ATTENTIONAL MODULATION AND PLASTICITY IN THE HUMAN SENSORY SYSTEM

Thesis of the Ph.D. Dissertation

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Introduction and aims

The perception and neural processing of a stimulus are influenced by the actual task to be solved, i.e. according to the given context. Sensory processing (including visual, tactile and pain processing) can be modulated by experience through neural plasticity and the related perceptual learning, but also by actual motivations through selective attention. Despite the fact that the research of pain perception, perceptual learning and of attentional mechanisms have been among the top research fields of cognitive neuroscience [18, 20, 28], very little is known about the interaction of these functions. This was the main reason for my choice to try to investigate these interactions.

It was long held that the topography of sensory areas was modifiable only during critical periods of development and could be considered "hard-wired" thereafter [26]. It is a fact that the plasticity of the human brain greatly decreases after approximately 6–10 years (at least for early sensory cortices) however in the later half of the 20th century, more evidence began to mount to demonstrate that the central nervous system does indeed adapt and is mutable even in adulthood; this broad idea is commonly termed neural plasticity. Neural plasticity refers to modulations and its different types and levels, which induce different extents of change in the neural system.

The dissertation – in line with the three theses – presents three studies. The experiments were carried out with various aims but it is common to all three that they represent examples of different

aspects of neural plasticity. The first thesis focuses on the topic of the interaction of attention, pain and –as a third factor- sensitization (few-hour modulation). The second thesis looks into the role of attention in relation to perceptual learning (as a result of one-week learning). The third thesis examines the spatio-temporal dynamics of the peri-personal spatial representation in relation to long term plasticity (when someone becomes an expert in a given field within a few years).

In the first experiment I aimed at investigating how distraction of attention from the noxious stimuli affects the perceived pain intensity in secondary hyperalgesia. Importantly, in this experiment I directly compared the attentional modulation of pain intensity reports during capsaicin-induced secondary hyperalgesia to that in the case of capsaicin-untreated, control condition [39, 53, 54].

In the second thesis, I review a study where I tested the hypothesis that perceptual learning involves learning to suppress distracting task-irrelevant stimuli [37, 46, 56, 57]. Moreover, parts of the EEG experiments in that study were to test whether attention-based learning influences perceptual sensitivity for the visual features present during training via modulating the sensory gain for the different features at the early stages of visual cortical processing and/or by biasing the decision processes at the higher processing stages.

In the experiment described in the third thesis, I examined whether the multisensory spatial information concerning sensory events are coded in a similar manner throughout peri-personal space

[43, 49] or might there instead be a difference between front and rear space (i.e. the space behind our backs), as a result of the existence of a detailed visual representations of the former but only occasional and very limited visual representation of the later [22, 27, 29]. To address this question, I compared the effect of crossing the hands on tactile temporal resolution when the hands were placed in front of participants versus when they were placed behind their backs. I compared two groups of participants, non-musicians as well as professional piano players, in order to uncover how extensive practice in playing piano – leading to altered tactile perception in pianists [25, 42] – will affect tactile temporal resolution performance in front and rear space in the latter group.

I believe that my results contribute to the better understanding of the human sensory system especially in relation to the attentional mechanisms and different aspects of plasticity.

This knowledge may also contribute to the diagnosis, monitoring and/or treatment strategies for adult patients with certain pathologic conditions within the sensory/ attentional system, like amblyopia [40], dyslexia, ADHD, chronic pain etc.

Methods Used in the Experiments

For my dissertation I worked with healthy normal subjects with the exception of the third study in which my participants were professional piano players. I used a wide array of experimental methods applicable in cognitive neuroscience research these included psychophysics, electrophysiology with classical ERP and several mathematical analytical approaches as well as functional magnetic resonance imaging (fMRI). I used several tasks: perceived pain intensity rating on a visual

