G Ital Med Lav Erg 2019; 41:3, 255-259
ISSN 1592-7830

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100 Hz Localized vibration increases ipsilateral cerebellar areas activity during a motor task in healthy subjects: Three Cases Report

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ABSTRACT. Background and Purpose. ***The exact mechanism thought which Localized vibration (LV) acts on the motor system at the suprasegmental level is still poorly understood. In this paper we have reported three cases of healthy men exposed to 100 Hz localized vibration during a motor task.***
Case Description. ***This case report describes 3 healthy men (age 23 years).***
Outcomes. ***During fMRI participants were engaged in a right-hand self-paced finger tapping (FT) task, with and without a 100 Hz LV of the right hand. After standard images preprocessing and normalization, a fix-effect GLM analysis was used to test the effect of vibratory stimulation on motor network. A bilateral activation, greater in the left hemisphere than in the right one, in the frontal premotor and supplementary motor areas (SMA), central gyrus (M1), postcentral gyrus, was found without any statistical significance between conditions. Activation in the left lenticular nucleus and thalamus was also found without differences between conditions. When using the FT activation map as a mask, the analysis showed that only the right cerebellum correlate positively with the vibratory stimulation.***
Discussion. ***Using fMR a localized vibratory stimulus was found to significantly increase the activity in homo-lateral motor cerebellar areas during a motor task. This finding aims to trigger new studies on how a LV can influence motor recovery in neurorehabilitation and to (re) consider the role of cerebellum in the rehabilitation strategy.***

Key words: *localized vibration, 100 Hz, sMNR, cerebellum, rehabilitation.*

RIASSUNTO. ***Introduzione.*** **L'esatto meccanismo con cui la vibrazione localizzata (LV) agisce sul sistema motore attraverso una azione neuro-mediata, non è ancora del tutto chiarito. Riportiamo qui il caso di tre soggetti normali sottoposti a LV a 100 Hz durante un task motorio alla mano Dx (finger tapping) e studiati con fMNR.
Dopo l'acquisizione standard delle immagini di fMNR e loro normalizzazione, una successiva elaborazione (fix-effect GLM) è stata utilizzata per valutare gli effetti della vibrazione sul network motorio. Una attivazione bilaterale maggiore nell'emisfero Sin, ma senza significatività statistica tra le due condizioni, è stata osservata nelle aree pre-motorie frontali e aree supplementari motorie (SMA) nel giro post-centrale. Un aumento non significativo della attività cerebrale è stata registrata anche a livello del nucleo lenticolare talamico Sin ma anche qui senza una significatività tra le due condizioni. Una attività statisticamente differente è stata invece osservata a livello dell'emisfero cerebellare Dx dopo applicazione di una maschera di sottrazione (FT activation map) che correla positivamente con l'applicazione di uno stimolo vibratorio sovrapposto ad un movimento.**

Introduction

Detection of mechanical forces is essential for living organisms to interact with external environments and to maintain stable biological systems (1,2). Moreover mechanotransduction in response to mechanical forces of different intensity and frequencies locally applied, such as touch, pressure and vibration is the first step toward corticalization.

Vibration in medicine has a double-faced aspect. On one side mechanical vibration has been shown to induce a work related pathology (3,4) leading to several attempts to reduce risks and increase surveillance (5,6).

However on the other side vibratory stimulations locally applied (LV) (3) on the skin overlaying muscles and tendons have been used for many years in clinical neurophysiology to study spinal cord reflex activity (4). LV has been also used as a non-invasive physical modality for the management of several conditions such as pain (5-12) and spasticity (13-16).

LV has been also proposed as a non-invasive methodology to improve motor functions in normal subjects as well as in hemiplegic subject (17). Although the exact mechanisms thought which LV acts on the sensory motor integration system is still a matter of deepening. It has been postulated that LV can act at several neural level both at spinal cord (18-20) as well as at supra segmental level both in normal and in patients (17,12,21).

With technical improvements in the last decades, investigations pertaining to human brain functions by non-invasive methods have become possible. Likewise, because of its improved spatial resolution and whole brain coverage, fMRI can demonstrate differences between brain images at rest or during various conditions. Accordingly, assessment of sensory-motor activity by the use of functional imaging with positron emission tomography and fMRI have been reported in the recent literature during a wide range of physiological settings such as controlled movements (22).Only very few data are present in fMRI literature on the central effects of LV (23, 24).

