Abstract
Autism spectrum disorders (ASD) comprise a number of heterogeneous neurodevelopmental diseases characterized by core behavioral symptoms in the domains of social interaction, language/communication and repetitive or stereotyped patterns of behavior. In utero exposure to valproic acid (VPA) has evolved as a highly recognized rodent ASD model due to the robust behavioral phenotype observed in the offspring and the proven construct-, face- and predictive validity of the model. The number of parvalbumin-immunoreactive (PV+) GABAergic interneurons has been consistently reported to be decreased in human ASD subjects and in ASD animal models. The presumed loss of this neuron subpopulation hereafter termed Pvalb neurons and/or PV deficits were proposed to result in an excitation/inhibition imbalance often observed in ASD. Importantly, loss of Pvalb neurons and decreased/absent PV protein levels have two fundamentally different consequences. Thus, Pvalb neurons were investigated in in utero VPA-exposed male ("VPA") mice in the striatum, medial prefrontal cortex (mPFC) and somatosensory cortex (SSC), three ASD-associated brain regions. Unbiased stereology of PV+ neurons and Vicia Villosa Agglutinin-positive (VVA+) perineuronal nets (PNNs), which specifically enwrap Pvalb neurons, was carried out. Analyses of PV protein expression and mRNA levels for Pvalb, Gad67, Kcnc1, Kcnc2, Kcns3, Hcn1, Hcn2 and Hcn4 were performed. We found a ~15% reduction in the number of PV+ cells and decreased Pvalb mRNA and PV protein levels in the striatum of VPA mice compared to controls, while the number of VVA+ cells was unchanged, indicating that Pvalb neurons were affected at the level of the transcriptome. In selected cortical regions (mPFC, SSC) of VPA mice, no quantitative loss/decrease of PV+ cells was observed. However, expression of Kcnc1, coding for the voltage-gated potassium channel Kv3.1 specifically expressed in Pvalb neurons, was decreased by ~40% in forebrain lysates of VPA mice. Moreover, hyperpolarization-activated cyclic nucleotide-gated channel (HCN) 1 expression was increased by ~40% in the same samples from VPA mice. We conclude that VPA leads to alterations that are brain region- and gene-specific including Pvalb, Kcnc1 and Hcn1 possibly linked to homeostatic mechanisms. Striatal PV down-regulation appears as a common feature in a subset of genetic (Shank3B-/-) and environmental ASD models.

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Functional alterations of the praxis network underlying limb kinetic apraxia in Parkinson's disease

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Parkinson's disease (PD) patients frequently suffer from dexterous deficits, which adds to the burden of the disease. Recent studies indicate that impaired dexterity may stem from limb kinetic apraxia (LKA) rather than core symptoms of PD. LKA is a disorder of fine finger movements not explained by bradykinesia. We hypothesized that altered activation and functional connectivity in brain areas involved in praxis planning and execution may underlie dexterous deficits in PD. We used functional magnetic resonance imaging (fMRI) to investigate the underlying neural mechanisms of LKA. Therefore, we used coin rotation (CR) task paradigm for limb kinetic apraxia and the finger tapping (FT) paradigm for bradykinesia. CR performance was significantly impaired in patients, thus pointing to a limb kinetic deficit. fMRI analysis revealed a significant task x group interaction in the left praxis network regardless of the motor output. Post-hoc t-tests revealed increased fMRI activation of the left inferior parietal lobe, superior parietal lobe and ventral premotor area during CR task in patients. Furthermore, whole-brain connectivity analysis revealed that the left inferior parietal lobe showed increased connectivity to the bilateral posterior hippocampi and decreased connectivity to the right the dorsolateral prefrontal cortex in patients compared to controls.
We revealed a differential activation of the left praxis network underlying dexterous deficits in Parkinson's disease, corroborating the behavioral dissociation of limb kinetic apraxia and bradykinesia. Moreover, altered connectivity of the praxis networks might reflect an insufficient compensatory mechanism that possible adds to dexterous deficits.

Cross-modal processing differentially affects attentional deployment in right-hemispheric patients with and without neglect

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Search tasks with cross-modal spatial cueing have been shown to improve healthy participants' search performance. However, the effects of such multisensory processing on the spatial deployment of attention in neurological patients with attentional disorders, particularly in patients with left-sided neglect, is not yet fully understood. The aim of the present study was thus to investigate the effects of cross-modal spatial cueing on the performance in a visual search task in patients with right-hemispheric lesions, with and without left-sided neglect. Two groups of patients with right-hemispheric lesions (with and without left-sided neglect) and a group of age-matched healthy controls completed a search task with cross-modal spatial cueing, i.e., a visual search task with spatially congruent, incongruent, non-informative, and without auditory cues. To further assess participants' accuracy in localizing the auditory cues, a unimodal sound localization task was also administered. Preliminary data analyses revealed that, in the unimodal visual search condition (i.e., without auditory cues), as expected neglect patients showed a worse performance for left- than right-sided targets. Additional auditory cues affected search performance exclusively in the left hemifield: spatial congruency improved search performance, incongruence deteriorated it, and spatially non-informative cues had no effect. Critically, patients' sound localization accuracy modulated these effects, as indicated by the results of the control task. In healthy participants and in right-hemispheric patients without neglect, visual search performance was affected both in the left and the right hemifield. Yet, whereas healthy controls showed no left/right asymmetries in performance, such asymmetries emerged with the additional presentation of a congruent auditory cue in right-hemispheric patients without neglect. The findings of the present study demonstrate that multisensory processing differentially influences spatial attentional deployment in patients with right-hemispheric lesions with or without neglect: in neglect patients, congruent auditory cues decreased, and incongruent auditory cues increased attentional asymmetries; in right-hemispheric patients without neglect, congruent auditory cues led to the emergence of an attentional asymmetry. Overall, these results are of potential relevance for neurorehabilitative trainings in patients with right-hemispheric lesions, both with and without neglect.