analog rating scale (VAS); face orientation detection on rapid serial visual presentation (RSVP); 2-interval forced choice speed discrimination task (QUEST); motion coherence thresholds detection (QUEST); motion discrimination thresholds with constant stimuli in a 2-alternative forced choice procedure; color discrimination task; and pairs of suprathreshold vibrotactile stimuli-TOJs performance task. I used bone-conducting hearing aids (Oticon) for the vibrotactile stimulation. To deliver mechanical and pain stimuli 1. TOUCH TEST TM von-Frey sensory filaments of different strengths and 2. a custom made PC controllable MR-compatible mechanical stimulator were used, which is being developed and tested by the members of MR Research Center (Szentágothai J. Knowledge Center - Semmelweis University, MR-RC and Neurobionics Research Group, Hungarian Academy of Sciences - Pázmány Péter Catholic University - Semmelweis University). For the experimental presentation and for analyzing the data, I used MATLAB 7.1. (MathWorks, Inc., Sherborn, MA) with various toolboxes: Psychtoolbox 2.54 [15, 38] psignifit toolbox (ver. 2.5.6) for Matlab (http://bootstrap-software.org/psignifit/); Cogent 2000 Software Toolbox (Cogent, www.vislab.ucl.ac.uk/Cogent/); Statistica 8 (StatSoft Inc.). To track the eye position, I used an iView XTM HI-Speed eye tracker (Sensomotoric Instruments, Berlin, Germany). EEG data were acquired using a BrainAmp MR EEG system (Brain Products GmbH, Münich, Germany) from 60 (Ag/AgCl) scalp electrodes mounted in an EasyCap (Easycap GmbH, Herrsching-Breitbrunn, Germany, extended 10–20 System). EEG pre-processing and pre-analyzing was implemented using BrainVision Analyzer (Brain Products GmbH) and for the source localization BESA 5.2, (MEGIS softwareGmbh, Germany) was used. I performed fMRI data acquisition and analysis at the MR-RC on a 3 Tesla Philips Achieva scanner (Philips, Best, The Netherlands) equipped with an eight-channel SENSE head coil. Data analysis was performed using BrainVoyager QX (v 1.74; Brain Innovation, Maastricht, The Netherlands) and custom time series analysis routines written in Matlab.

New Scientific Results

Thesis I. Attentional modulation of perceived pain intensity in capsaicin-induced secondary hyperalgesia

Perceived pain intensity is modulated by attention. However, it was not known how pain intensity ratings are affected by attention in capsaicin-induced secondary hyperalgesia.

I. I have shown that perceived pain intensity in secondary hyperalgesia is decreased when attention is distracted away from the painful stimulus with a concurrent visual task. Furthermore, it was found that the magnitude of attentional modulation in secondary hyperalgesia is very similar to that in capsaicin untreated, control condition. Interestingly, however, capsaicin treatment induced increase in perceived pain intensity did not affect the performance of the visual discrimination task. Finding no interaction between capsaicin treatment and attentional modulation suggest that capsaicin-induced secondary hyperalgesia and attention might affect mechanical pain via independent mechanisms.

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Consistent with earlier findings showing that attention modulates pain perception [16, 17, 35, 36]. The results of the first experiment provide evidence that attention affects the perceived pain intensity of pinprick stimulation in capsaicin-induced secondary hyperalgesia and that the magnitude of attentional modulation is similar to that found in the capsaicin untreated, control conditions *(Fig 1.)*.
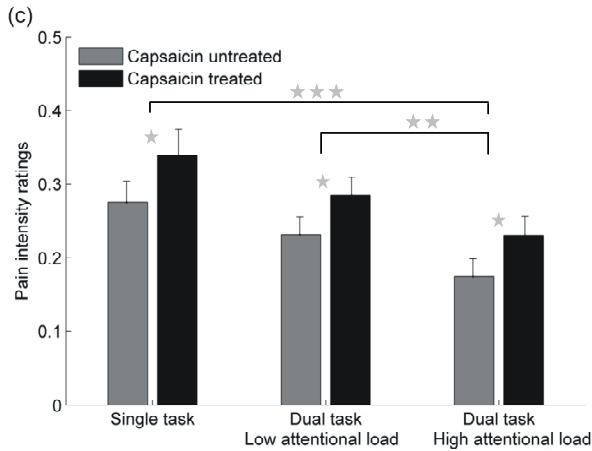

Figure.1 Attentional modulation of pain intensity ratings in the capsaicin untreated and capsaicin treated conditions in case of intermediate (300g) pinprick stimuli. Error bars indicate the SEM.

Nearly a decade of neuroimaging research has revealed that supraspinal activity is increased during mechanical hyperalgesia that is experimentally induced sensitisation by capsaicin in healthy volunteers. Increased activity is found in the brainstem, the thalami,

cerebellum, primary and secondary somatosensory cortices, insula and cingulate cortex [34, 58].

A recent study showed that it is the brainstem which is primarily responsible for the maintenance of central sensitization underlying secondary hyperalgesia, whereas activation of the cortical areas might be associated with the perceptual and cognitive aspects of hyperalgesia.

However, my results suggest that the short, 45 min sensitization period is restricted primarily to the brainstem mediated central sensitization mechanisms and involves very little or no modulation of anticipatory attentional processes.