No data are present on the possible effect of LV associated with a motor task on the central motor activity. A great interest for the use of vibration as a therapy would be to understand if and where these areas are activated and to what extent.

Conclusioni. **Mediante l'uso di fMNR è stato possibile documentare come una vibrazione localizzata a 100 Hz sovrapposta ad un movimento volontario è in grado di aumentare l'attività della corticale cerebellare omolateralmente al lato stimolato. Questo riscontro può aprire un nuovo campo di ricerca su come la vibrazione localizzata possa essere utilizzata in ambito neuroriabilitativo e pone nuova enfasi sul ruolo del cervelletto nel processo riabilitativo**

Parole chiave: vibrazione localizzata, 100 Hz, cervelletto, neuroriabilitazione.

The purpose of this case report is to describe central effect of a localized vibration during a motor task in healthy men.

Subjects History and Review of Systems

The subjects were 3 healthy men (all aged 23 years). All 3 subjects not exhibited substantial skeletal, muscular, neural, and neuromuscular impairments. Written informed consent was obtained from the subjects.

Clinical impression

The 3 young men included in this case series were all healthy university students of the Pavia Medical School. Subjects were assigned at different sequences of interventions during fMRI acquisitions: movement task alone and movement task with vibratory stimulus. All subjects completed the case series designed study.

Examination

Movement task

Participants were engaged in a right-hand self-paced finger tapping task (FT) (25). During the fMRI acquisition, all study participants were instructed to alternatively rest for 1 minute and tap using their index, middle and annular fingers for 2 minute for a total duration of 18 min and 15 sec. All subjects undergo the same procedure two times, one with finger tapping/rest conditions and one with finger tapping/rest conditions, but during the finger-tapping task each subject received a 100 Hz vibratory stimulus on the same hand. Thus, the data were composed, for each paradigm, of six 1-min segments acquired during the "rest" (non-tapping state) and six 2-min segments acquired during stimulation (finger-tapping state). During the first condition, a light sign was used to indicate the start of the FT; during the other condition the start of the movement corresponded with the start of the vibratory stimulus.

Vibratory stimulation

A single physiotherapist—trained in the application of the vibratory stimulation but not aware about the aim of the study—performed the vibration stimulation procedures applying the transducer on the dorsum of the hand. The transducer consisted of a cup (surface of 2 cm2) of material fMR compatible applied on the skin with elastic bands not interfering with the thumb opposition movement. The vibration stimuli was delivered with a mechano-acoustic device (VIBRA 3.0 AD Swiss Med Tech SA CH)) delivering a stimuli of 100 Hz with an amplitude of 2 mm and a mean pressure of 250 mBar of strength (15,17). The dorsal part of the hand was chosen because of the dimension of the mechano-acoustic transducer and to allow the thumb opposition movement without interference even if the highest concentration of mechanoreceptor units are in the glabrous skin of the distal phalanx (26).

Image acquisition and statistical analysis

Images were acquired on a 3T Discovery MR750 scanner (GE, Milwaukee, USA) with a 16-channel phased array head coil. The high-resolution anatomical images were acquired with a volumetric sequence BRAVO T1-weighted. For functional imaging a gradient-echo echo-planar BOLD technique was used. An fMRI time series lasted 18.15 min and comprised 360 measurements of 40 slices. During this time, after 15 sec of dummy, 6 "task-rest" cycles were performed, with 1 minute of rest and 2 minutes of thumb opposition.Following common procedures, for each subject, the images were realigned to the first image in the time series to correct for head motion. Different slice acquisition times and linear trends and non-linear drifts were also removed by temporal filtering. These preprocessed images were then co-registered to T1 images acquired for each subject and normalized into a standard stereotactic space (Talairach stereotactic system) (27,28). All the analysis were conduct using BrainVoyger QX 2.8 (Brain Innovation, Maastricht, The Netherlands) (29).

Outcome

We first run a GLM-FFX analysis to identify the area significantly active in the FT condition. We used motion correction predictors as covariate of no interests because during preprocessing the 3D motion correction was major than 1 mm. Statistical map was then created using a False Discovery Rate threshold correction ($q<0.01$), considering positive all clusters bigger than 9 voxels (30).

