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論文題目	Combining Multiple Indices of Diffusion Tensor Imaging Can Better Differentiate Patients with Traumatic Brain Injury from Healthy Subjects 拡散テンソル画像の複数の指標を組み合わせることで外傷性脳損傷と健常対象との判別能力が上昇する		

（論文内容の要旨）

Background: Traumatic brain injury (TBI) is a common cause of mortality and morbidity worldwide. Individuals with TBI have an elevated risk of developing numerous neurocognitive and psychiatric illnesses. Diffuse axonal injury (DAI) is one of the most common pathological features of traumatic brain injury (TBI). DAI may include extensive microscopic axonal damage, even in the absence of abnormal findings on conventional computed tomography (CT) and magnetic resonance imaging (MRI). Unlike conventional imaging techniques, diffusion tensor imaging (DTI) can be used to identify and quantify white matter microstructural changes following DAI. A variety of parameters can be obtained from a DTI scan (DTI indices), including fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD). In recent years, several studies have investigated the use of machine learning (ML) approaches for studying DTI indices for the prediction of white matter microstructural changes in TBI patients at the individual level to aid in the classification and/or diagnosis of TBI patients. In the current study, four DTI indices (FA, MD, AD and RD) were extracted from all white matter tracts to study the spatial and pathological heterogenous changes in white matter microstructures following TBI. PCA as a feature reduction method was applied to the extracted indices images maps followed by support vector machine (SVM) to identify a classification model that can best differentiated between TBI patients and healthy control group.

Methods: Participants were adult patients with chronic TBI (n = 26) with DAI pathology, and age- and sex-matched healthy controls (n = 26). DTI images were obtained from all participants. Tract-based spatial statistics (TBSS) analyses were applied to DTI images. Classification models were built using PCA and SVM. Receiver operator characteristic curve analysis and area under the curve were used to assess the classification performance of the different classifiers.

Results: TBSS analysis revealed significantly decreased FA as well as increased MD, AD, and RD in patients with TBI compared with healthy controls (all p-values < 0.01).

Feature reduction and feature extraction: PCA was applied to FA, MD, AD, RD and ALL (combined FA, MD, AD and RD dataset) during cross validation in both training and test datasets.

SVM classification: using SVM with five-fold cross validation was able to classify the patients with TBI and healthy control groups using PCs of the skeletonized maps of each DTI index and the ALL dataset. A high level of accuracy (90.5%) was achieved by the classifier trained on the combined indices dataset (ALL) and (86.5%) by the classifier trained on the FA maps (all p-values < 0.01). The AUCs were 93% and 89% for the ALL and FA classifier tasks, respectively.

Discussion and Conclusions: The present study investigated the utility of using combined DTI indices with SVMs for the classification/diagnosis of TBI. Four DTI indices were extracted from all white matter tracts instead of a specific region or tract to elucidate the spatial and pathological heterogeneity of white matter microstructural changes following TBI. Despite the small sample size and other limitations in this study, the high accuracy achieved by the combined indices classification model suggests its potential usefulness as a tool to aid in the objective classification/diagnosis of TBI. We plan to validate the robustness of our model in a larger independent sample while incorporating other clinical variables including neuropsychiatric comorbidities in future studies.

（論文審査の結果の要旨）

本研究は、26 名のびまん性軸損傷の症例を対象として、脳画像を用いた健常者との判別方法について検討を行った研究である。方法としては、拡散強調画像を用いた Tract-Based Spatial Statistics（TBSS）の手法を用いて、拡散テンソル画像から得られる 4 つの指標である fractional anisotropy（FA）、mean diffusivity（MD）、axial diffusivity（AD）、そして radial diffusivity（RD）の値を、それぞれ単独、あるいは 4 つの値すべてを TBSS の Skelton 上のボクセル情報として用い、主成分分析によって次元を減らしたうえで機械学習（support vector machine）を利用して、ROC 曲線（Receiver Operatorating Characteristic curve）を作成し、Area Under the Curve（AUC）面積を算出し、判別能力について検討を行った。結果、DTI の 4 つの指標すべてを用いた方法が、90.5%の正確性でびまん性軸索損傷症例と健常者を判別できる結果となり、4 つの指標単独で用いた場合と比較し、より正確な判別につながることが分かった。この結果は、過去の同様の検討と比較しても、同等あるいは良好な判別能力を示しており、DTI の 4 つの指標が、すでに臨床家にとってもなじみのあるものであることを考えると、臨床への応用可能性が高い結果と考えられる。

以上の研究は、症例によって多様な白質損傷パターンを呈するびまん性軸索損傷における MRI 画像の特性の解明に貢献し、今後の外傷性脳損傷の診断の向上に寄与するところが多い。

したがって、本論文は博士（医学）の学位論文として価値あるものと認める。

なお、本学位授与申請者は、令和 5 年 1 月 6 日実施の論文内容とそれに関連した試問を受け、合格と認められたものである。

要旨公開可能日：　　年　　月　　日　以降