Thesis II. Psychophysical and electrophysiological correlates of learning-induced modulation of visual motion processing in humans

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Gál, V., Kozák, L.R., **Kóbor**, I., Bankó, É.M., Serences, J.T., and Vidnyánszky, Z. (2009). Learning to filter out visual distractors. European Journal of Neuroscience, 29(8):1723-1731.

When learning to master a visual task in a cluttered natural environment, it is important to optimize the processing of task-relevant information and to efficiently filter out distractors. Previous studies have not examined how training influences the neural representation of task-irrelevant information to facilitate learning. Moreover, the mechanisms that suppress task-irrelevant information are not well understood.

Additionally, the time course of these attention-based modulations of neural sensitivity for visual features has not been investigated before. Another important unresolved question concerns the temporal dynamics of these attention-based learning effects on the neural responses to attended and neglected visual features.

II.1. **The results of my study propose that in cases when there is direct interference between task-relevant and task-irrelevant information that requires strong attentional suppression, training will actually produce decreased sensitivity for the task-irrelevant information.**

I investigated how training on a speed discrimination task affects perceptual sensitivity to different motion directions by measuring motion detection thresholds for three different directions before and after training [52, 55].

The results revealed that training had a strong effect on the observers' performance. The motion coherence threshold for the

task-relevant direction was significantly lower than the threshold for the task-irrelevant direction *(Fig. 2)* after training.
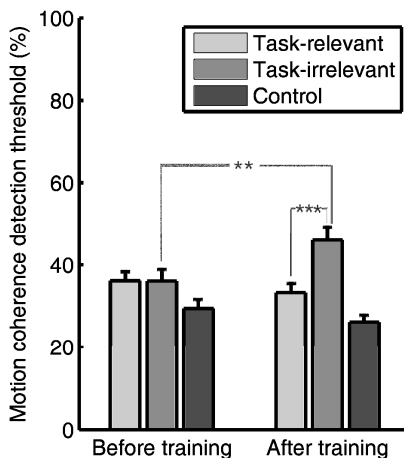

Figure 2. Perceptual sensitivity for the different motion directions. Before training, there was no difference between the motion coherence detection thresholds for the directions that were task-relevant and task-irrelevant during training as well as for a control direction. After training, sensitivity for the direction that was task-irrelevant during training was strongly reduced. Error bars indicate the SEM.

Furthermore, a comparison of the motion coherence thresholds before and after training reveals that thresholds for the task-relevant direction decreased non-significantly whereas thresholds for the irrelevant direction significantly increased.

Importantly, in this study, task-relevant and task-irrelevant stimuli were spatially overlapping and structurally similar. Therefore, the stimuli were likely competing for access to the same

neural processing mechanisms, which would be expected to drastically increase the amount of competition.

II.2. **I found that the strength of a coherent motion signal modulates the ERP waveforms in an early (300ms) and a late (500ms) time-window. The early component is most pronounced over the occipitotemporal cortex and may reflect the process of primary visual cortical extraction, the late component is focused over the parietal cortex and can be associated with higher level decision making mechanisms. I demonstrated training related modulation of the ERP in both the early and late time-windows suggesting that learning affects via modulating the sensory gain for the different features at the early stages as well as the integration and evaluation of motion information at decisional stages in the parietal cortex.**

The main goal of my EEG study was to test whether attention-based learning influences perceptual sensitivity for the visual features present during training via modulating the sensory gain for the different features at the early stages of visual cortical processing and/or by biasing the decision processes at the higher processing stages [32, 33, 41, 48, 50, 51].

My ERP results revealed that training on a task which requires object-based attentional selection of one of the two competing, spatially superimposed motion stimuli will lead to strong modulation

of the neural responses to these motion directions when measured in a training-unrelated motion direction discrimination task *(Fig. 3)*.
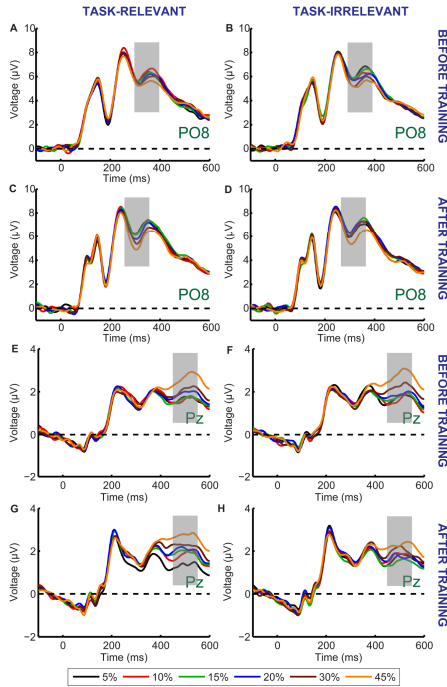

