# Ⅱ　研究成果の刊行に関する一覧表

厚生労働科学研究費補助金研究報告書

別紙４

研究成果の刊行に関する一覧表

書籍

| 著者氏名 | 論文タイトル名 | 書籍全体の編集者名 | 書　籍　名 | 出版社名 | 出版地 | 出版年 | ページ |
|---|---|---|---|---|---|---|---|
| Inoue Y | Reflex epilepsy | Duchowny M, Helen Cross J, Arzimanoglou A | Pediatric Epilepsy | McGraw Hill | New York | 2013 | 84-85 |
| Gelisse P, Wolf P, Inoue Y | Juvenile absence epilepsy | Bureau M, Genton P, Dravet C, Delgado-Escueta AV, Tassinari CA, Thomas P, Wolf P | Epileptic syndromes in infancy, childhood and adolescence 5th edition | John Libbey | Montrouge | 2012 | 329-339 |
| Wolf P, Inoue Y | Complex reflex epilepsies | Bureau M, Genton P, Dravet C, Delgado-Escueta AV, Tassinari CA, T | Epileptic syndromes in infancy, childhood and adolescence 5t | John Libbey | Montrouge | 2012 | 529-543 |
| 臼井桂子、井上有史、十一元三 | てんかん | 斉藤万比古、金生由紀子 | 子どもの強迫性障害診断・治療ガイドライン | 星和書店 | 東京 | 2012 | 152-159 |
| 井上有史 | ラコサミドの使い方 | 高橋幸利 | 新規抗てんかん薬マスターブック | 診断と治療社 | 東京 | 2012 | 84-85 |
| 臼井桂子 | ガバペンチンの使い方：成人 | 高橋幸利 | 新規抗てんかん薬マスターブック | 診断と治療社 | 東京 | 2012 | 74-75 |
| 寺田清人 | レベチラセタムの使い方：成人 | 高橋幸利 | 新規抗てんかん薬マスターブック | 診断と治療社 | 東京 | 2012 | 70-71 |
| 井上有史 | 災害に備えて | 井上有史、池田仁 | 新てんかんテキスト | 南江堂 | 東京 | 2012 | 155-156 |
| 馬場好一 | 外科治療の方法 | 井上有史、池田仁 | 新てんかんテキスト | 南江堂 | 東京 | 2012 | 95-97 |
| 寺田清人 | 脳波検査 | 井上有史、池田仁 | 新てんかんテキスト | 南江堂 | 東京 | 2012 | 38-40 |

| 著者氏名 | 論文タイトル名 | 書籍全体の編集者名 | 書　籍　名 | 出版社名 | 出版地 | 出版年 | ページ |
|---|---|---|---|---|---|---|---|
| 臼井桂子 | てんかんと高次脳機能 | 井上有史、池田仁 | 新てんかんテキスト | 南江堂 | 東京 | 2012 | 53-54 |
| 臼井桂子 | てんかんと性格・行動 | 井上有史、池田仁 | 新てんかんテキスト | 南江堂 | 東京 | 2012 | 57-58 |
| 寺田清人、井上有史 | 抗てんかん薬 | 治療薬ハンドブック2012 | 高久文麿 | じほう | 東京 | 2012 | 44-69 |
| 荒木邦彦、井上有史 | 疫学 | 最新医学別冊、新しい診断と治療のABC74/神経5、てんかん | 辻貞俊 | 最新医学社 | 大阪 | 2012 | 32-39 |
| 山本吉章、池田仁、井上有史 | 赤芽球癆 | 副作用軽減化新薬開発 | | 技術情報協会 | | 2012 | 359-362 |
| 寺田清人、井上有史 | 抗てんかん薬 | 高久史麿 | 治療薬ハンドブック2011 | じほう | 東京 | 2011 | 43-68 |
| 寺田清人 | てんかん | 泉孝英 | ガイドライン外来診療2011-今日の治療のために | 日系メディカル開発 | 東京 | 2011 | 482-485 |
| 井上有史 | MOSESワークブック：トレーナー教本 | MOSES企画委員会 | MOSESワークブック：トレーナー教本 | クリエイツかもがわ | 京都 | 2011 | 1-180 |
| 井上有史 | 「けいれん」で搬送されてきた患者 | 日本心とからだの救急学会 | 心とからだの救急患者対応 | MCメディカ | 大阪 | 2011 | 139-144 |
| 井上有史 | てんかん | 日本心とからだの救急学会 | 心とからだの救急患者対応 | MCメディカ | 大阪 | 2011 | 73-82 |
| 井上有史 | てんかん | 山内俊雄、小島卓也、倉知正佳、鹿島晴雄 | 専門医を目指す人の精神医学 | 医学書院 | 東京 | 2011 | 356-364 |
| 寺田清人、井上有史 | 抗てんかん薬 | 高久史麿 | 治療薬ハンドブック2010 | じほう | 東京 | 2010 | 43-67 |
| Inoue Y, Hashimoto M, Matsuda K | Epilepsy surgery and employment | Matsuura M, Inoue Y | Neuropsychiatric issues in epilepsy | John Libbey | Montrouge | 2010 | 225-234 |
| Inoue Y | Seizures Induced by Thinking and Praxis | Panayiotopoulos CP | The Atlas of Epilepsies | Springer-Verlag | London | 2010 | 1105-1107 |

| 著者氏名 | 論文タイトル名 | 書籍全体の編集者名 | 書　籍　名 | 出版社名 | 出版地 | 出版年 | ページ |
|---|---|---|---|---|---|---|---|
| Nishida T, Inoue Y | Affective and anxiety disorders in children with ep.. | Matsuura M, Inoue Y | Neuropsychiatric issues in epilepsy | John Libbey | Montrouge | 2010 | 105-114 |
| 小出泰道、井上有史 | てんかん | 門脇孝、小室一成、宮地良樹 | 診療ガイドラインup-to-date2010-2011 | メディカルレビュー | 東京 | 2010 | |
| 寺田清人、井上有史 | レベチラセタムのてんかん治療における意義 | 兼子直 | てんかんの薬物療法 | 新興医学出版社 | 東京 | 2010 | 99-115 |
| 寺田清人 | レベチラセタム | 藤原建樹、高橋幸利 | 小児てんかん診療マニュアル改訂第２版 | 診断と治療社 | 東京 | 2010 | 129-130 |

雑誌

| 発表者氏名 | 論文タイトル名 | 発表誌名 | 巻号 | ページ | 出版年 |
|---|---|---|---|---|---|
| Fujitani S, Matsuda K, Nakamura F, Baba K, Usui N, Tottori T, Mihara T, Terada K, Usui K, Inoue Y, Kajita Y, Wakabayashi T | Statistical parametric mapping of interictal 123I-iomazenil SPECT in temporal lobe epilepsy surgery | Epilepsy Res | Epub ahead of print | | 2013 |
| Terada K, Umeoka S, Usui N, Baba K, Usui K, Fujitani S, Matsuda K, Tottori T, Nakamura F, Inoue Y | Uneven interhemispheric connections between left and right primary sensori-motor areas | Hum Brain Mapp | 33 | 14-26 | 2012 |
| Usui K, Terada K, Inoue Y | Diagnostic approach for studying epileptic seizure | Rinsho Shinkeigaku | 52 | 857-860 | 2012 |
| Sato W, Kochiyama T, Uono S, Matsuda K, Usui K, Inoue Y, Toichi M. | Temporal profile of amygdala γ oscillations in response to faces | J Cogn Neurosci | 24 | 1420-1433 | 2012 |
| Yamamoto Y, Inoue Y, Matsuda K, Takahashi Y, Kagawa Y | Influence of concomitant antiepileptic drugs on plasma lamotrigine concentration in adult Japanese epilepsy patients | Biol. Pharm. Bull | 35 | 487-493 | 2012 |

