current study we aimed to compare the potential specificity of the role of GAD 65 in anxiety and in learning under stress, by comparing modulation of its expression in the VH compared to the dorsal hippocampus (DH). We used a lentivirus vector to down regulate GAD 65 directly in the ventral or dorsal hippocampus of adult SD rats (VH GAD65 Vs DH GAD65). The experiment groups were compared to control groups, which were injected with a control virus. The Elevated Plus Maze (EPM) test was performed in order to test changes in anxiety behavior. Learning ability and stress coping behavior were measured in the two-way shuttle test (TWS). VH GAD65 rats spent more time in the open arms and exhibited higher mobility rates, indicative of lower levels of anxiety. DH GAD65 rats did not display any changes in levels of anxiety relative to control. As for the learning abilities tested in the TWS, while Rats injected with the control virus showed high rates of performance, the VH GAD65 virus injected rats were impaired. DH GAD65 KO rats did not display any indication of learning. These results suggest that GAD65 down regulation in the VH leads to increased anxiety effects in rats and to a mild impairment in learning under stress. However, GAD65 down regulation in the DH, while does not alter anxiety levels, induces severe impairment in the ability to cope under stress. The results suggest that GAD65 expression contributes to the more emotional role of the VH and to the more cognitive role of the DH.

Intermittent explosive disorder: characterizing the phenotype through brain-behavior modeling

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Intermittent explosive disorder (IED) is quite prevalent and can complicate course of illness and recovery across many psychiatric disorders. Although explosive anger takes a heavy toll on patients and their victims, this problem is severely understudied. Here we present a series of fMRI paradigms interrogating basic brain and behavior mechanisms of IED. Compared to controls, results from the color-word Stroop task revealed higher (less optimized) error-related activity in IED in two core task regions relevant to conflict monitoring, error processing and cognitive control (anterior cingulate and dorsolateral PFC). Results from threat Stroop revealed higher activation to threat words in thalamus and parahippocampus and lower activation in dorsomedial PFC in IED . From the passively viewed emotional pictures, two-way interactions between group x valence emerged in the right pallidum/thalamus and midcingulate. Group x arousal were found in bilateral inferior frontal gyrus, right medial PFC, and pallidum (For all, p-uncorrected < 0.005). These interactions show abnormalities in PFC regulation and limbic reactivity in IED in both intensely pleasant or negative stimuli. Notably, across participants and tasks, trait anger correlated with activations in most of these regions of difference: pallidum/thalamic ($r = -0.485$, $p < 0.05$) midcingulate ($r = 0.505$, $p < 0.05$) and dorsolateral PFC ($r=0.41$, $p < 0.005$). The emerging brain behavior patterns in IED suggest a deficit in executive function commonly observed in disorders of self-control, while pointing to subcortical (instead of prefrontal) management of threat and emotional stimuli of intense valence and arousal. It appears that underlying these abnormalities in IED are their individual differences in trait anger. Treatment strategies might be focused on strengthening cortical control while reappraising hyper-responsivity to emotionally arousing cues.

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Small Molecule Scavengers for mitigating nerve agents poisoning: in vitro and in vivo efficacy

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The need for more effective medical countermeasures toward toxic organophosphorus (OP) nerve agents was accentuated by the recent tragic events in Syria. In contrast toenzyme bioscavengers that may create immunogenic response and excessivepayload due to their large molecular size (MW 40-80KD), we have developed new small molecules scavengers (SMS, MW 300-600D) for active detoxification of nerveagents. The molecular design was based on combining two functions in onemolecule i.e. direct degradation of OPs and reactivation of OP-inhibited AChE. Degradation of OPs was achieved by substituted benzhydroxamic (BHA) and pyridinehydroxamic acid (PHA) derivatives. Certain BHAs and PHAs were coupled via various linkers to pyridine oximes providing hybrid compounds. Thus, 12 new bifunctional SMS were synthesized. Two hybrid compounds 2-PAM-Pr-4PHA (PAPP) and 2-PAM-Me-BHA (PAMB) displayed rapid detoxification toward sarin, cyclosarin and soman as well as reactivation toward OP-AChE in *vitro*. PAPP displayed a 10-fold faster kinetics than 2-PAM toward cyclosarin-inhibited AChE. Both hybrid compounds exhibited high decontamination activity (88-98%) toward VX on pig-ear skin in *vitro*. PAPP and PAMB are relatively non-toxic compounds LD_{50}, im >568, 508 μmole/kg in rats and 144, 203 μmole/kg in guinea pigs, respectively. Pharmacodynamics (PD) of PAPP and PAMB in rats in pre- and post-exposure to $0.8xLD_{50}$sarin demonstrateda