In the FT>REST condition (Figure 1) we found a significant bilateral activation, greater in the left hemisphere than in the right one, in the frontal premotor area, SMA, central gyrus (M1), postcentral gyrus, cerebellum. Only in the left hemisphere we found activation in the lenticular nucleus and in the thalamus.

We also found a bilateral activation of the visual area due to the stimulus signal.

We run a second analysis using the FT activation map as a mask, excluding the negative signals, to verify the hypothesis that the vibratory stimulation associated with Finger Tapping movement could amplify the activity of the motor network. This analysis showed that only the right cerebellum correlate positively with the vibratory stimulation (Figure 2).

Discussion

As far as we know this is the first observation using fMRI in which a vibratory stimulus was found able to activate, as expected, not only different sensory areas (both homo- and contralateral) but also to significantly increase the activity in ipsilateral motor cerebellar areas when applied during a motor task.

Vibratory stimulation is transduced through the activation of mechanoreceptor located at the distal end of sensory neurons and innervated by Aβ afferents that transmit tactile sensory signals to the central nervous system. Their activation elicit a somatosensory, tactile, perception: from a sensation of light touch to flutter and vibratory sensation (31-35). These afferents are not intermingled as they transmit the tactile sensory signals to the cortex in a segregated way. This segregation is at the basis of different responses according to the types of vibration. Imaging studies in animals have demonstrated a specific spatial patterns in the primary sensory cortical area (S1) activity in response to the sustained pressure (1 Hz), flutter (30/50 Hz) and vibration (200 Hz). A frequency inducing flutter sensation increased cortical activity in contralateral S1 and S2, whereas a frequency inducing vibration increased activity in contralateral sensory cortical area S2 respectively (36-40).

Since the 60s LV has been demonstrated to induce different neurophysiological effects such as an initial inhibition of spinal monosynaptic reflex (41), a tonic prolonged contraction of the vibrated muscle (Tonic Vibratory Reflex-TVR) (42), and a post vibratory potentiation (43). Indeed all these effects are mainly related to the impact of LV on the spinal cord network and were found short lasting.

The exact mechanism thought which LV acts on the motor system at the suprasegmental level is still poorly understood. In a previous work, we observed that LV, acts at a central system level generating a long lasting modification in the motor unit recruitment pattern reducing the recruitment of fast fatigable motor unit. The conditioning was able to maintain the same mechanical output requested, reducing the myoelectric manifestations of fatigue, thus increasing the neuromuscular efficiency of the system (17).

The brain maintains the capacity of reorganizing its neural network architecture following environmental changes (17,44,45). The fMRI findings of an increase motor activity in the cerebellar cortex could be related to this ability of the nervous system to modify its activity depending on the continuous inflow of relevant inputs (46).

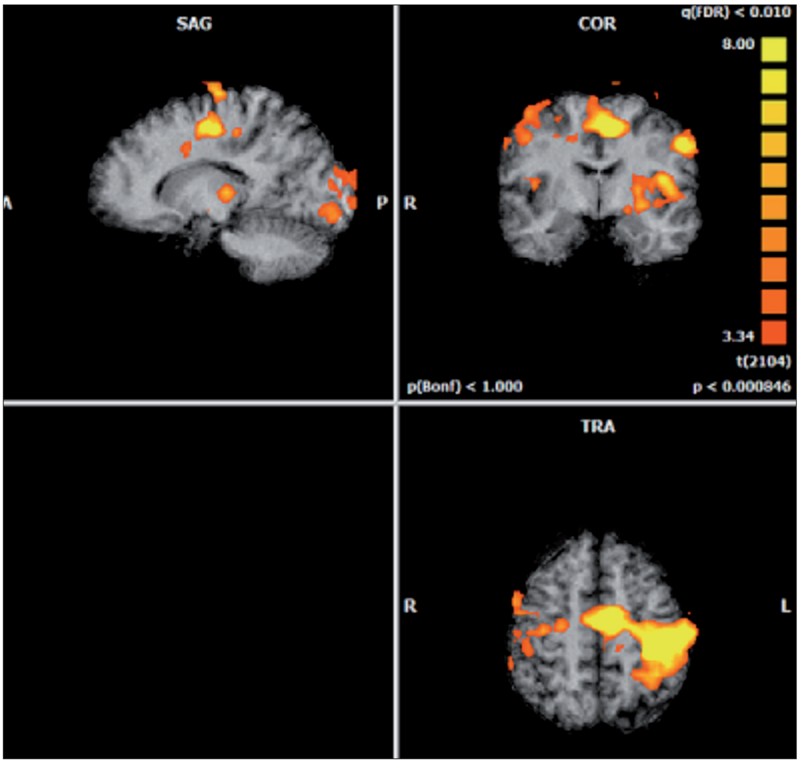

Figure 1. ***FT activations map***
This analysis show the activation of a huge number of cortical areas ipsi-and contralateral to the stimulated side