| 発表者氏名 | 論文タイトル名 | 発表誌名 | 巻号 | ページ | 出版年 |
|---|---|---|---|---|---|
| Yamamoto Y, Takahashi Y, Suzuki E, Mishima N, Inoue K, Itoh K, Kagawa Y, Inoue Y | Risk factors for hyperammonemia associated with valproic acid therapy in adult epilepsy patients | Epilepsy Res | 101 | 202-209 | 2012 |
| Beniczky S, Guaranha MSB, Conradsen I, Singh MB, Rutar V, Lorber B, Braga P, Fressola AB, Inoue Y, Yacubian EMT, Wolf P | Modulation of epileptiform EEG discharges in juvenile myoclonic epilepsy: An investigation of reflex epileptic traits | Epilepsia | 53 | 832-839 | 2012 |
| Cao D, Ohtani H, Ogiwara I, Ohtani S, Takahashi Y, Yamakawa K, Inoue Y | Efficacy of stiripentol in hyperthermia-induced seizures in a mouse model of Dravet syndrome | Epilepsia | 53 | 1140-1145 | 2012 |
| Suriadi M, Takahashi Y, Nishimura S, Tsunogae H, Inoue Y | Dysfunction of blood-brain barrier in epileptic patients after acute encephalitis | Epileptologia | 20 | 51-61 | 2012 |
| Takayama R, Takahashi Y, Mogami Y, Ikegami M, Mukaida S, Ikeda H, Imai K, Shigematsu H, Suzuki Y, Inoue Y | Self-induced seizures presumably by peri-orbital somatosensory self-stimulation: a report of two cases | Brain Dev | 34 | 685-690 | 2012 |
| Mogami Y, Takahashi Y, Takayama R, Ohtani H, Ikeda H, Imai K, Shigematu H, Inoue Y | Cutaneous adverse drug reaction in patients with epilepsy after acute encephalitis | Brain Dev | 34 | 496-503 | 2012 |
| Inoue Y, Usui N, Hiroki T, Shimizu K, Kobayashi S, Shimasaki S | Bioavailability of intravenous fosphenytoin sodium in healthy Japanese volunteers | Eur J Drug Metab Pharmacokinet | Epub ahead of print | | 2012 |
| Ogiwara I, Nakayama T, Yamagata T, Ohtani H, Mazaki E, Tsuchiya S, Inoue Y, Yamakawa K | A homozygous mutation of voltage-gated sodium channel βI gene SCN1B in a patient with Dravet syndrome | Epilepsia | 53 | e200-e203 | 2012 |

| 発表者氏名 | 論文タイトル名 | 発表誌名 | 巻号 | ページ | 出版年 |
|---|---|---|---|---|---|
| Yamamoto Y, Takahashi Y, Imai K, Mishima N, Yazawa R, Inoue K, Itoh K, Kagawa Y, Inoue Y | Risk factors for hyperammonemia in pediatric patients with epilepsy | Epilepsia | Epub ahead of print | | 2013 |
| Takahashi Y, Yamazaki E, Mine J, Kubota Y, Imai K, Mogami Y, Baba K, Matsuda K, Oguni H, Sugai K, Ohtsuka Y, Fujiwara T, Inoue Y | Immunomodulatory therapy versus surgery for Rasmussen syndrome in early childhood | Brain Dev | Epub ahead of print | | 2013 |
| 山崎悦子、井上有史 | 成人てんかんの薬物治療 | Modern Physician | 32 | 319-322 | 2012 |
| 山本吉章、井上有史 | 抗てんかん薬 | 医薬ジャーナル、新薬展望2012 | 48(S-1) | 282-286 | 2012 |
| 小出泰道、須佐史信、池田浩子、井上有史 | もやもや病におけるてんかんの臨床的特徴：７例の検討 | 脳卒中 | 34 | 140-146 | 2012 |
| 兼子　直、井上有史、笹川睦男、加藤昌明 | 局在関連性てんかんに対するトピラマート（トピナ錠）治療における漸増法の二重盲検並行群間比較―Rapid 漸増法および Slow 漸増法― | 日本神経精神薬理学雑誌 | 32 | 73-84 | 2012 |
| 山本吉章、井上有史 | 新規抗てんかん薬レベチラセタムの概要 | 脳21 | 15 | 314-318 | 2012 |
| 井上有史 | てんかん患者の長期ケアとホットライン | Mebio | 29 | 107-112 | 2012 |
| 井上有史 | てんかん診療における医療連携と社会的医療資源：てんかんの一次・二次・三次医療 | 治療 | 94 | 1697-1702 | 2012 |
| 井上有史 | 長期的視野からのてんかん診療 | 臨床神経 | 52 | 1039-1042 | 2012 |
| 寺田清人、井上有史 | 新規抗てんかん薬の有用性 | 臨床神経 | 52 | 1088-1042 | 2012 |

| 発表者氏名 | 論文タイトル名 | 発表誌名 | 巻号 | ページ | 出版年 |
|---|---|---|---|---|---|
| 井上有史 | てんかん診療の最新状況 | Asahi Medical | 496 | 20-21 | 2013 |
| 中野友義、西田拓司、井上有史 | 成人てんかんの治療ガイドライン | 日本精神科病院協会雑誌 | 32 | 32-36 | 2013 |
| 最上友紀子、高橋幸利、福山智広、高山留美子、大谷英之、池田浩子、今井克美、重松秀夫、井上有史 | 脳炎・脳症後てんかん症例における抗てんかん薬の副作用の検討：眠気について | 脳と発達 | 44 | 472-476 | 2012 |
| Sato W, Kochiyama T, Uono S, Matsuda K, Usui K, Inoue Y, Toichi M | Rapid amygdala gamma oscillations in response to fearful facial expressions | Neuropsychologia | 49(4) | 612-617 | 2011 |
| Wrench JM, Matsumoto R, Inoue Y, Wilson SJ | Current challenges in the practice of epilepsy surgery | Epilepsy Beh | 22 | 23-31 | 2011 |
| Usui N, Terada K, Baba K, Matsuda K, Nakamura F, Usui K, Yamaguchi M, Tottori T, Umeoka S, Fujitani S, Kondo A, Mihara M, Inoue Y | Clinical significance of ictal high frequency oscillations in medial temporal lobe epilepsy | Clin Neurophysiol | 122 | 1693-1700 | 2011 |
| Yamazaki E, Takahashi Y, Akasaka N, Fujiwara T, Inoue Y | Temporal changes in brain MRI findings in Rasmussen syndrome | Epileptic Disord | 13 | 229-239 | 2011 |
| Ren L, Terada K, Baba K, Usui N, Umeoka S, Usui K, Matsuda K, Tottori T, Nakamura F, Mihara T, Inoue Y | Ictal very low frequency oscillation in human epilepsy patients | Ann Neurol | 69 | 201-206 | 2011 |
| Ikeda H, Imai K, Ikeda H, Shigematsu H, Shishido T, Takayama R, Fujiwara T, Takahashi Y, Inoue Y | Lamotrigine is favorable for startle-induced seizures | Epileptic Disord | 13 | 277-283 | 2011 |
| Usui N, Mihara T, Baba K, Matsuda K, Tottori T, Umeoka S, Kondo A, Nakamura F, Terada K, Usui K, Inoue Y | Versive seizures in occipital lobe epilepsy: Lateralizing value and pathophysiology | Epilepsy Res | 97 | 157-161 | 2011 |

| 発表者氏名 | 論文タイトル名 | 発表誌名 | 巻号 | ページ | 出版年 |
|---|---|---|---|---|---|
| Sato W, Kochiyama T, Uono S, Matsuda K, Usui K, Inoue Y, Toichi M | Rapid amygdala gamma oscillations in response to eye gaze | PLoS One | 6 | e28188 | 2011 |
| Hitomi T, Ikeda A, Kondo T, Imamura H, Inouchi M, Matsumoto R, Terada K, Kanda M, Matsuhashi M, Nagamine T, Shibasaki H, Takahashi R | Increased cortical hyperexcitability and exaggerated myoclonus with aging in benign adult familial myoclonus epilepsy | Movement Disord | 26 | 1509-1514 | 2011 |
| Sato W, Kochiyama T, Uono S, Matsuda K, Usui K, Inoue Y, Toichi M | Temporal Profile of Amygdala Gamma Oscillations in Response to Faces | J Cogn Neurosci | Epub ahead of print | | 2011 |
| Shimizu-Okabe C, Tanaka M, Matsuda K, Mihara T, Okabe A, Sato K, Inoue Y, Fujiwara T, Yagi K, Fukuda A | KCC2 was downregulated in small neurons localized in epileptogenic human focal cortical dysplasia | Epilepsy Res | 93 | 177-184 | 2011 |
| 臼井桂子、寺田清人、井上有史 | Wadaテストによる言語・記憶機能検査-てんかん外科の手術前検査における役割- | Epilepsy | 15 | 117-123 | 2011 |
| 小出泰道、長尾雅悦、福島克之、宇留野勝久、笹川睦男、高橋幸利、岡田久、渡邉宏雄、星田徹、井上美智子、後藤一也、馬場啓至、石津棟暎、井上有史 | トピラマートの有効性と安全性についての多施設共同研究 | てんかん研究 | 29 | 3-13 | 2011 |
| 大谷英之、田中正樹、笹川睦男、溝渕雅弘、井上有史 | 抗てんかん薬と妊娠に関するヨーロッパを中心とした国際共同研究 | てんかん研究 | 29 | 28-35 | 2011 |
| 木村記子、井上有史、岡田俊 | てんかんに併存する強迫性・衝動性とてんかん治療の影響 | 臨床精神医学 | 14 | 615-621 | 2011 |
| 馬場好一、臼井直敬、寺田清人、臼井桂子、松田一己、鳥取孝安、井上有史、三原忠紘 | 内側側頭葉てんかんの頭蓋内脳波における発作時高周波成分の臨床的意義に関する研究 | 財)てんかん治療研究振興財団研究年報 | 22 | | 2011 |
| 井上有史 | てんかんにおける医療連携 | 精神医学 | 53 | 461-467 | 2011 |

