the progression of amyloid deposition in AD (Fig. 5).

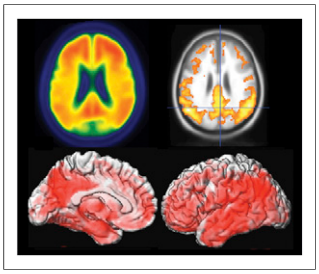

FIGURE 3. Hypometabolism in cognitively normal ^{11}C-PiB–positive subjects. Top left: composite PiB uptake in normal subjects with PiB SUV ratio > 2.05. Top right: hypometabolism on axial view in these subjects as compared to normal subjects with PiB SUV ratio < 1.40. Bottom: 3D renderings of hypometabolism in subjects with PiB SUV ratio > 2.05.

When amyloid tracers or any other new PET agents are introduced in research, they face a difficult path to eventual clinical adoption. One element in routine adoption is the need for training in interpreting images with the new agent. Sabri et al. from the University of Leipzig (Germany), MNI (New Haven, CT), Nippon Medical School (Tokyo, Japan), Technical University Munich (Germany), IBRI (Kobe, Japan), Kobe University Hospital (Japan), and Bayer Healthcare (Berlin, Germany) reported on "Close to clinical routine phase 2 trial on florbetaben PET imaging of β-amyloid (Aβ) in Alzheimer's disease" [299]. This was a Web-based training program using PET data acquired in 22 centers on 4 continents, with images from 116 early AD patients and 120 healthy controls. After Web training, 5 readers previously untrained in ^{18}F-florbetaben interpretation achieved a median sensitivity of 79% and median specificity of 89%, with good intra- and interreader reproducibility. New tracers will continue to appear, and Web-based training is a promising method through which physicians can keep up to date on their interpretation skills.

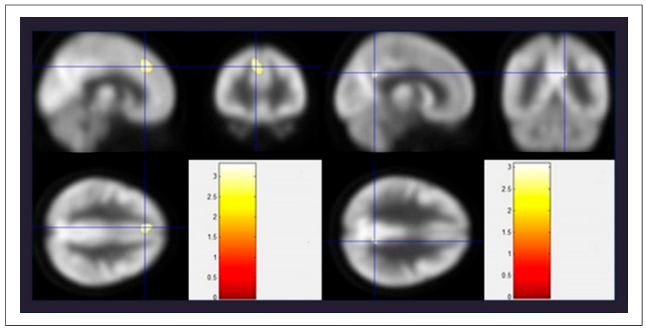

FIGURE 4. Apoε4-positive vs. Apoε4-negative subjects (old and young). No significant metabolic decreases were noted; instead, focally increased glucose metabolism was noted in Apoε4 carriers in the left superior frontal gyrus (BA 9), adjacent anterior cingulate (BA 32), and right posterior cingulate.

To help those interpretations, tremendous effort has been put into automatic and semiquantitative software development. For example, Thurfjell et al. from GE Healthcare (Uppsala, Sweden; London, UK; Princeton, NJ) reported on "Automated quantification of ^{18}F-flutemetamol data—comparison with standard of truth based on histopathology" [302]. The group used a semiquantitative

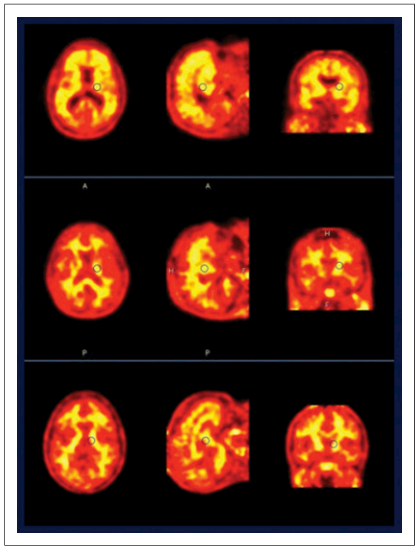

FIGURE 5. ^{18}F-florbetaben brain PET images in: a 52-y-old with Down syndrome (top row); a 41-y-old with Down syndrome (middle row); and a 21-y-old non–Down syndrome volunteer (bottom row).

method to identify positive amyloid imaging in PET, and achieved 91% sensitivity and 88% specificity.

