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学位論文題目	Mapping of FGF1 in the Medulla Oblongata of Macaca fascicularis (カニクイザル延髄における FGF1 の分布図)
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論文内容要旨

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学位論文題目	Mapping of FGF1 in the medulla oblongata of <i>Macaca Fascicularis</i> (カニクイザル延髄における FGF1 の分布図)		
<p>Background and Purpose</p> <p>Acidic fibroblast growth factor-1 (FGF1) is a growth factor in the FGF growth factor super family. It was the first to be discovered, alongside basic FGF (FGF2), isolated from bovine brain. Since its discovery, FGF1 has been found to have a potent mitogenic and proliferation effect on cells. In the brain it is mainly expressed in neuronal cells where it plays a neuroprotective role. Low expression of FGF1 was been linked with increased vulnerability of cholinergic neurons.</p> <p>In the medulla oblongata, neurons of the dorsal motor nucleus of the vagus (DMNV) are more vulnerable to injury and clinically, have been reported to have a slower recovery rate than neurons from other cholinergic neurons of the medulla. It is a postulation that low expression of FGF1 may be a potential contributor to this unique characteristic of the DMNV. Previous studies in rat and mouse have yielded results that corroborated this hypothesis; markedly lower expression of FGF1 was observed in the DMNV as compared to other cranial nuclei of the medulla oblongata.</p> <p>The current studied sought to corroborate these results in non-human primate studies, with the study of fgf-1 in the brainstem of Cynomolgus monkey.</p> <p>Materials and methodology</p> <p>Sample collection – Brain stem samples were obtained from 4 cynomolgus monkeys (<i>Macaca fascicularis</i>), euthanized under deep anesthesia using pentobarbital; after use for separate research purposes by other researchers. 3 samples were processed for use in immunohistochemistry (IHC) assays, while one sample was used for antibody specificity assay.</p> <p>Antibody specificity assay: We determined the specificity of the antibody against FGF1; by western blott analysis of anti-FGF1 antibody using crude extract protein of monkey brainstem.</p>			

- (備考) 1. 論文内容要旨は、研究の目的・方法・結果・考察・結論の順に記載し、2千字程度でタイプ等で印字すること。
2. ※印の欄には記入しないこと。

Immunohistochemistry and double fluorescent immunohistochemistry: To determine the distribution of FGF1, Brainstem samples were cryosectioned into 20 μ M sections and the sections immunostained in free-floating medium with antibodies against FGF1 and Choline acetyltransferase (ChAT) - biomarker for cholinergic neurons. The percentage of FGF1 immunoreactivity in cholinergic neurons was also quantified for each cholinergic nucleus. Immunostaining was also carried out using anti-Tyrosine Hydroxylase (TH) for catecholaminergic neurons.

Mapping of FGF1 immunoreactivity: To determine the distribution of FGF1 in the medulla oblongata, we mapped the FGF1 using camera lucida technique; preparing diagrammatic representations of the Immunostaining observed in IHC.

Results & Discussion

FGF1 immunoreactivity was observed in the neuronal cell bodies and neural processes, with no staining observed in glial cells. We observed an extensive FGF1 immunoreactivity of ChAT-stained neurons in the hypoglossal nucleus (HG), the nucleus ambiguus (NA) and the facial nucleus (FN). The fgf-1 immunoreactivity was highly colocalized to ChAT in these nuclei; HG - 70.5%, NA - 83.9%, and Hg - 71.7%. We also observed scattered neurons in the raphe magnus and inferior olive stained for FGF1.

In the dorsal motor nucleus of the vagus (DMNV), we observed markedly lower FGF1 immunoreactivity as compared to other cranial nuclei. Colocalization of FGF1 to ChAT-positive neurons was also markedly lower, at 16.3%. FGF1 immunoreactivity was observed mainly in the lateral region of the DMNV and was relatively higher in the rostral DMNV (20.1%) as compared to caudal DMNV (11.9%).

FGF1 immunoreactivity was also observed in neurons that were not ChAT-positive neurons, in the DMNV. The DMNV is presorted to contain catecholaminergic neurons (adrenergic and noradrenergic) apart from cholinergic neurons. TH-immunoreactivity did not colocalize to FGF-1 immunoreactivity.

Conclusion:

Mapping of FGF1 distribution in brainstem of cynomolgus monkey (*Macaca fascicularis*) was successfully carried out. FGF1 was found to distribute to cholinergic nuclei of the medulla oblongata. Similar to previous report in rodents; FGF1 immunoreactivity was markedly lower in the DMNV as compared to other cranial nuclei.

学位論文審査の結果の要旨

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論文審査委員			
<p>(学位論文審査の結果の要旨) (明朝体11ポイント、600字以内で作成のこと。)</p> <p>FGF1は神経細胞によく発現しており、神経保護や神経再生作用を有している。コリン作動性ニューロンにおけるFGF1の低発現は、その脆弱性に関連している。これまでに、げっ歯類の脳におけるFGF1の発現分布や機能についての報告はみられるが、霊長類の脳における分布や機能は明らかになっていない。そこで、カニクイザルの延髄を用いてFGF1、およびコリン作動性ニューロンのマーカーであるコリンアセチルトランスフェラーゼ (ChAT) の分布と共局在について検討を行い、以下の点を明らかにした。</p> <ol style="list-style-type: none"> 1) FGF1は舌下神経核、迷走神経背側運動核 (DMNV)、疑核、顔面神経核、大縫線核およびオリーブ核のニューロンに発現していた。 2) DMNVでは外側部にFGF1陽性細胞が認められ、その割合は他の神経核に比較して明らかに少なかった。 3) 舌下神経核、疑核および顔面神経核では、FGF1とChATの共発現細胞が多く認められるが、DMNVでは共発現の割合が顕著に低い。 4) DMNVにおけるFGF1陽性ニューロンは、ノルアドレナリン作動性ニューロンおよびドーパミン作動性ニューロンではなかった。 <p>本論文は、霊長類の延髄におけるFGF1陽性コリン作動性ニューロンの分布について新しい知見を与えたものであり、最終試験として論文内容に関連した試問を受け合格したので、博士(医学)の学位論文に値するものと認められた。</p> <p style="text-align: right;">(総字数587字)</p> <p style="text-align: right;">(平成26年 1月29日)</p>			