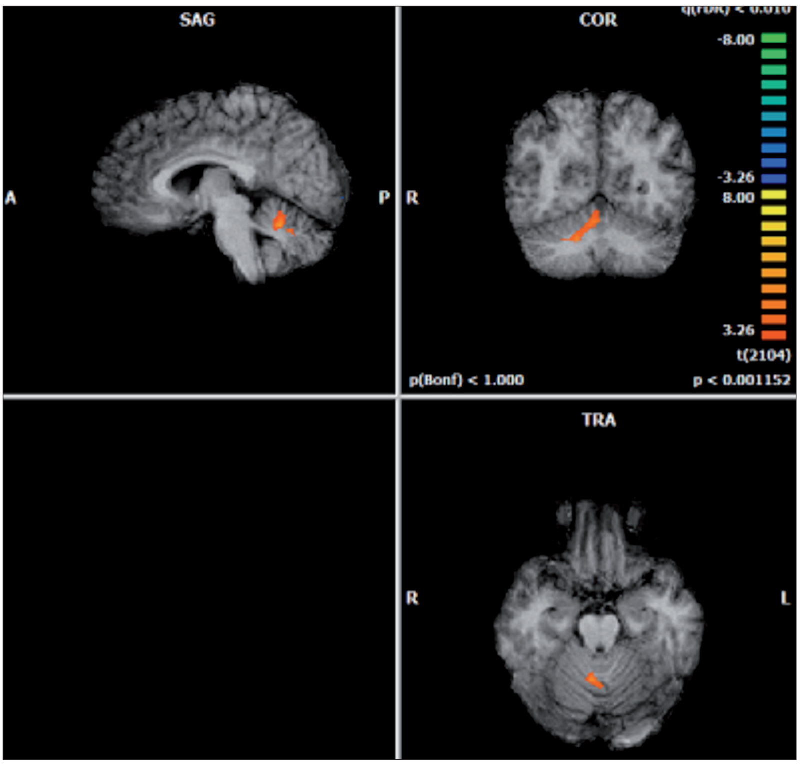

Figure 2. ***VIBRA >FT in the GLM-FFX analysis with FT mask***
Pictures clearly show an activation of cerebellar areas ipsilateral to the stimulation side

The cerebellum is placed at the crossroads of sensory-motor integration. Purkynjě cells are its landmark. While Purkynjě cells are the only output neurons of the cerebellar cortex, they receive two distinct afferent pathways convey

Box 1. ***Mechanoreceptors classification according to the type of mechanical forces and frequency of stimulation***
(from: Delmas et al., 2011, Lumpkin and Caterina, 2007 and McGlone and Reilly, 2010)

Name	Action	Type	Cortical areas
Merkel cell-neurite complexes	detect a light touch and a sustained indentation	type 1 slowly adapting receptors (SA1)	contralateral primary somatosensory (S1) and the bilateral secondary somatosensory cortex (S2)
Ruffini corpuscles	detect kinesthetic senses and static forces	type 2 slowly adapting receptors (SA2)	contralateral primary somatosensory (S1) and the bilateral secondary somatosensory cortex (S2)
Meissner corpuscles	detect texture and a relatively low frequency stimulation of cutaneous flutter whose frequency range is 5–50 Hz	type 1 rapidly adapting receptors (RA)	contralateral primary somatosensory (S1) and the bilateral secondary somatosensory cortex (S2)
Pacinian corpuscles	detect high-frequency rapid stimulation of cutaneous vibration whose frequency range is 50–400 Hz	type 2 rapidly adapting receptors (PC)	contralateral primary somatosensory (S1) and the bilateral secondary somatosensory cortex (S2)

information from the periphery. Mossy and climbing fibres inputs from cutaneous mechanoreceptors reach Purkynjĕ cells and can be accounted for the anatomical pathway trough which mechanical stimulations can reach the cerebellum (47). Moreover the cerebellar distribution of these mechanoreceptive inputs are highly somatotopical and mainly ipsilateral to the side of the mechanostimulation (48). These data are congruous with our results of an ipsilateral activation of the cerebellum. Indeed in animal experiments most of the short latency responses via mossy fibers resulted from activation of the receptors of the ipsilateral side and that also climbing fibre discharges from the ipsilateral side were more frequently evoked than from the contralateral side (47).