One unique study was somewhat unexpected and perhaps may be the beginning of a new research direction. Patel et al. from the University of California, Irvine, reported on "Norepinephrine effects on Aβ-amyloid plaques in post-mortem AD brain" [1790]. Their work suggests that amyloid deposition and tracer binding to amyloid deposition can potentially be influenced by the presence of neurotransmitters. They showed that ^{11}C-PiB binding in hippocampal and frontal cortex brain sections from AD patients could be displaced with different concentrations of neuroepinephrine (Fig. 6). This raises interesting possibilities for chemical alterations and interactions among amyloid deposition, tracers, and neurotransmitters in neurodegeneration.

Molecular imaging is also making new inroads in understanding PD. Meyer et al. from the University of Leipzig (Germany) and Hannover Medical School (Germany) reported on "Progressive decline of α4β2* nicotinic acetylcholine receptor (α4β2*-nAChR) binding in early stage PD: A 5-year follow-up 2-[^{18}F]F-A-85380 (2FA) PET study" [189]. Over 5 years in PD patients, PET images (Fig. 7) clearly showed continuing deterioration of nAChRs, a decline that was closely correlated with motor and clinical decline.

A range of acetylcholine receptors are under current investigation in PD research, including efforts to create new nAChR imaging agents. Gallezot et al. from Yale University (New Haven, CT) reported on "Evaluation of [^{18}F] NCFHEB and its sensitivity to increases in endogenous acetylcholine in nonhuman primates" [412]. Figure 8 shows excellent uptake in the target. Binding is also sensitive to increases in endogenous acetylcholine concentration induced by physostigmine and donepezil. This tracer gives us an opportunity not only to look at receptor densities but at the mechanisms involved when acetylcholine is released in the brain.

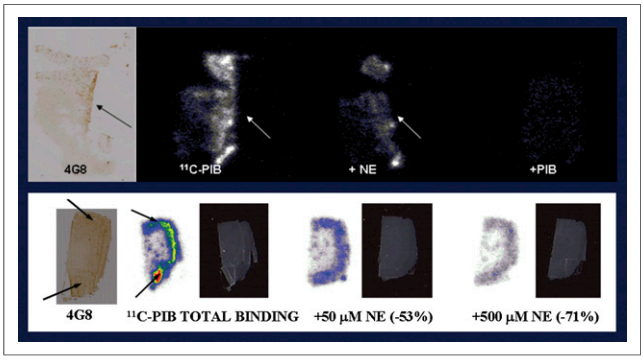

FIGURE 6. Top row: ^{11}C-PIB binding to AD hippocampal brain sections, displaced with norepinephrine (NE). Bottom row: ^{11}C-PIB binding to AD frontal cortex brain sections, displaced with different concentrations of NE.

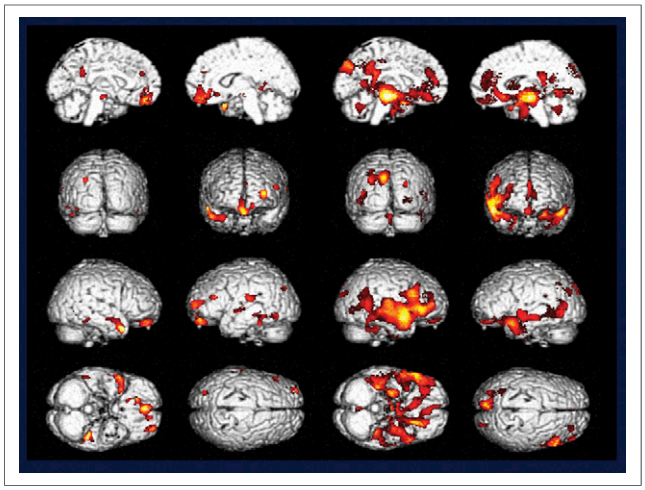

FIGURE 7. α4β2*-nAChR reductions in PD assessed with 2FA-PET at baseline (PD + 1 y) and at 5-y follow-up (PD + 5 y). Left to right: PD at baseline, healthy controls at baseline, PD at 5-y follow-up, and healthy controls at 5-y follow-up.