| 発表者氏名 | 論文タイトル名 | 発表誌名 | 巻号 | ページ | 出版年 |
|---|---|---|---|---|---|
| 宍戸文郎、井上有史 | てんかん薬物治療ガイドライン | 綜合臨床 | 60 | 601-602 | 2011 |
| 清水秀明、井上有史 | 特発性全般てんかん | 臨床精神医学 | 40増刊号 | 400-402 | 2011 |
| 鎌田泉、井上有史 | “てんかん”と“けいれん”：静注用フェノバ | 臨床評価 | 38 | 895-897 | 2011 |
| 兼子直、井上有史、飯島正文、石田篤子、井尻章 | てんかん患者を対象としたラモトリギン錠の使用成績調査 | 新薬と臨床 | 60 | 431-457 | 2011 |
| Usui K | Basal temporal language area | Clin Neurophysiol | 121(S1) | S59 | 2010 |
| Yu L, Terada K, Usui N, Usui K, Baba K, Inoue Y | Ear movement induced by electrical cortical stimulation | Epilepsy Behav | 18 | 488-490 | 2010 |
| Usui K, Matsuda K, Terada K, Nikaido K, Matsuhashi M, Nakamura F, Umeoka S, Usui N, Tottori T, Baba K, Inoue Y | Epileptic negative myoclonus: a combined study of EEG and [123I]iomazenil (123I-IMZ) single photon emission computed tomography indicating involvement of medial frontal area | Epilepsy Res | 89 | 220-226 | 2010 |
| Ren L, Terada K, Baba K, Usui N, Umeoka S, Usui K, Matsuda K, Tottori T, Nakamura F, Mihara T, Inoue Y | Ictal very low frequency oscillation in human epilepsy patients | Ann Neurol | 121 | | 2010 |
| Usui N, Terada K, Baba K, Matsuda K, Nakamura F, Usui K, Tottori T, Umeoka S, Fujitani S, Mihara T, Inoue Y | Very high frequency oscillations (over 1000 Hz) in human epilepsy | Clin Neurophysiol | 121 | 1825-1831 | 2010 |
| Kawamata J, Ikeda A, Fujita Y, Usui K, Shimohama S, Takahashi R | Mutations in LGI1 gene in Japanese families with autosomal dominant lateral temporal lobe epilepsy: the first report from Asian families | Epilepsia | 51 | 690-693 | 2010 |

| 発表者氏名 | 論文タイトル名 | 発表誌名 | 巻号 | ページ | 出版年 |
|---|---|---|---|---|---|
| Nakayama T, Ogiwara I, Ito K, Kaneda M, Mazaki E, Osaka H, Ohtani H, Inoue Y, Fujiwara T, Uematsu M, Haginoya K, Tsuchiya S, Yamakawa K | Deletions of SCN1A 5' genomic region with promoter activity in Dravet syndrome | Hum Mutat | 31 | 820-829 | 2010 |
| Fukao K, Inoue Y, Yagi K | Magnetoencephalographic correlates of different types of aura in temporal lobe epilepsy | Epilepsia | 51 | 1846-1851 | 2010 |
| Koide Y, Inoue Y, Bayasgalan B | Epilepsy care in Mongolia: current problems and future prospects | Neurology Asia | 15 | 263-266 | 2010 |
| 臼井桂子、寺田清人、臼井直敬、馬場好一、松田一己、鳥取孝安、 | てんかん外科治療における言語機能温存のための側頭葉底部言語野 | てんかん治療研究振興財団研究年報 | 21 | 99-106 | 2010 |
| 千葉茂、Bernhard Steinhoff、武田洋司、寺田清人、松本理器 | 再考「てんかん治療のゴールとは何か？」 | 臨床精神薬理 | 13 | 2355-2363 | 2010 |
| 井上有史 | てんかん。特集：この10年間で精神科治療はどう変わったか | 精神科 | 16 | 434-440 | 2010 |
| 寺田清人、井上有史 | Levetiracetam の臨床効果 | 臨床精神薬理 | 13 | 1685-1691 | 2010 |

# Ⅲ　研究成果の刊行物・別冊

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# Very high frequency oscillations (over 1000 Hz) in human epilepsy

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ABSTRACT

*Objective:* High frequency oscillations (HFO) of 100–500 Hz have been reported in epileptic human brain. However, the questions of how fast these oscillations can reach, and which frequency range is clinically important remain unanswered. We recorded interictal and ictal very high frequency oscillations (VHFO) of 1000–2500 Hz by subdural electrodes using 10 kHz sampling rate. We describe the characteristics of VHFO, and discuss their underlying mechanism and clinical significance.

*Methods:* Five patients with neocortical epilepsy were studied. All patients underwent intracranial EEG monitoring with subdural electrodes. EEG recording with sampling rate of 10 kHz was conducted. Histopathology revealed malformation of cortical development in all cases.

*Results:* In four of five patients, very high frequency activities of 1000–2500 Hz were detected in highly localized cortical regions (one to four electrodes in individual patient). We named these activities "very high frequency oscillations (VHFO)". Interictally, VHFO appeared intermittently, and were interrupted by spikes. Sustained VHFO without spikes appeared around the start of seizures.

*Conclusions:* Both interictal and ictal VHFO can be recorded by subdural electrodes. Compared to HFO previously reported, VHFO have much higher frequency, more restricted distribution, smaller amplitude, and different timing of onset.

*Significance:* Recording of VHFO may be useful for identifying the epileptogenic zone.



## 1. Introduction

Animal studies of strychnine discharges have already elucidated the association between high frequency oscillations (HFO) and ictal phenomena (Gastaut and Fischer-Williams, 1959). The occurrence of HFO having frequencies higher than the conventionally analyzed range in focal epilepsy has attracted attention. Most studies reported interictal HFO in the medial temporal lobe using microelectrodes (Bragin et al., 1999, 2002; Staba et al., 2002), or a combination of microelectrodes and macroelectrodes (Worrell et al., 2008). Recent reports have described ictal HFO during focal seizures recorded by macroelectrodes (Ochi et al., 2007; Jirsch et al., 2006; Khosravani et al., 2009; Yamaguchi et al., 2008; Nakamura et al., 2008). In these reports, the frequency range of ictal HFO was less than 500 Hz at sampling rate of 2–5 kHz. Because HFO were observed only at a limited number of electrodes within the epileptogenic zone, ictal HFO have been suggested to be clinically useful in epilepsy surgery. However, the questions of how fast these oscillations can reach, and which frequency range is clinically important remain unanswered.

In four of five patients with intractable neocortical epilepsy, we recorded interictal and ictal very high frequency oscillations (VHFO) of 1000–2500 Hz by routinely used subdural electrodes using a very high sampling rate of 10 kHz. Such high frequency EEG activities have never been reported previously. In this report, we describe the characteristics of VHFO, and discuss their possible underlying mechanism and clinical significance.

