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EDITORIAL

Application of Artificial Intelligence in Nuclear Neuroimaging

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Deep learning techniques are increasingly being applied in the field of nuclear medicine, and the diagnosis of neurodegenerative and neurological disorders is also being studied utilizing these techniques. This editorial introduces four recent studies that demonstrate the potential of deep learning methods in: (1) improving the diagnosis of Alzheimer's disease using tau PET imaging, (2) auto-quantification for amyloid PET imaging, (3) diagnosing parkinsonian syndromes using ^{18}F-FDG PET, and (4) diagnosing pediatric temporal lobe epilepsy using ^{18}F-FDG PET. These studies demonstrate the ability of deep learning to extract meaningful features, overcome limitations of conventional methods, and enhance diagnostic accuracy. As the field continues to evolve, the integration of deep learning in nuclear medicine imaging holds great promise for early detection, personalized treatment, and improved patient outcomes.

Deep Learning Detection of Informative Features in Tau PET for Alzheimer's Disease Classification [1]

Taeho Jo, Kwangsik Nho, Shannon L. Risacher, Andrew J. Saykin.

Indianapolis in USA.

Highlights

- Addressing the critical need for early and accurate diagnosis of Alzheimer's disease (AD), the study has developed an innovative deep learning framework that identifies informative features in tau PET images. By combining 3D convolutional neural networks (CNN) and layer-wise relevance propagation (LRP), their approach offers an innovative solution to the challenges faced in early AD detection, setting it apart from traditional diagnostic methods.
- The CNN-based model outperforms existing methods, achieving an impressive accuracy of 90.8% in classifying AD from cognitively normal (CN). Moreover, the LRP algorithm's ability to identify critical brain regions, such as the hippocampus, parahippocampus, thalamus, and fusiform, that contribute most to AD classification sets this study apart from others that lack such interpretability. The integration of CNN and LRP provides a powerful tool for detecting AD-related pathology, surpassing the limitations of earlier approaches.
- The deep learning approach holds great promise for the early detection of AD during prodromal stages, demonstrating its potential for clinical utility. The correlation between AD probability scores generated by the classifier and tau deposition in the medial temporal lobe in mild cognitive impairment (MCI) participants underscores the model's ability to identify individuals at risk of developing AD. This could facilitate timely intervention and improve patient outcomes, making the approach a valuable asset for clinical decision-making and disease management. The study's findings pave the way for the integration of advanced deep learning techniques into clinical practice, offering a more accurate and efficient means of diagnosing AD compared to current standard diagnostic procedures.

Comments

This study successfully applies a deep learning model to tau PET imaging for the classification of AD, addressing the critical need for early detection methods in AD. The authors' approach is commendable, as tau pathology is closely associated with cognitive symptoms, and the proposed model offers a more efficient and convenient way to measure the

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extent and amount of tau deposition, which is typically a time-consuming and labor-intensive process.

The authors' efforts to create an explainable AI model through the use of LRP are noteworthy. This approach not only enhances the interpretability of the results but also provides valuable insights into the spatial distribution of tau pathology in AD. Furthermore, the comparison of the deep learning model with traditional methods, such as statistical parametric mapping (SPM), demonstrates that the transition from conventional techniques to deep learning is well-validated in this study. The use of data from the ADNI cohort is another strength of this work, as it allows for the verification of the results and enables other researchers to reproduce the study. This transparency and accessibility are essential for advancing our understanding of AD pathology and progression.

However, future studies should consider validating the model's performance and clinical utility through prospective longitudinal studies. Such studies would provide a more comprehensive assessment of the model's ability to detect and monitor AD progression over time in real-world clinical settings.

Clinical Performance Evaluation of an Artificial Intelligence-Powered Amyloid Brain PET Quantification Method [2]

Seung Kwan Kang, Mina Heo, Ji Yeon Chung, Daewoon Kim, Seong A Shin, Hongyoon Choi, Ari Chung, Jung-Min Ha, Hoowon Kim, Jae Sung Lee

Seoul, Gwangju in Korea.

Highlights

- Accurate quantification of amyloid PET images is crucial for the diagnosis and treatment planning of Alzheimer's dementia. However, the subjectivity and variability inherent in visual interpretation pose challenges to the clinical utility of brain PET imaging. BTXBrain-Amyloid, an AI-powered software, addresses these limitations by providing objective and reproducible quantitative parameters from PET images, streamlining the quantification process without relying on additional imaging modalities such as MRI.
- BTXBrain-Amyloid demonstrates superior spatial normalization accuracy compared to traditional methods using SPM12, achieving higher similarity to the standard template and greater consistency across individuals. The improved spatial normalization enhances the sensitivity of detecting regional differences, particularly in deep brain structures critical for neurodegenerative disease research and diagnosis.
- The adoption of BTXBrain-Amyloid not only improves the accuracy and reproducibility of amyloid PET quantification but also significantly reduces the processing time compared to conventional methods. The enhanced precision and efficiency of BTXBrain-Amyloid can aid in the early diagnosis and effective treatment planning for patients with neurodegenerative diseases. Moreover, the ability to detect subtle regional differences in deep brain structures can provide valuable insights into disease progression and treatment response, ultimately leading to more personalized patient care.