Neuroinflammation

At this meeting we saw that inflammation is the topic of much research interest, particularly in cardiac and neuroimaging. Many disease investigators have interests in development of new radiotracers that can better characterize and explore neuroinflammatory activity in the brain. Shukuri et al. from the Center for Molecular Imaging Science, RIKEN (Kobe, Japan), National Center of Neurology and Psychiatry (Kodaira, Japan), Hamamatsu University School of Medicine (Japan), and National Center for Geriatrics and Gerontology (Obu, Japan) reported on "*S*-enantiomer of ^{11}C-ketoprofen-methyl ester, a potent imaging probe for COX-1 in microglial activation" [413]. Several recent studies suggest that COX-1, traditionally considered merely as the isoform involved in homeostasis, plays an important role in several neurodegenerative diseases, including AD, with a neuroinflammatory component. In a mouse model of

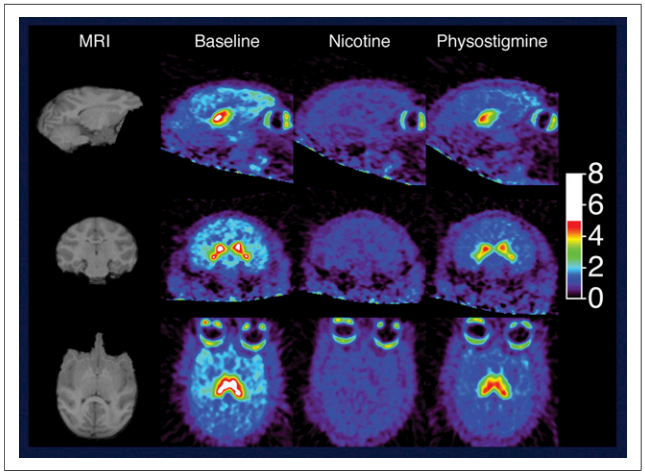

FIGURE 8. ^{18}F-NCFHEB in nonhuman primates. Left to right: MR imaging, ^{18}F-NCFHEB PET at baseline, ^{18}F-NCFHEB PET with nicotine challenge, and ^{18}F-NCFHEB PET with physostigmine challenge.

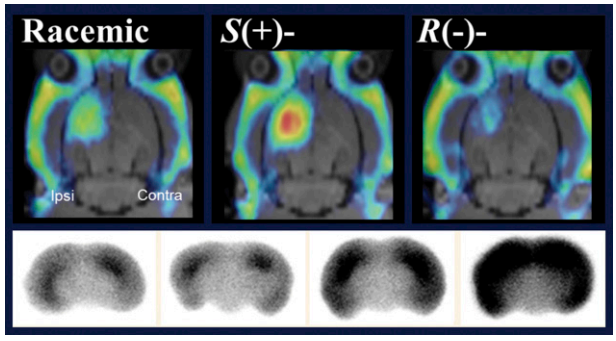

FIGURE 9. Top: ^{11}C-(S)KTP-Me PET images in mouse model of AD at d 1 after lipopolysaccharide injection. ^{11}C-(S)KTP-Me could detect neuroinflammation more specifically than R-enantiomer and also a racemic mixture of ^{11}C-KTP-Me. Bottom: Ex vivo autoradiographic images showing apparent increase in accumulation of ^{11}C-(S)KTP-Me at (left to right) 8, 13, 16, and 24 mo, corresponding with histopathologic assessment of Aβ plaque and CD11b-positive activated microglia.

AD, the authors showed that their tracer, ^{11}C-(S)KTP-Me, could detect neuroinflammation with a high degree of specificity and also that it was highly accumulated in those areas where COX-1–expressing activated microglia tightly surrounded and enclosed Aβ plaque (Fig. 9).

Colasanti from Imperial College and Imanova (London, UK) reported that "[^{18}F]PBR111 binding is increased in lesional and perilesional white matter of multiple sclerosis (MS) patients" [82]. They showed that MS patients with extensive overlap between white matter lesions on MR imaging and ^{18}F-PBR111 uptake on PET progressed much more quickly than those patients who did not have this overlap (Fig. 10).