## 2. Methods

Five patients with intractable neocortical epilepsy (one with parietal lobe epilepsy, and four with frontal lobe epilepsy) were monitored with a sampling rate of 10 kHz. Histopathology revealed malformation of cortical development in all cases. The clinical characteristics of the patients are shown in Table 1. All patients underwent intracranial EEG monitoring as a part of presurgical evaluation. Subdural electrodes (Ad-tech Medical Instrument Corporation, Racine, WI, 2.3 mm contact, effective area 4.15 $mm^2$, 10 mm spacing, platinum/iridium alloy) were implanted over the cortical areas depending on the finding of the noninvasive presurgical evaluation (Fig. 1). Reference electrodes were placed on the

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**Table 1**
Clinical characteristics of the patients.

| Patient | Diagnosis | Age at onset (yrs) | Age at surgery (yrs) | Seizure | Interictal scalp EEG | Ictal scalp EEG | MRI |
|---|---|---|---|---|---|---|---|
| 1 | PLE | 4 | 14 | Tonic posturing | Right parietal sharp waves | Right hemisphere | Right medial parietal |
| 2 | FLE | 4 | 27 | Gestural Automatism | Right F-T spikes | Right F-T | Right frontal operculum |
| 3 | FLE | 3 | 19 | Gestural Automatism | Normal | Right hemisphere | Right basal frontal |
| 4 | FLE | 5 | 14 | Tonic facial contraction | Left frontal sharp waves | Left frontal | Left frontal operculum |
| 5 | FLE | 0 | 22 | Tonic posturing | Left central spikes | Nonlateralizing | Left posterior frontal |

PLE, parietal lobe epilepsy; FLE, frontal lobe epilepsy; F-T, fronto-temporal.

surface of the skull, with the contacts of the electrodes facing away from the skull to avoid the referential activation. The EEG signals were digitally recorded by EEG-1000 (Nihon-Kohden Corporation, Tokyo) at a sampling rate of 200 Hz and time constant of 10 s for clinical purposes. After completing the routine EEG recording at a sampling rate of 200 Hz, EEG recording using a higher sampling rate of 10 kHz was conducted. The time constant was set at 10 s. Due to the limitation of the EEG machine, only 16 channels could be monitored simultaneously. To visualize high frequency activities, the horizontal (time) and vertical (amplitude) axes of the EEG display were expanded, and EEG was digitally high-pass filtered at 160 Hz (a time constant of 0.001 s) and low-pass filtered at 3 kHz. Peaks of high frequency activities were visually identified on CRT screen, and the frequency, amplitude, and duration of these activities were measured by cursors with computer assistance (Fig. 2). In this study, high frequency activities faster than 200 Hz are defined as HFO, and those faster than 1000 Hz as VHFO.

Both ictal and interictal recordings were analyzed. Interictal sections of more than two hours were visually analyzed. They were distant from the seizures from 20 h to more than 40 h in each patient.

## 3. Results (Table 2)

Using 10 kHz sampling rate, two seizures were recorded in Patient 1, three seizures in Patient 2, four seizures in Patient 3, two seizures in Patient 4, and two seizure in Patient 5. In Patient 5, no high frequency activities faster than 200 Hz were detected both ictally and interictally. Fig. 1 shows the MRI lesion and the locations of subdural electrodes in Patient 2. In both interictal and preictal recordings, intermittent VHFO of very low amplitude were detected at two electrodes in Patient 1, one electrode in Patient 2, two electrodes in Patient 3, and four electrodes in Patient 4. VHFO were not detected at other electrodes (Figs. 3 and 4). The frequencies of intermittent VHFO ranged from 1000 to 2500 Hz. VHFO were interrupted by spikes. Interictal VHFO and preictal VHFO had identical characteristics in terms of frequency, amplitude, duration, temporal relationship with spikes, and distribution. The amplitudes of VHFO were 3.5–29.4 μV in Patient 1, 4.4–24.7 μV in Patient 2, 3.5–19.4 μV in Patient 3, and 5.3–15.0 μV in Patient 4. The VHFO durations were 4–45 ms in Patient 1, 2–75 ms in Patient 2, 20–226 ms in Patient 3, and 6–18 ms in Patient 4 (Fig. 5).

Sustained VHFO without interrupting spikes appeared at the start of seizures, superimposing on slower rhythmic activities (70–100 Hz) (Figs. 3 and 4). The VHFO lasted approximately 10 s in Patient 1, 12–13 s in Patient 2, 35–53 s in Patient 3, and 10–12 s in Patient 4. The frequencies of sustained VHFO were 1000–2000 Hz in Patient 1, 1000–2500 Hz in Patient 2, and 1000–1500 Hz in Patients 3 and 4. The amplitudes of sustained VHFO were 3.5–19.6 μV in Patient 1, 7.4–26.5 μV in Patient 2, 5.3–15.0 μV in Patient 3, and 6.2–10.6 μV in Patient 4. VHFO were detected in all seizures recorded with 10 kHz sampling rate. The characteristics of sustained VHFO were consistent among seizures in each patient.

On interictal recordings, HFO of 300–700 Hz were detected at ten electrodes including the three electrodes detecting VHFO in Patient 1 (Figs. 5A and 6A). HFO of 350–600 Hz were detected at nine electrodes including the one electrode detecting VHFO in Patient 2 (Figs. 5B and 6B). No HFO were detected in Patient 3 (Fig. 6C). HFO of 400–600 Hz were detected at six electrodes including the four electrodes detecting VHFO in Patient 4 (Fig. 6D). The amplitudes of interictal HFO were 11.8–279.4 μV in Patient 1, 8.8–150.0 μV in Patient 2, and 10.3–71.5 μV in Patient 4. The durations of interictal HFO were 7–33 ms in Patient 1, 8–35 ms in Patient 2, and 18–29 ms in Patient 4. Ictally, no HFO (over 200 Hz) were observed when sustained VHFO were recorded, while 70–100 Hz rhythmic activities were seen.

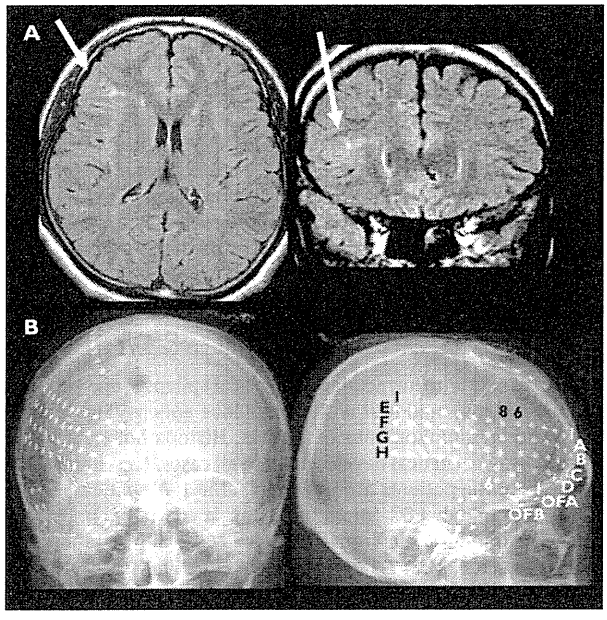


**Fig. 1.** MRI lesion and subdural electrodes (Patient 2). (A) Brain MRI with FLAIR sequences showing a high intensity area in the right frontal operculum (arrow). (B) X-ray photographs showing subdural electrodes. Subdural grid electrodes were implanted over the right fronto-temporal, and parietal areas.

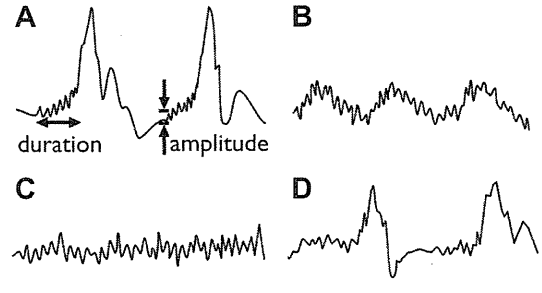


**Fig. 2.** Schematic illustrations of typical VHFO waveform. (A) Interictally and preictally, intermittent VHFO are followed by spikes. (B) VHFO become sustained at the start of the seizures. They are superimposed on slower rhythmic activities. (C) Then, slower rhythmic activities become less prominent, and disappear. (D) Thereafter, VHFO are intermixed with spikes.