These data pin point a possible new role of cerebellar activation in the rehabilitation as well as in training setting of the healthy person. A congruous LV stimulation seems able to induce plastic rearrangement in the sensory motor coupling involving the cerebellar structure. This could be the basis for a better coordination in health subject, as well as a novel approach to patients with the activation of a non-lesioned pathway in case of central nervous lesions such as in hemiplegia.

The importance of high frequency vibration versus lower frequency vibration is forwarded by laboratory acquisition showing that only when muscle stretch receptors are driven maximally by a high frequency vibration, neurones in the motor cortex and in area 3a in monkeys are effectively activated (49). This could indicate a supremacy in cortical activation of high frequencies versus lower frequencies.

This report is aiming to trigger new studies on how a LV can influence motor recovery in neurorehabilitation and to (re) consider the role of cerebellum in the rehabilitation strategy.

It is thus possible if not mandatory to speculate further experimental protocols aimed to better assess other conditioning effects of a vibratory stimulus on the central nervous system and in particular on the cerebellum and the role played by different stimulus parameters. Future studies using larger sample sizes and blinded randomization are required to further enhance our understanding on the cerebellar activation areas of localized vibration in patients.

References

1) Delmas P, Hao J, Rodat-Despoix L. Molecular mechanisms of mechanotransduction in mammalian sensory neurons. Nat Rev Neurosci 2011; 12: 139-153.
2) Lumpkin EA, Caterina MJ. Mechanisms of sensory transduction in the skin. Nature 2007; 445: 858-865.
3) van der Molen HF, Foresti C, Daams JG, Frings-Dresen MHW, Kuijer PPFM. Work-related risk factors for specific shoulder disorders: a systematic review and meta-analysis. Occup Environ Med 2017 Oct; 74(10): 745-755.
4) Nilsson T, Wahlström J, Burström L. Hand-arm vibration and the risk of vascular and neurological diseases-A systematic review and meta-analysis. PLoS One 2017 Jul 13; 12(7): e0180795.
5) Peretti A, Bonomini F, Pasqua di Bisceglie A. Forklifts: vibrations, drivers exposure, interventions to reduce risk.G Ital Med Lav Ergon 2012 Jul-Sep; 34(3): 335-42.
6) Riolfi A, Perbellini L. The combined use of capillaroscopy and skin thermometry in health surveillance of workers exposed to hand-arm vibration. G Ital Med Lav Ergon 2010 Oct-Dec; 32(4 Suppl): 153-5.
7) Casale R. Focal, local or segmental vibration: a commentary on Murillo and Coworkers review. Eur J Phys Rehabil Med. 2014 Sep 30. [Epub ahead of print]
8) Lance JW. The effect of vibration on afferent nerve conduction and spinal reflex mechanisms. Electroencephalogr Clin Neurophysiol 1968; 25(4): 407-8.
9) Lundeberg T, Nordemar R, Ottoson D. Pain alleviation by vibratory stimulation. Pain 1984; 20(1): 25-44.
10) Lundeberg T. Relief of pain from a phantom limb by peripheral stimulation. J Neurol 1985; 232(2): 79-82.
11) Vibration therapy for pain. Editorial. Lancet 1992; 339(8808): 1513-4.
12) Yarnitsky D, Kunin M, Brik R, Sprecher E. Vibration reduces thermal pain in adjacent dermatomes. Pain 1997; 69(1-2): 75-7.
13) Hollins M, Roy EA, Crane SA. Vibratory antinociception: effects of vibration amplitude and frequency. J Pain 2003; 4(7): 381-91.
14) Constantino C, Galuppo L, Romiti D. Efficacy of mechano-acoustic vibration on strength, pain, and function in poststroke rehabilitation: a pilot study. Top Stroke Rehabil 2014; 21(5): 391-9.
15) Hollins M, McDermott K, Harper D. How does vibration reduce pain? Perception 2014; 43(1): 70-84.