Another example of a new radiotracer was presented by Paul et al. from the University of Groningen (The Netherlands) and the Tokyo Metropolitan Institute of Gerontology (Japan), who reported on "Changes of binding of cerebral adenosine A1 receptor antagonist ^{11}C-MPDX in rodent encephalitis" [244]. In experimental encephalitis, microPET showed that tracer binding potential was significantly increased in the hippocampus, cerebellum, and medulla, with immunohistochemistry indicating that the number of adenosine 1 receptors was increased (Fig. 11). This suggests that upregulation of adenosine 1 receptors may afford neuroprotection in encephalitis and that this process may be monitored with imaging.

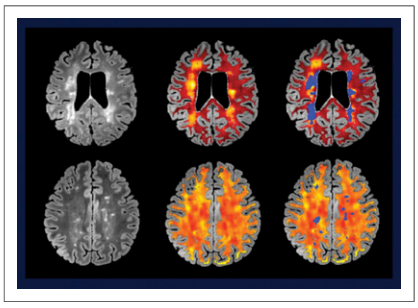

FIGURE 10. Overlap between white matter MS lesions and ^{18}F-PBR111 uptake on PET. Top row: High overlap seen in (left to right) T2-FLAIR MR, ^{18}F-PBR111 V_T PET, and PET/MR overlay in patient with aggressive MS course. Bottom row: Low overlap seen in corresponding images in patient with benign MS course.

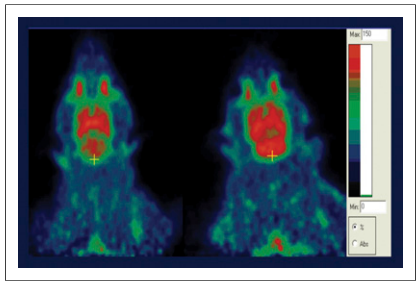

FIGURE 11. MicroPET images with cerebral adenosine A1 receptor antagonist ^{11}C-MPDX in rodent encephalitis. Left: Sham infected animal. Right: Encephalitis infected animal.

The broad range of current research on identifying new tracers is providing substantial and significant data that affects how we think about neuroinflammation. To what extent, for example, in any given disease entity or clinical instance, is it the cause or the consequence of some abnormal physiologic process? New tracers must be characterized thoroughly and well. In the study mentioned previously by Owen et al. from the Imperial College and Imanova (London, UK), "Determination of [^{11}C]PBR28 specific binding: A first human TSPO PET blocking study" [81], the group administered a blocking agent (XBD173) to displace a specific component of the TSPO ligand (used in PET to monitor neuroinflammation). Subsequent PET images show that the displaced component represents specific binding to the inflammatory pathway, providing the first direct estimate of specific TSPO signal in the living human brain (Fig. 12). These sorts of rigorous investigations are required before we can use new tracers for widespread research or as part of clinical applications.

Neurotransmission

Our brains work as a result of complex interactions of neurotransmitters, and investigations into neurochemistry using molecular imaging remain critical for better understanding of neurophysiology and neuropathophysiology. Numerous pathways and neurochemicals in the brain provide myriad opportunities for investigation. Fujita et al. from the National Institutes of Mental Health (Bethesda, MD) and the University of Oklahoma (Tulsa) reported on "Cyclic-AMP (cAMP) cascade in major depressive disorder. Downregulation in unmedicated patients and response to antidepressant" [33]. These researchers showed global decreases in ^{11}C-(*R*)-rolipram binding in patients with major depressive disorders compared with controls, indicating downregulation of the cAMP cascade (Fig. 13). Selective serotonin reuptake inhibitor treatment increased rolipram binding by 13% in patients, sug-

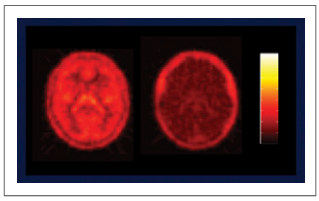

FIGURE 12. Estimation of ^{11}C-PBR28 V_{ND} using TSPO blockade with XBD173 provided direct estimation of specific TSPO signal in the living human brain. Left: Baseline. Right: After blockade.