**Table 2**
The characteristics of VHFO and HFO.

| Patient | Number of seizures | Number of electrodes with VHFO | Amplitude (interictal) (μV) | Duration (ms) | Amplitude (ictal) (μV) | Number of electrodes with HFO | Amplitude (μV) | Duration (ms) |
|---|---|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 3.5–29.4 | 4–45 | 3.5–19.6 | 10 | 11.8–279.4 | 7–33 |
| 2 | 3 | 1 | 4.4–24.7 | 2–75 | 7.4–26.5 | 9 | 8.8–150.0 | 8–35 |
| 3 | 4 | 2 | 3.5–19.4 | 20–226 | 5.3–15.0 | 0 | – | – |
| 4 | 2 | 4 | 5.3–15.0 | 6–18 | 6.2–10.6 | 6 | 10.3–71.5 | 18–29 |

In four patients with VHFO, the electrodes recording VHFO were located above the MRI lesions, and surgical resection of the MRI lesion together with the sites where the electrodes recorded VHFO was performed. The locations of the electrodes with VHFO, those with HFO, and those with interictal spikes, seizure onset zone defined by conventional EEG, MRI lesion, and the extent of surgical

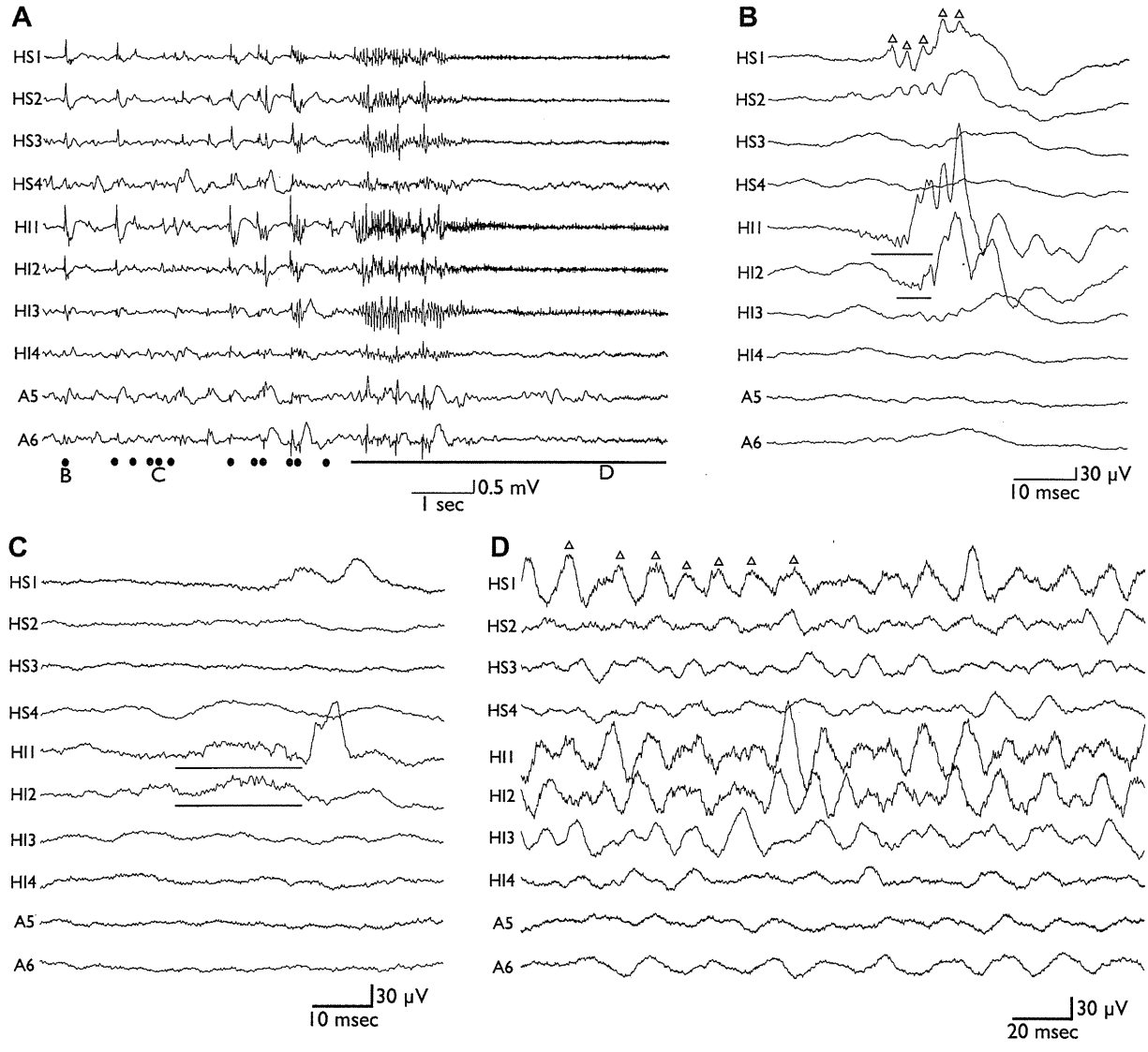


**Fig. 3.** Ictal EEG recorded at a sampling rate of 10 kHz (Patient 1). (A) Ictal EEG shown using conventional filter settings (low-pass filter 120 Hz, time constant 0.1 s). Only 10 channels are shown. Ictal EEG shows initial spike burst at HI1–4/HS1–4 and spike-and-waves at A5–6, followed by electrodecremental pattern and low amplitude fast activities at HI1–3/HS1. Filled circle and straight line indicate the presence of VHFO. The EEG at B, C, and D is shown using VHFO filter settings. (B and C) Preictal VHFO detected visually using low-pass filter of 3 kHz and time constant of 0.001 s. Preictal VHFO of 1000–2500 Hz are observed at HI1 and HI2 electrodes (underlined). They appear intermittently before the start of seizures, and are interrupted by spikes. The amplitudes are 3.5–22.1 μV (note the calibrations), and the durations were 12–27 ms. These activities are not observed at other electrodes. HFO of 350–550 Hz are seen at HS1–2 and HI1–2 electrodes, with durations of HFO of 10–14 ms and the amplitudes of 22.6–234.7 μV. Representative HFO peaks are marked by triangles (B). (D) VHFO recorded at HI1, HI2 (both electrodes also record preictal VHFO) and HS1 electrodes become sustained at the start of seizure. The frequencies of VHFO are 1000–2000 Hz and the amplitudes are around 8.8–14.1 μV. These activities superimpose on the slower rhythmic activities (70–90 Hz) (marked by triangles). Sustained VHFO lasted approximately 10 s. Again, these activities are not observed at other electrodes, although rhythmic activities are recorded.