16) Marconi B, Filippi GM, Koch G, Giacobbe V, Pecchioli C, Versace V, Camerota F, Saraceni VM, Caltagirone C. Long-term effects on cortical excitability and motor recovery induced by repeated muscle vibration in chronic stroke patients. Neurorehabil Neural Repair 2011 Jan; 25(1): 48-60.
17) Caliandro P, Celletti C, Padua L, Minciotti I, Russo G, Granata G, La Torre G, Granieri E, Camerota F. Focal muscle vibration in the treatment of upper limb spasticity: a pilot randomized controlled trial in patients with chronic stroke. Arch Phys Med Rehabil 2012; 93(9): 1656-61.
18) Tavernese E, Paoloni M, Mangone M, Mandic V, Sale P, Franceschini M, Santilli V. Segmental muscle vibration improves reaching movement in patients with chronic stroke. A randomized controlled trial. NeuroRehabilitation 2013; 32(3): 591-9.
19) Casale R, Damiani C, Maestri R, Fundarò C, Chimento P, Foti C. Localized 100 Hz vibration improves function and reduces upper limb spasticity: a double-blind controlled study. Eur J Phys Rehabil Med 2014; 50(5): 495-504.
20) Murillo N, Valls-Sole J, Vidal J, Opisso E, Medina J, Kumru H. Focal vibration in neurorehabilitation. Eur J Phys Rehabil Med 2014; 50(2): 231-42.
21) Casale R, Ring H, Rainoldi A. High frequency vibration conditioning stimulation centrally reduces myoelectrical manifestation of fatigue in healthy subjects. J Electromyogr Kinesiol 2009; 19(5): 998-1004.
22) Desmedt JE. Mechanisms of vibration-induced inhibition or potentiation: tonic vibration reflex and vibration paradox in man. Adv Neurol 1983; 39: 671-83.
23) Day Bl, Marsden CD, Obeso JA, Rothwell JC. Reciprocal inhibition between the muscles of the human forearm. J Physiol 1984; 349: 519-34.
24) Cody FW, Henley NC, Parker L, Turner G. Phasic and tonic reflexes evoked in human antagonistic wrist muscles by tendon vibration. Electroencephalogr Clin Neurophysiol 1998; 109: 24-5.
25) Schieppati, M. The Hoffmann reflex: A means of assessing spinal reflex excitability and its descending control in man. Progress in Neurobiology 1987; 28(4): 345-376
26) Stefanescu MR, Thürling M, Maderwald S, Wiestler T, Ladd ME, Diedrichsen J, Timmann D. A 7T fMRI study of cerebellar activation in sequential finger movement tasks. Exp Brain Res 2013; 228: 243-54.
27) Yoon Gi Chung, Junsuk Kim, Sang Woo Han, Hyung-Sik Kim, Mi Hyun Choi, Soon-Cheol Chung, Jang-Yeon Park, Sung-Phil Kim. Frequency dependent patterns of somato sensory cortical responses to vibrotactile stimulation in humans: A fMRI study. Brain Res 2013; 1504: 47-57.
28) Harrington GS, Hunter Downs J. III FMRI mapping of the somatosensory cortex with vibratory stimuli Is there a dependency on stimulus frequency? Brain Res 2001; 897: 188-192.
29) Goebel R, Esposito F, Formisano E. Analysis of functional image analysis contest (FIAC) data with brainvoyager QX: From single-subject to cortically aligned group general linear model analysis and self-organizing group independent component analysis. Hum Brain Mapp 2006; 27: 392-401.
30) Johansson RS, Vallbo AB. Spatial properties of the population of mechanoreceptive units in the glabrous skin of the human hand. Brain Res 1980; 184: 353-366.
31) Strother SC, Anderson JR, Xu XL, Liow JS, Bonar DC, Rottenberg DA. Quantitative comparisons of image registration techniques based on high-resolution MRI of the brain. J Comput Assist Tomogr 1994; 18: 954-62.
32) Migneco O, Darcourt J, Benoliel J, Martin F, Robert P, Bussiere-Lapalus F, Mena I. Computerized localization of brain structures in single photon emission computed tomography using a proportional anatomical stereotactic atlas. Comput Med Imaging Graph 1994; 18: 413-22.