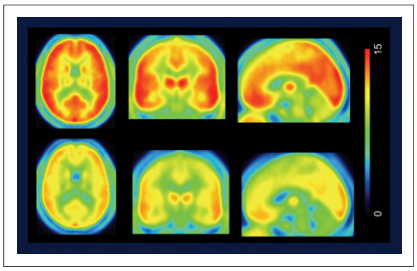

FIGURE 13. Unmedicated patients with major depressive disorder (bottom row) showed 18% global decreases of ^{11}C-(*R*)-rolipram binding compared with healthy controls (top row), indicating downregulation of the cAMP cascade.

gesting normalization of the cAMP cascade.

Wang et al. from Stony Brook University (Upton, NY), Brookhaven National Laboratory (Upton, NY), the National Institute on Drug Abuse (Bethesda, MD), and the National Institute on Alcohol Abuse and Alcoholism (Bethesda, MD) reported that "Peripheral insulin resistance affects brain dopaminergic signaling after glucose ingestion" [29]. ^{11}C-raclopride PET imaging of the brain indicated that insulin-resistant subjects have less brain dopamine release after a glucose drink than insulin-sensitive subjects. Those insulin-resistant subjects with greater disinhibition (i.e, who were prone to respond rapidly to eating and food opportunities) have less dopamine release in the nucleus accumbens after glucose ingestion. These findings suggest that insulin resistance and its association with less dopamine release in a central brain reward region might promote overeating to compensate for this deficit. This is an example of one of the many ways in which researchers are going beyond the brain in neuroimaging to explore mind/body interactions.

Explorations of neurorelease are becoming much more microscopic thanks to the incorporation of MR and other anatomic tools. Using MR diffusion-weighted imaging (DWI) and tractography we can now map out which parts of the brain are receiving and providing inputs to other areas. Tziortzi et al. from the University of Oxford (UK), Imperial College London (UK), and Imanova (UK) reported on "Quantification of dopamine release and dopamine D3R in the functional subdivisions of the human pallidum" [84]. Using MR DWI in dynamic baseline and postamphetamine ^{11}C-PHNO PET, the group provided evidence that endogenous dopamine release measured with PET is not governed by the relative proportions of the dopamine receptors. This kind of careful analysis is facilitated by state-of-the-art imaging technologies.

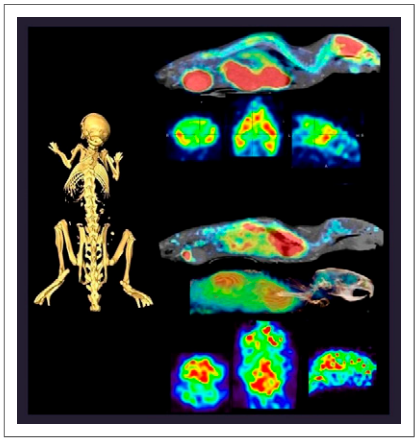

FIGURE 14. Enhanced expression of mGluR5 and peripheral benzodiazepine receptors as indicators of inflammation in ALS mouse model. Left: 3D CT. Right, top 2 rows: ^{11}F-FPEB PET. Right, bottom 3 rows: ^{11}C-PBR PET.

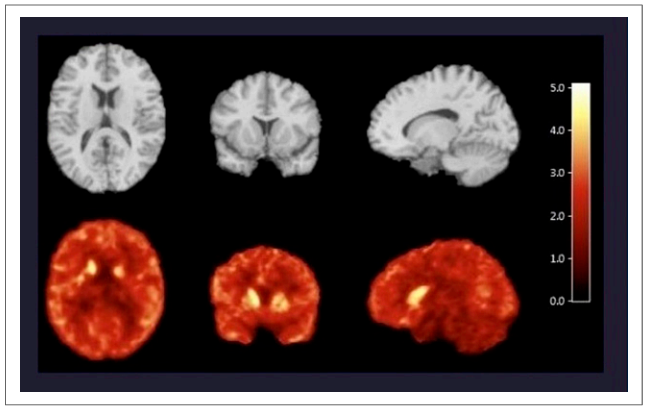

FIGURE 15. MR and ^{11}C-GSK215083 PET comparisons showed age-related decreases in receptor availability in the striatum and cortex. Example shows MR for anatomic comparison (top) and summed 60–90-min images (bottom) in a single subject.