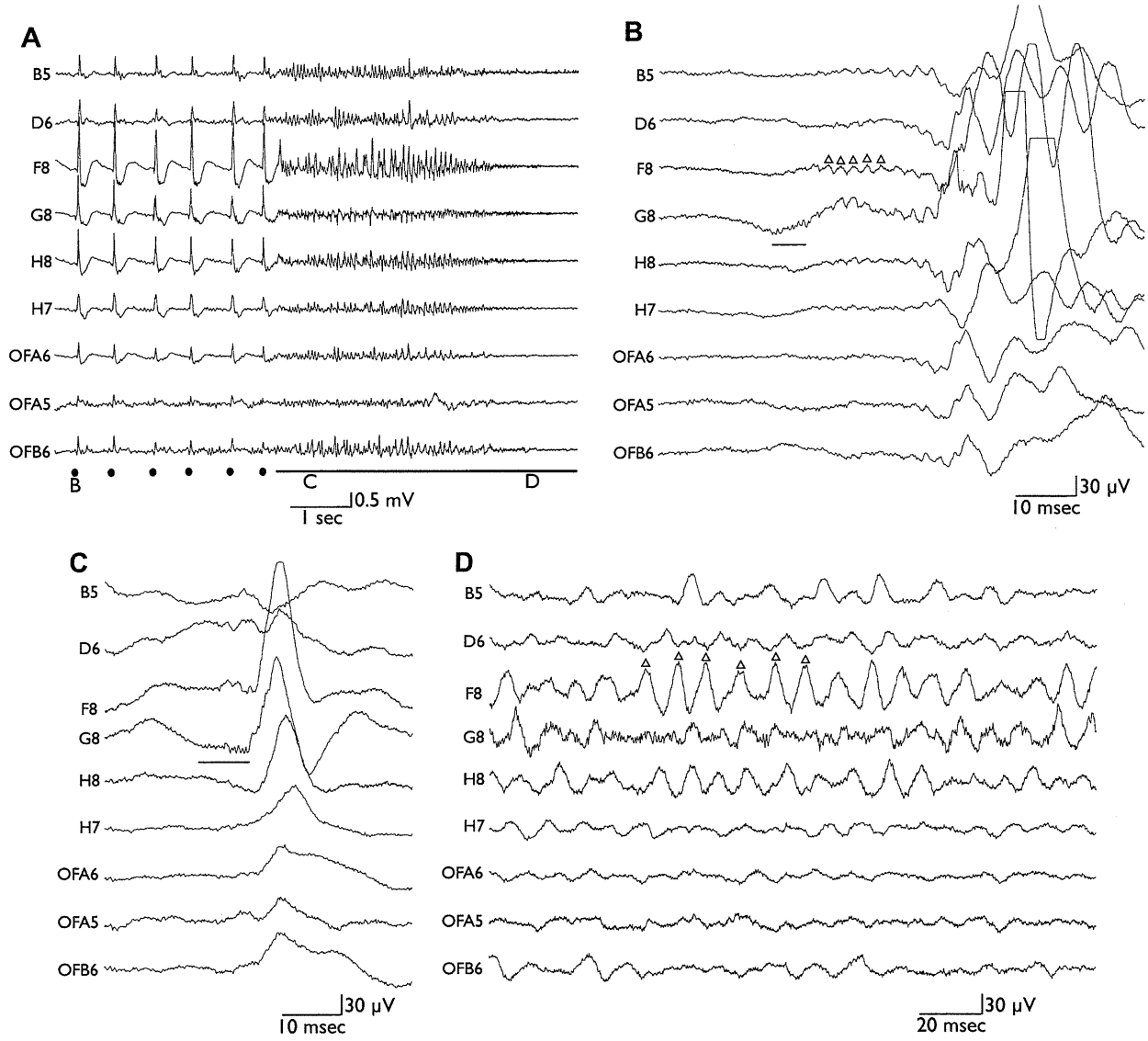


**Fig. 4.** Ictal EEG recorded at 10 kHz sampling rate (Patient 2). (A) Ictal EEG shown using conventional filter settings (low-pass filter 120 Hz, time constant 0.1 s). Only 9 channels are shown. Ictal EEG shows that repetitive spiking is replaced by spike bursts at ictal onset. Spike bursts are later followed by electrodecremental pattern. Filled circle and straight line indicate the presence of VHFO. The EEG at B, C, and D is shown using VHFO filter settings. (B) Preictal VHFO detected visually using low-pass filter of 3 kHz and time constant of 0.001 s. VHFO of 1000–2500 Hz are detected at G8 electrode. The duration of VHFO is 5 ms, and the amplitudes are 7.4–16.2 μV. HFO of 350–600 Hz are also observed at electrodes B5, D6, F8, G8, H8, and H7, with durations of 18–28 ms and amplitudes of 10.3–64.7 μV. Representative HFO peaks are marked by triangles. They are interrupted by spikes. (C) Intermittent VHFO of 1400–2000 Hz are recorded at G8 electrode around seizure onset. The duration is 7 ms, and the amplitudes are 8.8–17.6 μV. (D) VHFO of 1000–2500 Hz become sustained after the electrodecremental pattern appears using conventional EEG setting. The sustained VHFO superimpose on the slower rhythmic activity (80–100 Hz) (marked by triangles). The amplitudes are 8.8–20.6 μV.

resection in each patient are summarized in Fig. 6. The area with VHFO was always located within the seizure onset zone, the irritative zone, and area with HFO. In Patient 5, MRI lesion involved the left frontal lobe including the precentral gyrus, and the irritative zone and seizure onset zone defined by conventional EEG were located over the MRI lesion. Partial frontal resection sparing the precentral gyrus was performed. The postoperative follow-up period was nine months, seven months, ten months, two months, and four months, in Patients 1–5, respectively. Postoperatively, Patient 1 has only simple partial seizures characterized by lightheadedness and blurred vision for several seconds. The other three patients with VHFO (Patients 2–4) have been seizure free. Patient 5 had several motor seizures.

## 4. Discussion

Using routine subdural electrodes and 10 kHz sampling rate, we were able to identify visually low amplitude VHFO of 1000–2500 Hz both in the interictal and ictal states. Although we could record similar frequency "VHFO" in median nerve SEP (Sakura et al., 2009), such high frequency activities have never been reported before in association with spontaneous epileptic discharges in humans. Moreover, as described later, we suspect that the underlying pathophysiology of these activities is different from that of HFO. Therefore, we named these activities "very high frequency oscillations (VHFO)" to distinguish them from HFO.

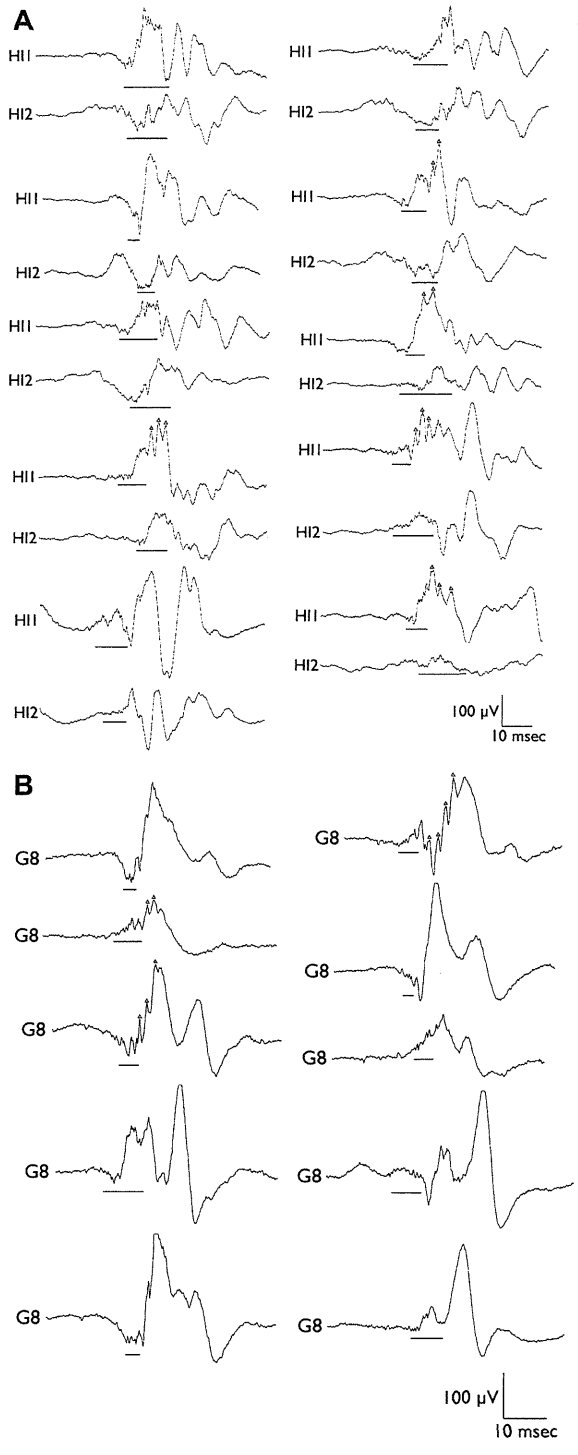


**Fig. 5.** Interictal EEG recorded at a sampling rate of 10 kHz (Patients 1 and 2). Interictal VHFO detected visually using low-pass filter of 3 kHz and time constant of 0.001 s. Only electrodes with VHFO are shown. Underlines indicate the presence of VHFO. Representative HFO peaks are marked by triangles. (A, Patient 1) Interictal VHFO of 1000–2500 Hz are observed at HI1 and HI2 electrodes. They are followed by spikes. Ten samples of VHFO for each electrode are shown. The amplitudes of interictal VHFO were 3.5–29.4 μV, and the durations were 4–45 ms. (B, Patient 2) Interictal VHFO of 1000–2500 Hz are observed at G8 electrode. Ten samples of VHFO are shown. The amplitudes of interictal VHFO were 4.4–24.7 μV, and the durations were 2–75 ms.

VHFO were highly localized and were recorded by one to four electrodes in each patient. Therefore, these activities were most likely not muscular or other artifacts although an extracranial reference electrode was used. VHFO were interrupted by spikes in the interictal state, while spikes were not seen when VHFO became sustained at the onset of seizures. Therefore, we speculate that the VHFO may be excitatory phenomena, and the spikes may have an inhibitory effect on VHFO, and probably inhibit seizure initiation. It has also been proposed that the after-inhibition produced by interictal spikes protects against the occurrence of ictal discharges by maintaining a low level of excitation in a general condition of hyperexcitability determined by the primary epileptogenic dysfunction (de Curtis and Avanzini, 2001).

Synchronously firing bursting neurons have been considered to be the mechanism of HFO generation (Bragin et al., 2002). Meanwhile, the amplitude of VHFO was very low, and the frequency was markedly higher than that of HFO. Considering that individual neuronal firing rates do not approach the VHFO range because of the presence of refractory period, we speculate that low amplitude VHFO recorded by macroelectrodes may represent summated activities from multiple subgroups of neurons with various, non-synchronous firing rates and phases. Synchronization of population activity may be important for the generation of HFO, whereas non-synchronized firing of many neuronal groups may be necessary for the generation of VHFO. The distribution of VHFO was more restricted than that of HFO. Considering that the distribution and the onset timing of VHFO are also different from those of HFO, VHFO and HFO may have different pathophysiological mechanisms.