Figure 3. Grand average ERP responses shown for the PO8 (A-D) and Pz (E-H) electrodes. There was no difference between the ERP responses to the task-relevant (A,E) and task-irrelevant (B,F) directions before training. After training, the magnitude of motion signal strength dependent modulation of the ERP responses in the 300 -550 ms time interval is reduced in the case of task-irrelevant direction (D,H) compared to that in the case of task relevant direction (C,G). Different colors represent different motion coherence levels. Grey shaded bars indicate the time-windows where motion signal strength dependent modulations are most pronounced.

The first motion coherence-related peak reflects the initial, feed-forward stage of representing the coherent motion signal in visual cortex. The fact that the learning effects related to this early motion-related ERP peak was most pronounced over the occipital cortex is in agreement with previous electrophysiological and neuroimaging studies *(Fig. 4)*, [31, 41, 45, 48, 50].

Learning also had a strong effect on the late motion strength-dependent peak of the ERP responses *(Fig. 3)*. The late peak of motion coherence-dependent modulation might reflect decision processes related to the motion direction discrimination task. This interpretation is also supported by our results showing that the late ERP response peaked over the parietal cortex *(Fig. 4)*, [21, 47].
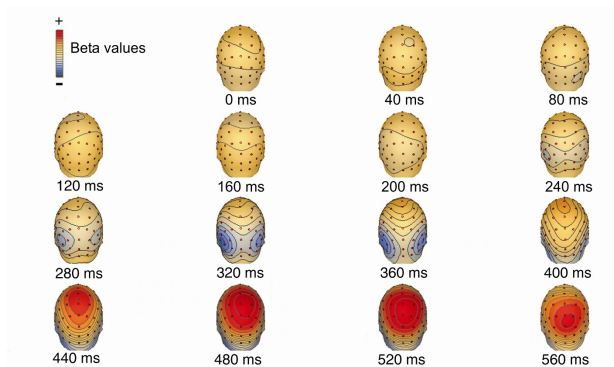

Figure 4. Spatial distribution of motion strength dependent modulation of the ERP responses: scalp maps of beta values related to task-relevant motion before training (the scalp map was similar to the map obtained in response to task-irrelevant motion.). The temporal evolution of the distribution shows an early (320-360ms) bilateral occipital and a late(480-520ms) parietal peak.

Thesis III. Spatiotemporal representation of vibrotactile stimuli

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Perceptual localization of tactile events are localized according to an externally-defined coordinate system, which is dominated by vision [22, 30]. The remapping of tactile stimuli from body-centred coordinates – in which they are coded initially – into external coordinates is fast and effortless when the body is in its "typical" posture but slow when more unusual body postures are adopted, such as crossing the hands [14, 23]. Moreover congenitally blind individuals do not show any such impairment in tactile Temporal Order Judgements (TOJ) as a result of crossing their hands [44].

Thus the following intriguing question arises: is the multisensory spatial information concerning sensory events coded in a similar manner throughout the peri-personal space or might there instead be a difference between front and rear space, as a result of the existence of detailed visual representations of the former but only occasional and very limited visual representation of the later?

III. I found that the spatiotemporal representation of non-visual stimuli in front versus rear space (in the human body-

based coordinate system) is different. My experiments show that crossing the hands behind the back leads to a much smaller impairment in tactile temporal resolution as compared to when the hands are crossed in front. My investigation have also revealed that even though extensive training in pianists resulted in significantly improved temporal resolution overall, it did not eliminate the difference between the temporal discrimination ability in front and rear space, demonstrating that the superior tactile temporal resolution I found in the space behind people's backs cannot simply be explained by incidental differences in tactile experience with crossed-hands at the rear versus in the front. These results suggest that the difference in the spatiotemporal representation of non-visual stimuli in front versus rear space originates in the differences in the availability of visual input.

I investigated differences in people's ability to reconstruct the appropriate spatiotemporal ordering of multiple tactile stimuli, when presented in frontal space (a region where visual inputs tend to dominate) versus in the space behind the back (a region of space that we rarely see) in professional piano players and in non-musicians.