Shumay et al. from Brookhaven National Laboratory (Upton, NY), the National Institute on Drug Abuse (Bethesda, MD), and the National Institute on Alcohol Abuse and Alcoholism (Bethesda, MD) reported that a "New genetic marker in the *AKT1* gene predicts brain levels of DRD2 in human brain" [523]. The group had noted considerable individual variability in brain dopaminergic tone, which can be assessed by ^{11}C-raclopride, which specifically binds to DRD2 receptors. They theorized that marked individual differences in ^{11}C-raclopride binding might be the result of genetic factors. Currently known genetic markers for dopaminergic pathways can explain only a small fraction of binding heterogeneity among individuals. The group discovered a new repeat polymorphism in the *AKT1* gene

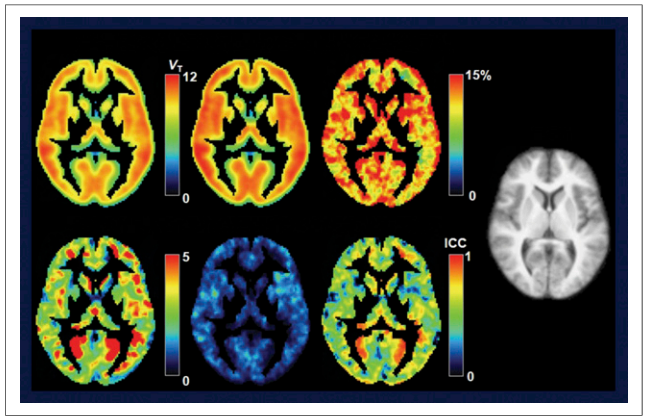

FIGURE 16. ^{11}C-NOP-1A PET accurately assessed nociceptin/orphanin FQ peptide receptors in healthy human brain. Top row, left to right: test, retest, and retest variability. Bottom row, left to right: mean of summed squares between subjects, mean of summed squares within subjects, and test reliability. Right: MR imaging.

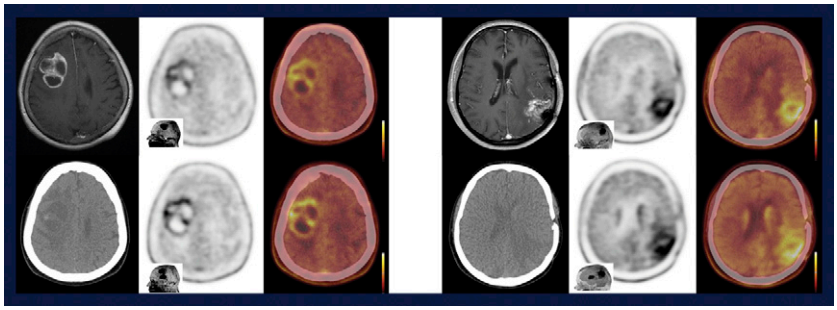

FIGURE 17. Comparison of ^{18}F-FET and ^{18}F-DOPA in glioblastoma patients. Left block: Primary glioblastoma manifestation. Top, left to right: T1 MR, ^{18}F-FET PET, fusion. Bottom, left to right: CT, ^{18}F-DOPA PET, fusion. Right block: corresponding images in recurrent glioma.

and tested its effect on striatal DRD2 availability in more than 100 healthy controls. They found not only that the AKT1 genotype significantly corresponds to this variability in all examined regions of interest, but that a model including age and AKT1 genotype is a robust predictor of striatal DRD2 availability. This reminds us of Dr. Wagner's prediction that genetics, pharmacology, and molecular imaging will be significantly interwined in future efforts to create smarter and more targeted health care.

Radiotracer Developments

Many individuals are working on new radiotracer development, which is central to the advancement of molecular imaging. One example came from Djekidel et al. from Yale University (New Haven, CT), who reported on "PET imaging of mGluR5 with [^{18}F]FPEB in medically refractory epilepsy" [83]. They showed that mGluR5 imaging with ^{18}F-FPEB in patients with medically refractory epilepsy is feasible and may demonstrate significant changes compared with controls. Brownell et al. from the Massachusetts General Hospital and the Harvard Medical School (Boston) looked at the same tracer and reported on "Modulation of mGluR5 expression and inflammation in amyotrophic lateral sclerosis (ALS)" [525]. They showed that mGluR5 expression was upregulated in animal ALS models. Imaging demonstrated enhanced expression of mGluR5 and peripheral benzodiazepine receptors as indicators of inflammation in the ALS mouse model (Fig. 14).