The next question is why previous studies did not demonstrate VHFO. Khosravani et al. (2009) used 5 kHz sampling rate and recorded 100–500 Hz HFO in patients with temporal lobe epilepsy, but they did not detect VHFO faster than 1000 Hz. Worrell et al. (2008) also did not observe VHFO faster than 1000 Hz from the temporal lobe even though they used 32 kHz sampling. This difference in VHFO detection may be due to the location of the epileptogenic zone (temporal in previous studies versus extratemporal in this study) or pathology of epileptogenic lesions. Considering that histology revealed malformation of cortical development in our four cases, abnormal cellular profiles of malformation of cortical development may be important for the generation of VHFO. Further studies of epileptogenic lesions other than malformation of cortical development are necessary.

VHFO were recorded in highly localized cortical regions (only one to four electrodes in individual patient). The electrodes at which ictal VHFO were recorded were located within the seizure onset zone identified by conventional EEG recordings. The ictal discharges captured by conventional EEG usually spread from ictal onset zone to the other cortical areas, whereas the distribution of VHFO never spread during seizures in our four cases. Therefore, VHFO may be very specific for epileptogenic zone and/or ictal onset zone. The detection of VHFO may be clinically useful for identifying core of the epileptogenic zone although the whole epileptogenic zone cannot be delineated by VHFO. Although the reason why VHFO were not detected in one patient (Patient 5) is not clear, the core of the epileptogenic zone might not be covered by the electrodes considering that the patient has not been seizure free postoperatively.

In summary, VHFO were recorded by routinely used subdural electrodes with 10 kHz sampling rate. Compared to HFO previously reported, VHFO have much higher frequency, more restricted distribution, smaller amplitude, and different timing of onset. Therefore, VHFO generation may involve mechanisms different from those of HFO. It is likely that VHFO may directly reflect summation of activities arising from non-synchronized multiple neuronal subgroups, and will provide further insight into epilepto-

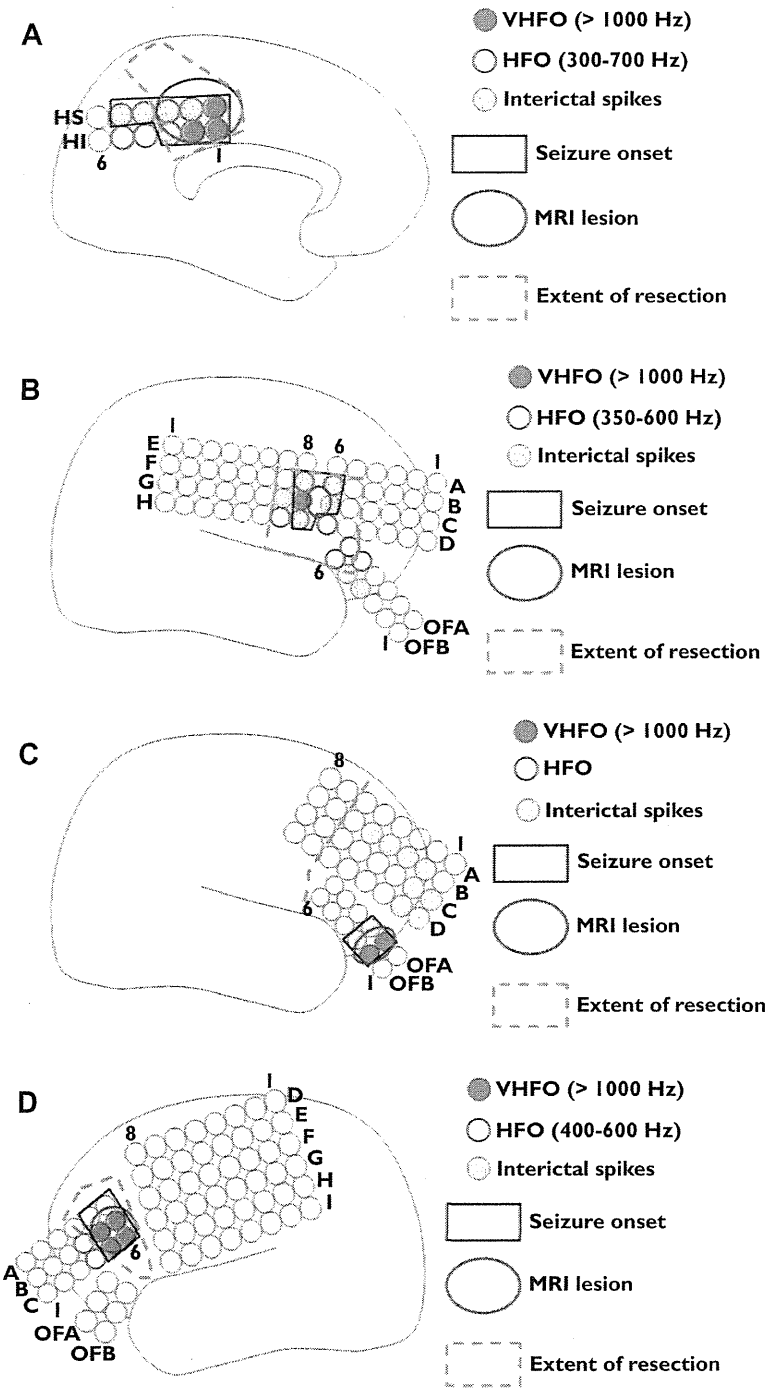


**Fig. 6.** The location of the electrodes with VHFO (red) and those with HFO (green circles), and those with interictal spikes (dotted circles), seizure onset zone defined by conventional EEG (solid line), MRI lesion (purple line), and the extent of surgical resection (orange broken line).

genesis and ictogenesis. The detection of VHFO may be very useful for identifying the epileptogenic zone. Further studies are necessary to clarify the clinical significance of VHFO.

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None of the authors has any conflict of interest to disclose.

## References

Bragin A, Engel Jr J, Wilson CL, Fried I, Mathern GW. Hippocampal and entorhinal cortex high-frequency oscillations (100–500 Hz) in human epileptic brain and in kainic acid-treated rats with chronic seizures. Epilepsia 1999;40:127–37.

Bragin A, Mody I, Wilson CL, Engel Jr J. Local generation of fast ripples in epileptic brain. J Neurosci 2002;22:2012–21.

De Curtis M, Avanzini G. Interictal spikes in focal epileptogenesis. Prog Neurobiol 2001;63:541–67.

Gastaut H, Fischer-Williams H. The physiopathology of epileptic seizures. In: American Physiological Society, editor. Handbook of physiology: a critical, comprehensive presentation of physiological knowledge and concepts. Washington, DC: American Physiological Society; 1959. p. 329–63.

Jirsch JD, Urrestarazu E, LeVan P, Olivier A, Dubeau F, Gotman J. High-frequency oscillations during human focal seizures. Brain 2006;129:1593–608.

Khosravani H, Mehrotra N, Rigby M, Hader WJ, Pinnegar CR, Pillay N, et al. Spatial localization and time-dependent changes of electrographic high frequency oscillations in human temporal lobe epilepsy. Epilepsia 2009;50:605–16.

Nakamura F, Terada K, Usui N, Usui K, Baba K, Tottori T, et al. Ictal high frequency oscillations in intracranial EEG of patients with medial temporal epilepsy. Ann Rep Jpn Epi Res Found 2008;19:81–8.

Ochi A, Otsubo H, Donner EJ, Elliott I, Iwata R, Funaki T, et al. Dynamic changes of ictal high-frequency oscillations in neocortical epilepsy: using multiple band frequency analysis. Epilepsia 2007;48:286–96.

Sakura Y, Terada K, Usui K, Baba K, Usui N, Umeoka S, et al. Very high-frequency oscillations (over 1000 Hz) of somatosensory-evoked potentials directly recorded from the human brain. J Clin Neurophysiol 2009;26:414–21.

Staba RJ, Wilson CL, Bragin A, Fried I, Engel Jr J. Quantitative analysis of high-frequency oscillations (80–500 Hz) recorded in human epileptic hippocampus and entorhinal cortex. J Neurophysiol 2002;88:1743–52.

Worrell GA, Gardner AB, Stead SM, Hu S, Goerss S, Cascino GJ, et al. High-frequency oscillations in human temporal lobe: simultaneous microwire and clinical macroelectrode recording. Brain 2008;131:928–37.

Yamaguchi M, Terada K, Baba K, Nakamura F, Inoue Y. Ictal high frequency oscillations in patients with mesial temporal lobe epilepsy. Jpn J Clin Neurophysiol 2008;36:615–23.

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# Clinical significance of ictal high frequency oscillations in medial temporal lobe epilepsy

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HIGHLIGHTS

- Ictal high frequency oscillations (HFO) were detected unilaterally.
- They were detected ipsilateral to the side of hippocampal sclerosis (HS).
- They were not propagated contralaterally except for one patient.
- In one case with bitemporal onset, ictal HFO were detected only on the side of HS.
- Ictal HFO in the medial temporal lobe is the electrophysiological signature of HS.