I found that the lack of a visual reference frame in the representation of peri-personal space that leads to improved tactile temporal resolution at the rear space of sighted individuals *(Fig. 5)*, so my results raise the following intriguing possibility: namely, that the spatiotemporal representation of tactile stimuli in the space

behind the backs of sighted individuals – especially in those who are trained in tasks requiring fine spatiotemporal analyses of tactile information – are used as a normal model for the spatial representation of tactile information in congenitally blind individuals.
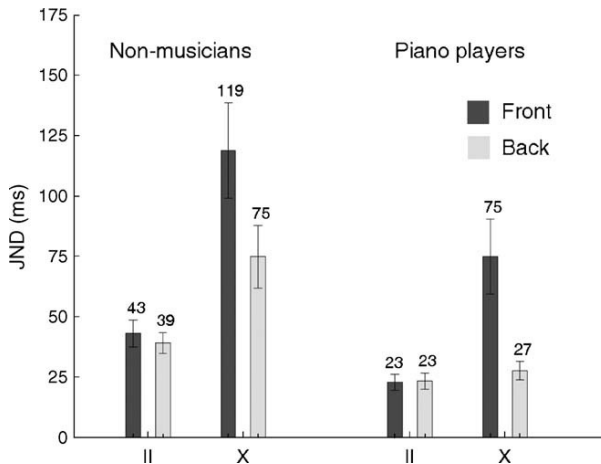

Figure.5 TOJ performance of the veridical group. Average JNDs (calculated by subtracting the SOA needed to achieve 75% performance from that needed to achieve 25% performance and dividing by two) are shown for the non-musicians and pianists for all four conditions tested (II = uncrossed posture; and X = crossed posture). JNDs were determined independently for all participants based on the slope of the Weibull functions that were fitted to the individual data obtained in the four conditions (see Fig. 3.3 for the Weibull fit to participants' mean performance). Error bars represent the between observer S.E.M.

The presented results also have important implications with respect to the learning processes leading to professional piano playing. Interestingly, it has also been shown that extensive practice

in playing the piano leads not only to improved motor skills but also to higher spatial tactile resolution in pianists as compared to non-musicians [42].

I showed for the first time that the temporal resolution of tactile stimuli is also significantly higher in professional piano players than in non-musicians. Thus, my results revealed that extensive piano practice has a broad effect on somatosensory information processing and sensory perception, even beyond training-specific constraints.

A possible application

I developed and experimentally compared three psychophysics methods to accurately and reproducibly measure subjective perception of pain and hyperalgesia induced by capsaicin treatment. I demonstrated that using these methods subjective pain perception can be well characterized even in case of a small number of subjects (N~10). My psychophysics experiments have shown that the exact temporal- and spatial parameters of stimulation greatly influence pain perception and the detection of hyperalgesia. I determined the optimal parameters for measuring secondary hyperalgesia evoked by capsaicin treatment – and in the background of which there is central sensitization.

My fMRI experiments demonstrated that in accordance with relevant earlier publications, BOLD responses in certain brain areas reflect primarily the subjective pain perception and not the intensity

of physical stimulation. Furthermore, my fMRI results have also demonstrated that several pain perception related brain areas (primarily in S2 and insula) stimuli of the same physical intensity result in bigger BOLD responses when the subjects perceive them as painful rather than as non-painful. The results of my psychophysics and fMRI experiments suggest that my behavioural biomarkers and my preliminary fMRI results could be applied to exactly and effectively measure subjective pain perception and changes in sensitivity to pain in both normal and pathologic (allodynia, hyperalgesia) circumstances.

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Publications

The Author's Journal Publications

[1] **Kóbor**, I., Füredi, L., Kovács, G., Spence, C., Vidnyánszky, Z. (2006). Back-to-front: Improved tactile discrimination performance in the space you cannot see Neurosci. Lett. 400(1-2):163-7.

[2] **Kóbor**, I., Gál, V., Vidnyánszky, Z. (2009). Attentional modulation of perceived pain intensity in capsaicin-induced secondary hyperalgesia. Exp. Brain. Res. 195(3):467-72.

[3] Gál, V., **Kóbor, I.**, Kozák. L.R., Bankó, É.M, Serences, JT., and Vidnyánszky, Z. (2010). Electrophysiological correlates of learning induced modulation of visual motion processing in humans. Front. Hum. Neurosci. 6;3:69.

[4] Gál, V., Kozák, L.R., **Kóbor**, I., Bankó, É.M., Serences, J.T., and Vidnyánszky, Z. (2009). Learning to filter out visual distractors. European Journal of Neuroscience, 29(8):1723-1731.

The Author's conference Publications

[5] **Kóbor**, **I.,** Füredi, L., Kovács, Gy., Spence, C., Vidnyánszky, Z. (2006): Back-to-front: Improved tactile discrimination performance in the space you can't see Annual Meeting of the Hungarian Neuroscience Society.

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