Comments

The authors have identified a crucial unmet need in the field of amyloid PET imaging and have developed an innovative solution to address it. The limitations of visual assessment, such as interobserver variability, have long been a challenge in the interpretation of amyloid PET images. The development of BTXBrain-Amyloid, an AI-based software for quantifying amyloid uptake in brain PET images, is a significant step forward in addressing the unmet needs. The ability to perform accurate and fast quantification without the need for MRI is a major advantage of this method. This not only simplifies the process but also makes it more accessible, as MRI may not always be available for all patients.

The results of the study are impressive, demonstrating the superiority of BTXBrain-Amyloid in several aspects. The higher spatial normalization accuracy, greater consistency, and reproducibility compared to the SPM method are notable strengths. The ability to detect statistically significant differences in regions such as the dorsal caudate and thalamus, which were not detected by SPM, highlights the improved sensitivity of BTXBrain-Amyloid in detecting group differences. Although exploration in large-scale data sets will be necessary, future studies using amyloid PET imaging are expected to have clinical utility by reducing differences between various centers and finding small differences through BTXBrain-Amyloid.

Differential Diagnosis of Parkinsonism Based on Deep Metabolic Imaging Indices [3]

Ping Wu, Yu Zhao, Jianjun Wu, Matthias Brendel, Jiaying Lu, Jingjie Ge, Alexander Bernhardt, Ling Li, Ian Alberts, Sabrina Katzdobler, Igor Yakushev, Jimin Hong, Qian Xu, Yimin Sun, Fengtao Liu, Johannes Levin, Günter U.

Höglinger, Claudio Bassetti, Yihui Guan, Wolfgang H. Oertel, Wolfgang Weber, Axel Rominger, Jian Wang, Chuantao Zuo, Kuangyu Shi.

Shenzhen, Shanghai in China; Munich, Hannover, Marburg in Germany; Bern in Switzerland.

Highlights

- Accurate and early differential diagnosis of idiopathic Parkinson's disease (IPD) and atypical parkinsonian syndromes, such as multiple system atrophy (MSA) and progressive supranuclear palsy (PSP), remains a challenge due to overlapping clinical presentations, particularly in the early stages. This study addresses this unmet need by developing deep metabolic imaging (DMI) indices based on ^{18}F-FDG PET using a novel 3D deep CNN, termed PD Diagnosis Network (PDD-Net), to support the differential diagnosis of these conditions.
- The proposed DMI indices demonstrated superior performance compared to conventional methods, such as principal component analysis (PCA), in differentiating IPD, MSA, and PSP. The DMI indices achieved high sensitivity and specificity for each condition in both cross-validation and blind-test cohorts, with less ambiguity space in the differential diagnosis. Furthermore, the method exhibited robustness when dealing with discrepancies between populations and imaging acquisitions, as evidenced by its performance on an independent German cohort with different imaging protocols.
- The DMI indices developed in this study show great potential for providing an early and accurate differential diagnosis of parkinsonism, which can complement diagnoses made by expert clinicians. The automated nature of the method and its ability to handle discrepancies in imaging acquisitions make it suitable for clinical translation. Early and accurate diagnosis of parkinsonian disorders using these DMI indices can assist in determining appropriate therapeutic strategies and facilitate the development of disease-modifying treatments. Moreover, the interpretability of the DMI indices was enhanced using saliency maps, which highlighted the contribution of parkinsonism-related brain regions to the diagnostic probabilities.

Comments

This study addresses a crucial challenge in the field of nuclear medicine: the differential diagnosis of IPD, MSA, and PSP. The authors' approach to overcoming the limitations of PCA by utilizing the PDD-Net is innovative and commendable. The developed DMI indices demonstrate high accuracy in differentiating parkinsonian syndromes, as evidenced by the impressive performance metrics in both cross-validation and blind-test cohorts. Furthermore, the authors have taken the important step of validating their approach using an external dataset from a German cohort. This evaluation of robustness and generalizability is crucial for assessing the potential for clinical translation. The comparable performance of the DMI indices in the German cohort, despite differences in imaging protocols and patient populations, suggests that the deep learning approach may be more adaptable and better suited for real-world application compared to conventional methods like PCA.

