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学位論文題目	Somatosensory Evoked Magnetic Fields In Humans
論文審査委員	主　査　教　授　伊佐　正 教　授　柿木 隆介 教　授　小松 英彦 助教授　松山 清治 教　授　加藤　元博（九州大学）

She mainly studied MEG results on somatosensory functions in humans, termed "somatosensory evoked magnetic fields (SEF)". By examining SEF, detailed functional anatomy of the primary and secondary somatosensory cortex (SI and SII) in humans have been elucidated.

She reported three studies on SEF in this thesis. In the first study, she analyzed receptive fields in SI for lower limb stimulation in detail. This is the first systematic study on this matter. In the second and third studies, she analyzed the intracerebral interactions caused by simultaneous stimulation of the same nerve of the upper limb (median nerve) and lower limb (posterior tibial nerve). By these studies, they found that not only SI but also SII is the most important area for sensory processing of stimulation applied to the bilateral sides of the body.

1. Differentiation of receptive fields in the sensory cortex following stimulation of various nerves of the lower limb in humans: a magnetoencephalographic study.

They investigated magnetoencephalography (MEG) following siimulation of the posterior tibial (PT) and sural nerve (SU) at the ankle, the peroneal nerve (PE) at the knee and the femoral nerve (FE) overlying the inguinal ligament in 7 normal subjects (14 limbs), and confirmed its usefulness to clarify the detailed differentiation of the receptive fields in the lower limb area of the primary sensory cortex (SI) in humans. The results were summarized as follows; (1) The location of the equivalent current dipole (ECD) estimated by the magnetic fields following stimulation of the PT and SU were very close to each other, along the interhemispheric fissure in all 14 limbs. They were directed horizontally to the hemisphere ipsilateral to the stimulated nerve. (2) ECD following stimulation of FE was clearly different from others, in terms of the location and/or direction, in all 14 limbs. The ECD of 14 limbs were classified into two types according to the distance of ECD location between PT and FE; type 1 (longer than 1 cm, 9 limbs) and type 2 (shorter than 1 cm, 5 limbs). The ECD following FE stimulation was located on the crown of the postcentral gyrus, or at the edge of the interhemispheric fissure in type 1, and was close to those following PT and SU stimulation along the interhemispheric fissure in type 2. (3) ECD following PE stimulation was along the interhemispheric fissure in all 14 limbs like PT and SU. Its location was slightly but significantly higher than that of PT and SU in type 1, and was close to those following PT and SU in type 2. The present findings indicated that

approximately 65 % (9/14) of the limbs show the particular receptive fields compatible with the homunculus. Large inter- and the intraindividual (left-right) difference found in the present study indicated a large anatomical variation in the area of the lower limb in SI in humans.

2. Magnetoencephalographic study of intracerebral interaction caused by bilateral posterior tibial nerve stimulation in man.

They studied somatosensory evoked magnetic fields (SEFs) following stimulation of bilateral posterior tibial nerves ("bilateral" waveform) in normal subjects to determine the inter- and intra-hemispheric interference effects caused by activation of sensory areas in bilateral hemispheres. Activated areas in the primary and second sensory cortices (SI and SII) in each hemisphere following bilateral stimulation were clearly identified by estimation of the double best-fitted equivalent current dipoles (ECD) using the spherical head model, and the large inter-individual differences were identified. SEFs following the right posterior tibial nerve stimulation and those following the left stimulation were summated ("summated" waveform). The "difference" waveform was induced by a subtraction of "bilateral" waveforms from the "summated" waveform. Short-latency deflections showed no consistent changes between the "summated" and "bilateral" waveforms, but the long-latency deflection, the N100m-P100m, in the "bilateral" waveform was significantly ($P<0.02$) reduced in amplitude as compared with the "summated" waveform. The differences were clearly identified in the "difference" waveform, in which the main deflections, U100m-D100m, were found. The ECDs of the short-latency deflections were located in SI contralateral to the stimulated nerve, but the ECDs of the N100m-P100m were located in bilateral SII which are considered to receive ascending signals from the body bilaterally. Therefore, some inhibitory interactions might take place in SII by receiving inputs from the body bilaterally.