33) Causby R, Reed L, McDonnell M, Hilljier S. Use of objective psychomotor tests in health professionals. Percept Mot Skills 2014; 118: 765-804.
34) Maldjian JA, Gottschalk A, Patel RS, Pincus D, Detre JA, Alsop DC. Mapping of secondary somato sensory cortex Brain Res 1999; 824(2): 291-5.
35) Nguyen HD, McLachlan GJ, Cherbuin N, Janke AL. False discovery rate control in magnetic resonance imaging studies via Markov random fields. IEEE Trans Med Imaging 2014; 33: 1735-48.
36) Disbrow E, Roberts T, Krubitzer L. Somatotopic organization of cortical fields in the lateral sulcus of Homo sapiens: evidence for SII and PV. J Comp Neurol 2000; 418: 1-21.
37) Ruben J, Schwiemann J, Deuchert M, Meyer R, Krause T, Curio G, Villringer K, Kurth R, Villringer A. Somatotopic organization of human secondary somatosensory cortex. Cereb Cortex 2001; 11: 463-73.
38) Kopietz R, Sakar V, Albrecht J, Kleemann AM, Schopf V, Yousry I, Linn J, Fesl G, Wiesmann M. Activation of primary and secondary somatosensory regions following tactile stimulation of the face. Clin Neuroradiol 2009: 19: 135-144.
39) Hu L, Zhang ZG, Hu Y. A time-varying source connectivity approach to reveal human somatosensory information processing. Neuroimage 2012; 62: 217-228.
40) Talbot WH, Darian-Smith I, Kornhuber HH, Mountcastle VB. The sense of flutter-vibration: comparison of the human capacity with response patterns of mechanoreceptive afferents from the monkey hand. J Neurophysiol 1968; 31: 301-34.
41) Bolanowski Jr. SJ,Gescheider GA,Verrillo RT, Checkosky CM. Four channels mediate the mechanical aspects of touch. J Acoust Soc Am 1988; 84: 1680-1694.
42) Gescheider GA, Bolanowski SJ, Hardick KR The frequency selectivity of information-processing channels in the tactile sensory system. Somatosens Mot Res 2001; 18: 191-201.
43) Chen LM, Friedman R, Roe AW. Somatosensory: imaging tactile perception. In Roe AW (Ed) Imaging the Brain with Optical Methods. Springer Verlag, 2010; 65-92.
44) Tommerdahl M, Favorov OV, Whitsel BL. Dynamic representations of the somatosensory cortex. Neurosci Biobehav Rev 2010; 34: 160-7.
45) Lance JW, De Gail P, Neilson PD. Differential effects on tonic and phasic reflex mechanisms produced by vibration of muscles in man. J Neurol Neurosurg Psychiatry 1966; 29: 1-11.
46) Eklund G, Hagbarth KE. Normal variability of tonic vibration reflexes in man. Exp Neurol 1966; 16: 80-92.
47) Delwade PJ. Human monosynaptic reflexes and presynaptic inhibition. In: Desmedt JE (Ed) New Development in Electromyography and Clinical Neurophysiology. Basel: Karger; 1973; vol 3: 508-522.
48) Sterr A, Muller MM, Elbert T, Rockstroh B, Pantev C, Taub E. Perceptual correlates of changes in cortical rapresentation of fingers in blind multifinger Braille readers. J Neurosci 1998; 18: 4417-23.
49) Flor H. Cortical reorganisation and chronic pain: implications for rehabilitation. J Rehabil Med 2003; 41: 66-72.
50) Elbert T, Rockstroh B. Reorganization of human cerebral cortex: the range of changes following use and injury. The neuroscientist 2004; 10: 129-41.
51) Leicht R, Rowe MJ, Schmidt RF. Mossy and climbing fiber inputs from cutaneous mechanoreceptors to cerebellar Purkynjě cells in unanesthetized cats. Exp Brain Res 1977; 27: 459-77.
52) Garwicz M, Jorntell H, Ekerot CF. Cutaneous receptive fields and topography of mossy fibres and climbing fibres projecting to cat cerebellar C3 zone. J Physiol 1998; 512: 277-93.
53) Lucier GE, Rüegg DC, Wiesendanger M. Responses of neurones in motor cortex and in area 3A to controlled stretches of forelimb muscles in cebus monkeys. J Physiol 1975; 251: 833-53.

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