However, using ^{18}F-FDG PET instead of the more commonly used dopamine transporter imaging such as ^{18}F-FP-CIT PET may have both advantages and disadvantages. In routine clinical practice, it is not uncommon for patients with IPD to undergo FDG scanning simultaneously with dopamine transporter imaging. This may limit the immediate applicability of the proposed approach. Nevertheless, research is ongoing, such as that of Choi [4], which aims to generate FDG-like images from early-stage FP-CIT scans. If these related studies are successfully combined with the current work, they may complement each other and enhance the practical utility of the DMI indices. Moreover, the use of FDG PET offers the additional benefit of potentially detecting other diseases beyond parkinsonian syndromes, which is a notable strength of this approach.

A deep Learning Framework for ^{18}F-FDG PET Imaging Diagnosis in Pediatric Patients with Temporal lobe Epilepsy [5]

Qinming Zhang, Yi Liao, Xiawan Wang, Teng Zhang, Jianhua Feng, Jianing Deng, Kexin Shi, Lin Chen, Liu Feng, Mindi Ma, Le Xue, Haifeng Hou, Xiaofeng Dou, Congcong Yu, Lei Ren, Yao Ding, Yufei Chen, Shuang Wu, Zexin Chen, Hong Zhang, Cheng Zhuo, Mei Tian.

Zhejiang in China.

Highlights

- Accurate localization of the epileptic focus in pediatric patients with temporal lobe epilepsy (TLE) remains challenging, as the focus may present either hypo- or hyper-metabolic abnormality with unclear boundaries on ^{18}F-FDG PET imaging. The study introduces a novel symmetricity-driven deep learning framework to address this unmet need, utilizing a pair-of-cube

(PoC)-based Siamese CNN for precise identification of epileptic foci.

- The proposed deep learning framework outperformed conventional methods such as visual assessment by physicians with different experience levels and SPM analysis in terms of dice coefficient and AUC. The framework demonstrated higher sensitivity and specificity in detecting epileptic foci and determining metabolic abnormality levels compared to visual assessment, even when physicians were unblinded to clinical information. The PoC training strategy employed in the study effectively addressed the challenges associated with limited and imbalanced pediatric ^{18}F-FDG PET datasets.
- The deep learning framework developed in this study has the potential to serve as a computer-assisted diagnostic tool for accurate and efficient localization of epileptic foci in pediatric patients with TLE. By providing precise identification of the focus and its metabolic abnormality level, the proposed method can assist in the early diagnosis and treatment planning for epilepsy patients. The automated nature of the framework reduces the reliance on physician experience and subjectivity, potentially improving the consistency and reliability of epilepsy diagnosis in clinical settings.

Comments

The authors present a novel approach to localize epileptic foci in pediatric patients with temporal lobe epilepsy using ^{18}F-FDG PET imaging. The strength of this study lies in its two-step approach: first, validating the hypothesis that epilepsy is related to high-dimensional symmetricity changes in PET images through radiomics analysis, and then developing Siamese CNN architecture with the PoC concept that exploits symmetricity to accurately identify epileptic foci.

The radiomics analysis used to validate the hypothesis provides a foundation for the development of the deep learning framework. The authors have done a commendable job in comparing their proposed method with various other approaches, including SPM analysis and visual assessments by physicians with varying levels of experience. However, it is important to keep in mind that while this study has validated the hypothesis, further research is needed to establish it as a widely accepted theory. The use of symmetricity-focused PoC and Siamese CNN architecture, based on the hypothesis, is innovative and demonstrates superior performance compared to conventional methods and visual assessments by physicians. This methodology has the potential to be applied not only to epilepsy but also to various fields of medical imaging.

The proposed deep learning framework has demonstrated impressive performance in localizing epileptic foci and determining metabolic abnormality levels, outperforming both conventional methods and visual assessments by physicians. The model's ability to accurately identify subtle metabolic changes, particularly in cases of hypermetabolism, which were missed by all physicians, underscores its potential for clinical implementation. With further validation and refinement, this innovative approach could significantly improve the diagnosis and treatment planning for pediatric patients with temporal lobe epilepsy, ultimately leading to better patient outcomes. The authors' work represents a significant step forward in the application of AI in medical imaging and raises excitement for its potential to revolutionize clinical practice in the near future.

Conclusion

Neuroimaging in nuclear medicine contain a wealth of information, yet their interpretation remains challenging. Various analytical methods have been employed, and now deep learning techniques are emerging as a powerful tool in this domain. As illustrated by the studies highlighted in this editorial, deep learning approaches are overcoming obstacles that previously hindered progress, effectively extracting meaningful features and enhancing diagnostic accuracy. Entering the 2020s, exciting advancements in diagnosis and therapeutic development are being reported in the field of nuclear medicine, driven by the integration of deep learning [6, 7]. It is anticipated that, hand in hand with artificial intelligence, this field will continue to thrive, ushering in an era of unprecedented growth, early detection, personalized treatment strategies, and improved patient outcomes.

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Declaration of Generative AI in Scientific Writing I utilized Claude, Anthropic's large language model, enhance the readability and fluency. However, I meticulously revised and verified the sentences to ensure the content's accuracy and credibility.

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