ABSTRACT

*Objective:* To clarify the clinical significance of ictal high frequency oscillations (HFO) in the medial temporal lobe.
*Methods:* This study included 19 patients who underwent intracranial electrode implantation in bilateral temporal lobes and had at least one seizure recorded at 1 kHz sampling rate. The characteristics of ictal HFO in the medial temporal lobe, and the relations between the presence of HFO, pathology, and postoperative seizure outcome were analyzed.
*Results:* Ictal HFO were detected from medial temporal structures in 11 patients with medial temporal lobe epilepsy (MTLE). Among eight patients without HFO, only three were diagnosed with MTLE. Ictal HFO were detected from unilateral medial temporal structures ipsilateral to the side of hippocampal sclerosis (HS). In one patient with bitemporal independent seizure onset, ictal HFO were detected only on the side of HS. HS was detected in all 11 patients with HFO, but in only one of four patients without HFO. Seizure outcome did not differ between patients with and without HFO.
*Conclusions:* Ictal HFO in the medial temporal lobe may be a specific marker for MTLE with HS.
*Significance:* Recording of ictal HFO in the medial temporal lobe may be useful for presurgical evaluation of MTLE.


## 1. Introduction

Electrophysiological studies in animals revealed that high frequency oscillations (HFO) with frequencies of 400–1000 Hz were recorded in the vicinity of epileptogenic foci (Gastaut and Fischer-Williams, 1959). Recently, HFO have attracted attention in epilepsy surgery. Previous studies have reported the characteristics of HFO in medial temporal lobe epilepsy (MTLE) as follows; (1) recorded from hippocampus or entorhinal cortex; (2) frequencies ranging from 170 to 400 Hz, usually with fast frequencies of 260–270 Hz [fast ripple: FR (Bragin et al., 1999), very high frequency band: VHF (Jirsch et al., 2006)]; (3) usually detected on the side of surgical resection; (4) not detected in the region of secondary propagation; (5) can be recorded ictally or interictally; (6) appear as clusters of short bursts with a duration of 6–53 ms; (7) usually associated with ictal spikes on conventional EEG; (8) detected by only 1–2 macroelectrode channels; and (9) low amplitudes of 5–30 μV (Bragin et al.,1999, 2002; Jirsch et al., 2006; Yamaguchi et al., 2008).

As for ictal HFO, Jirsch et al. (2006) reported ictal HFO in 10 patients with focal seizures, including four with medial temporal onset seizures. They used the EEG seizure onset as a surrogate for the epileptogenic area, and did not evaluate the postoperative seizure

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**Table 1**
Clinical characteristics of 19 patients.

| Patient | Age (yrs)/sex | Age at onset (yrs) | Semiology | Interictal EEG | Ictal EEG |
|---|---|---|---|---|---|
| 1 | 20/M | 7 | Automotor | Lt | Rt |
| 2 | 21/F | 1 | Automotor | Bil (Lt predominant) | Rt |
| 3 | 32/F | 10 | Dysmnestic aura → automotor | Rt | Rt |
| 4 | 36/F | 15 | Aura → automotor | Rt | Lt |
| 5 | 43/F | 9 | Dialeptic | Bil (Lt predominant) | Lt |
| 6 | 34/F | 1 | Aura → automotor | Bil (Lt predominant) | Bil (Lt predominant) |
| 7 | 30/F | 4 | Automotor | Rt | Lt |
| 8 | 19/M | 3 | Abdominalaura → automotor | Bil (Lt predominant) | Bil (Rt predominant) |
| 9 | 43/F | 9 | Aura → dialeptic | Rt | Lt |
| 10 | 37/F | 18 | Automotor | Bil | Lt |
| 11 | 39/M | 10 | Aura → automotor | Bil (Rt predominant) | Rt |
| 12 | 36/M | 27 | Dialeptic | Bil | Lt |
| 13 | 21/M | 15 | Abdominal aura → dialeptic | Rt | Rt |
| 14 | 29/M | 16 | Aura → automotor | Bil | Lt |
| 15 | 26/F | 15 | Automotor | Rt | Rt |
| 16 | 26/M | 5 | Hypermotor | Bil | Bil |
| 17 | 16/F | 11 | Automotor | Bil | Bil (Lt predominant) |
| 18 | 31/F | 11 | Automotor | Lt | Bil (Lt predominant) |
| 19 | 21/M | 15 | Aura → automotor | Bil | Lt |

M: male; F: female; Rt: right; Lt: left; Bil: bilateral independent spikes on right and left.

outcome. Khosravani et al. (2009) also studied ictal HFO in seven TLE patients. However, the clinical significance of ictal HFO on surgical decision-making has not been fully examined.

To clarify the clinical relevance of ictal HFO, we analyzed their characteristics including the spatial distribution of ictal HFO in the medial temporal lobe, and compared the presence or absence of ictal HFO with hippocampal pathology and postoperative seizure outcome. We also demonstrated the clinical usefulness of detecting ictal HFO in surgical decision-making for bitemporal epilepsy.

## 2. Patients and methods

### 2.1. Patients

Previously, we proposed the following criteria for omitting intracranial EEG monitoring in patients with temporal lobe epilepsy; (1) appearance of focal epileptic discharges in unilateral sphenoidal lead during the phase of simple partial seizures, or unilateral discharges predominantly in the sphenoidal lead during the early phase of complex partial seizures; (2) interictal spikes on scalp-recorded EEGs localizing unilaterally in the anterior region of the temporal lobe, and if bilaterally independent, presenting with unilateral predominance in a ratio of greater than 4:1; (3) presence of autonomic signs in the initial phase of signal symptoms; and (4) neuroimaging findings in the mesial temporal region showing elongated T2 on MRI and HS, or a tumorous lesion (Mihara et al., 1992). Consequently, between May 2005 and May 2008, 19 patients underwent implantation of combined depth and subdural electrodes in bilateral temporal lobes (Mihara and Baba, 2001), and had at least one seizure recorded at 1 kHz sampling rate. These 19 patients were included in this study. Before intracranial video/EEG monitoring, all patients underwent noninvasive presurgical evaluations including history-taking, video/scalp sphenoidal EEG monitoring, neuroimagings, and neuropsychological tests. Brain MRI was performed at 1.5 tesla and 5-mm slice thickness, and axial, coronal, and sagittal T1-weighted, T2-weighted, and FLAIR images were acquired. The clinical characteristics of the 19 patients are shown in Table 1. Seizures were classified by the semiological seizure classification proposed by Lüders et al. (1998).

Depth electrodes (Unique Medical, Japan, 0.8 mm diameter, 1 mm length, either 5 or 10 mm center-to-center spacing) were placed in bilateral hippocampi and amygdala using MRI stereotaxy. Subdural electrodes (Ad-tech Medical Instrument, Racine, WI. 2.3 mm contact, effective area 4.15 $mm^2$, 10 mm spacing) were also placed over bilateral temporal regions including the basal and anterior aspects, and the adjacent parieto-occipital areas (Fig. 1). Reference electrodes were placed on the surface of the skull, with the contacts of the electrodes facing away from the skull to avoid the referential activation. Analyses were performed on referential montages. Antiepileptic medications were reduced, and EEG recording was started approximately 1 week after electrode placement and continued for approximately 2 weeks. The EEG signals were digitally recorded by EEG-1000 (Nihon Kohden) at a sampling rate of 200 Hz and a time constant of 10 s for conventional EEG analysis. For detection of HFO, EEG was low pass filtered at 300 Hz, recorded at a sampling rate of 1 kHz and a time constant of 10 s.

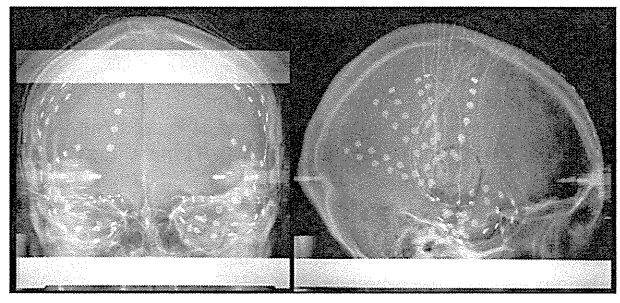

**Fig. 1.** Skull X ray showing the location of intracranial electrodes. Left: anteroposterior view. Right: lateral view. Two depth electrodes are inserted into the medial temporal structure on each side. RA and LA are aimed at amygdala, and RH and LH are at hippocampus. Basal temporal areas are covered by subdural electrodes.