Matuskey et al. from Yale University (New Haven, CT) reported on "Age decline in subcortical 5-HT$_6$ receptor availability as imaged in male volunteers" [28] in a first-in-human study using ^{11}C-GSK215083 PET and MR for anatomic comparison. The study showed an age-related decrease in receptor availability in the striatum and cortex (Fig. 15).

Zoghbi et al. from the National Institutes of Health (Bethesda, MD) and Eli Lilly & Co. (Indianapolis, IN) reported on "Retest imaging of nociceptin/orphanin FQ peptide (NOP) receptors using a new PET radioligand [^{11}C]NOP-1A in healthy human brain" [417]. Images show that test/retest reproducibility with this agent is excellent and that the NOP receptors can be precisely measured in individual voxels (Fig. 16). This novel target in treatment of pain, anxiety, and drug abuse is quite promising and is sure to have many applications in the near future.

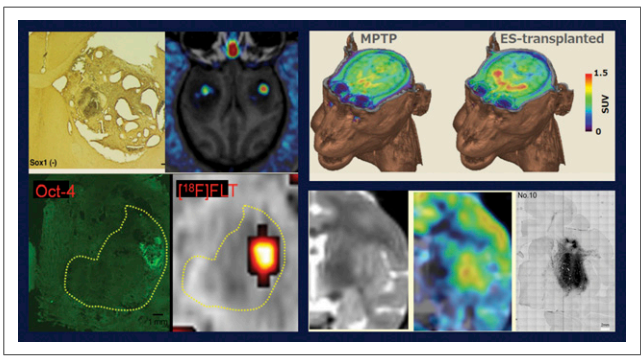

FIGURE 18. Three PET tracers illuminated 3 different aspects of stem cell–related treatment. Left block of 4: ^{18}F-FLT showed oncogenic transformation; right top: ^{18}F-DOPA showed functionality and migration in MPTP-treated (left) and embryonic stem cell–transplanted (right) animals; and right bottom: ^{11}C-KTP-Me monitored inflammation and immunologic reactions.

Brain Tumors

Jansen et al. from LMU University Munich (Germany) reported on "Prognostic value of [^{18}F]FET-PET in newly diagnosed low-grade glioma" [355], a condition in which ^{18}F-FDG is known to be challenging. The study was designed to evaluate prognostic factors using dynamic FET PET for the identification of biologically aggressive low-grade glioma. Among other observations, the researchers concluded that dynamic acquisition of ^{18}F-FET PET enables identification of aggressive gliomas and should be implemented for optimized treatment management.

Lapa et al. from Würzburg University (Germany) and the University of California at Los Angeles reported on "Comparison of the amino acid tracers FET and F-DOPA in glioblastoma patients" [357]. They showed that the 2 tracers performed equally well in primary and recurrent glioblastoma (Fig. 17).

Regenerative Medicine

The Nobel Prize in Physiology or Medicine in 2012 was awarded jointly to Sir John B. Gurdon and Shinya Yamanaka "for the discovery that mature cells can be reprogrammed to become pluripotent." The application of regenerative medicine to treat brain disorders will be a very important element in the future of brain imaging. Onoe et al. from RIKEN, Center for Life Science Technologies (Kobe, Japan) and Kyoto University (Japan) reported on "Assessment of tumorigenicity and efficacy of transplantation therapy with embryonic stem cell (ESC)–derived neural cells by PET imaging" [1739]. The group used 3 tracers (^{18}F-DOPA, ^{18}F-FLT, and ^{11}C-KTP-Me) to look at 3 different aspects