3. Intracerebral interactions caused by bilateral median nerve stimulation in man. A magnetoencephalographic study.

Somatosensory evoked magnetic fields (SEFs) following stimulation of the median nerves bilaterally ("bilateral" waveform) were examined in normal subjects to determine the interference effects of activations of sensory areas in bilateral hemispheres. SEFs following right median nerve stimulation and those following left median nerve stimulation were summated ("summated" waveform). A "difference"

waveform was induced by subtraction of the "bilateral" waveform from "summated" waveform. Short-latency deflections showed no consistent differences between the "summated" and "bilateral" waveforms, but the middle-latency deflection, N60m-P60m, in the "bilateral" waveform was significantly ($P<0.01$) smaller than that in the "summated" waveform. The long-latency deflection, the N90m-P90m, in the "bilateral" waveform was markedly ($P<0.001$) reduced in amplitude as compared with "summated" waveform. The differences were clearly identified in the "difference" waveform, in which the main deflections, U90m-D90m, were found in all subjects. Equivalent current dipoles (ECDs) of the short- and middle- latency deflections were located in the primary sensory cortex (SI) contralateral to the stimulated nerve, but ECDs of the N90m-P90m and U90m-D90m were located in bilateral second sensory cortices (SII) which are considered to receive ascending signals from bilateral sides of the body.

論文の審査結果の要旨

かつて、Penfield らが手術中に脳の直接刺激を行って作成した第１次体性感覚野の受容野マップ、いわゆる homunculus は、その後、倫理上の問題のため追試が行えず、確認ができなかった。ところが、脳磁図は mm 単位の高い空間分解能を有し、全く非侵襲的にヒトの脳機能を検索することができる。このような脳磁図の利点を活用して、本研究では体性感覚刺激による脳磁図（somatosensory evoked magnetic fields, SEF）を記録して、非侵襲的に homunculus を再評価するとともに、両側の末梢神経を同時刺激した場合の脳内の干渉効果を解析して、ヒトの体性感覚野の生理的機能を検索した。

まず、下肢の異なる４つの神経を刺激して、SEF を記録した。下肢の感覚野は大脳半球間裂に面した部分に存在するため、通常の脳波検査ではその詳細な検討は不可能であり、脳磁図研究の最も良い適応の１つといえる。後脛骨神経と腓腹神経は足首部で、腓骨神経は膝か部で、大腿神経はそけい部にて電気刺激して、SEF を記録した。個人差の影響がもっとも少なかった、刺激後最初に出現する成分について分析を行った。結果は、受容野分布が homunculus によく一致していたタイプ１と、４つの神経の受容野は近接していたが推定双極子の方向が異なり、受容野の位置も微妙に異なると考えられるタイプ２に明瞭に分かれた。また、同一個人においても左右の半球でタイプの異なる例も多くみられた。これは、下肢の感覚受容野が大脳半球間裂部という解剖学的に特殊な位置にあるためと考えられた。

次に、両側神経同時刺激に対する SEF 波形を、片側刺激による SEF 波形と比較検討することにより、脳内での両側四肢に加えられた体性感覚間の干渉効果について検討した。上肢では両側の正中神経手首部、下肢では両側の後脛骨神経足首部に電気刺激を与えて、記録した。両側刺激による波形を"bilateral"波形、右刺激による波形と左刺激による波形を数学的に加算したものを"summated"波形とした。すると、第１次体性感覚野が発生源である初期反応は、"bilateral"波形と"summated"波形の間には有意差は見られなかったが、第２次感覚野を発生源とする中潜時反応（約 80-120msec）は、"bilateral"波形で有意に振幅が減少した。これは、第２次感覚野の多くのニューロンが左右いずれの刺激に対しても反応する、いわゆる両側反応を呈するため、抑制（inhibition）あるいは閉塞（occlusion）現象による特異的な干渉作用がおこったものと考えられた。

この研究から得られた結果は、ヒトの体性感覚野の機能解析において脳磁図の持つ高い空間分解能が、極めて有用であることを示している。本研究におけるヒトにおける第２次感覚野の存在およびその機能の解明は、脳磁図研究により初めて明らかにされたものであり、また末梢神経両側同時刺激による第２次感覚野での干渉作用は、世界で初めて明らかにされた知見である。よって、申請者の論文は、学位論文として十分ふさわしい内容であるものと審査委員会の委員一致で判定した。

さらに、実験手法や実験結果の解釈及び学問的背景について口頭試問を行ったが、いずれに対する応答も満足すべきものであった。本論文の内容は、既に申請者が筆頭著者の３篇の論文として、国際的学術雑誌に発表されており、英語力も十分なものであると判定した。以上を総合的に判断して、学位を取得するに足る水準に十分達しているものと判断した。