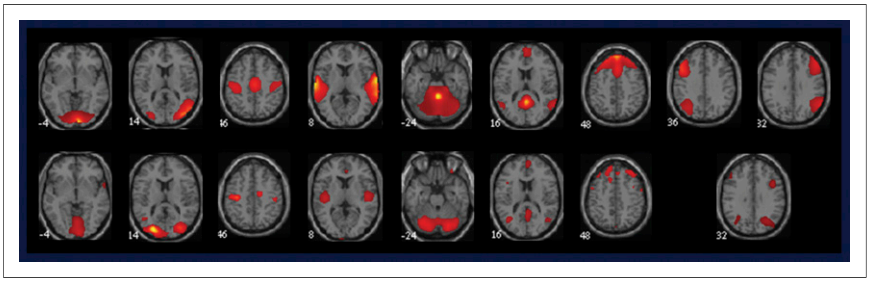

FIGURE 19. Functional and metabolic resting state networks as captured with simultaneous PET/MR (bottom/top). Left to right: primary visual, secondary visual, sensorimotor, auditory, cerebellar, default mode, frontal, and frontoparietal networks.

of stem cell–related treatment: functionality and targeted migration, oncogenic transformation, and inflammation and immunologic reactions. They showed restoration of dopaminergic function by transplantation of neural cells derived from human ESCs without tumorigenicity and neuroinflammation in a primate model of PD and demonstrated that PET molecular imaging is undeniably capable of assessing efficacy and safety in stem cell transplantation therapy in PD patients (Fig. 18).

Wu et al. from Case Western Reserve University (Cleveland, OH), Imperial College London (UK), and GlaxoSmithKline Research and Development (Brentford, UK) reported on "In vivo PET characterization of myelination in the spinal cord" [1767]. The researchers showed that myelination can be improved using stem cells and a growth hormone. The PET approach to monitoring myelin damage and repair in the spinal cord is unique in that it does not require invasive surgeries or biopsies. Use of this newly developed myelin-imaging technique to serially quantify local myelination should enable more efficient development of therapeutics directly focused on facilitating remyelination and the protection or regeneration of neural tissue.

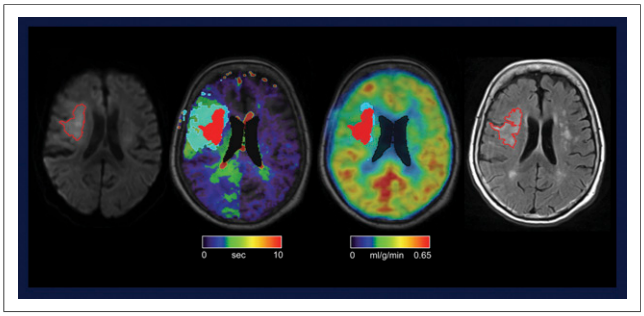

FIGURE 20. Simultaneous ^{15}O-H_2O PET/MR in acute stroke. Left to right: infarction core (DWI MR); MR penumbra (MR contrast media dynamics); PET penumbra (CBF as determined by H_2O kinetic modelling), and outcome (FLAIR MR) on d 6.

PET/MR Imaging

Multimodal imaging with PET/MR is now becoming a clinical reality. Yakushev et al. from the Technical University of Munich (Germany) and University Hospital of Cologne (Germany) reported on the "Functional and metabolic resting state networks as captured with simultaneous PET/MR imaging" [527]. They found close similarity between resting-state BOLD networks on MR and group-based covariance in glucose metabolism on PET (Fig. 19). Their validation study shows that multivariate analyses can provide consistent and reliable data from PET and MR acquired simultaneously. This contributes to our understanding of the increasingly complex information that imaging biomarkers can provide.

Werner et al. from University Hospital Leipzig (Germany) reported on the "Feasibility of combined $[^{15}O]H_2O$ PET/MRI in patients with acute stroke" [87]. Images show the first use of simultaneous ^{15}O-H_2O PET/MR in this indication (Fig. 20).

As I noted last year, Dr. Wagner often quoted Dag Hammerskjöld, former secretary general of the United Nations, who said "only he who keeps his eye fixed on the far horizon will find his right road." I strongly believe that our neuroscience community and SNMMI are on the right path—we can see the direction in which we must go to pursue a cure for AD, help PD patients, guide therapies for brain tumor patients, and better understand behavioral disorders and psychiatric conditions.

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Erratum

In the Newsline article "SNMMI 2013 Annual Meeting: Awards and Recognitions" (J Nucl Med. 2013;54[8]:12N–17N), the SNMMI-TS Presidential Distinguished Service Award was mistakenly described as having been awarded to Pamela S. Alderman. Ms. Alderman in fact won the SNMMI-TS Outstanding Educator Award. We regret the error.