of both receptors have created a new hypothesis about the cortisol effects on behaviour and sleep (De Kloet et al, 1999; Lupien et al, 2007). Elevated levels of cortisol due to stress have commonly detrimental effects on performance, such as on memory, but it is more than once reported that cortisol could have positive effects on cognition. The Type I/Type II ratio hypothesis suggests that performance by cortisol can be enhanced when Type I receptors are activated. However, when both Type I and Type II receptors are saturated, shifting the ratio towards Type II occupancy, performance and sleep are affected. It is in this way that the double function of cortisol as a sleep/wake–hormone as well as a stress-hormone, can be understood. The hypothesis is now that the inverted-U shaped relationship between arousal and stress at one side and behavioural and cognitive performance at the other, might be explained by the presence of two different types of glucocorticoid receptors.

THE NEUROSCIENTIFIC BASIS OF EVIDENCE-BASED TREATMENTS FOR PTSD – A SELECTIVE REVIEW

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Key words: posttraumatic Stress Disorder , selective serotonin reuptake inhibitors, memory, cognitive behavioral therapies

Posttraumatic Stress Disorder (PTSD) includes a) exposure to a significant traumatic event, b) intrusive recollections, c) avoidant symptoms d) increased physiological arousal or amnesia for the traumatic event). While up to 90% of the US adult civilian population has a lifetime exposure to at least one significant traumatic event, only 8-10% develop PTSD. While PTSD can result in significant morbidity and dysfunction, evidence-based treatments can now be matched with an emerging understanding of underlying neurobiology.

Meta-analysis demonstrates that certain selective serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs) are superior to placebo in attenuating PTSD symptoms. Unfortunately, the effect size is small (0.23), side-effects are common and these drugs may be less efficacious when PTSD results from combat trauma rather than from civilian trauma.

Recurring nightmares of the triggering event contribute to the sleep disturbances that affect some 70% of patients with PTSD. Although available data unequivocally support the efficacy (effect size ~ 1.0) of prazosin, an α1-adrenergic receptor antagonist, it remains underutilized in most clinical settings.

Patients with PTSD are more sensitive to the anxiogenic effects of an intravenously administered 5HT2C agonist or an adrenergic α2 receptor antagonist. This suggests that SSRIs and SNRIs may act by downregulation hypersensitive 5HT2C receptors. Analogously, since presynaptic α2 receptors are inhibitory to efflux of noradrenaline, symptoms of PTSD could be mediated by excessive stimulation of postsynaptic α1 receptors. Prazosin may act to attenuate this stimulation.

Brain regions involved in modulation of emotion, such as the dorsal and rostral anterior cingulate cortices, as well as the ventromedial prefrontal cortex show decreased activity in PTSD, resulting in excessive input from the amygdala, an evolutionarily older brain region dominant in threat responses. Thus, PTSD can be conceptualized as a dysregulation of brain circuits that integrate historical information of a traumatic event (memory) and autonomic responses.

Fortunately, memory storage is not a onetime event but a process repeated with each use of that memory. Retrieval of a memory renders it temporarily available for modification at the cellular and systems level. This principle is thought to underlie several independently developed psychotherapeutic approaches. The observation that recurring, disturbing thoughts of PTSD could be permanently abolished, if the subject's eyes were automatically moving in a multi-saccadic manner while the disturbing thought was

being held in consciousness, catalyzed the development of Eye movement desensitization and reprocessing therapy (EMDR). Analogous neurobiological mechanisms are likely operative in other trauma focused cognitive behavioral therapies (TFCBTs). Indeed, the favorable side effect profile and relatively large effect sizes (~ 1.0) of EMDR and TFCBTs have led to their designation as first line treatments for PTSD, ahead of pharmacological approaches. Available studies show that EMDR and TFCBTs affect memory-driven activation of cortical regions implicated in emotional processing, including the amygdala.

Neuroscience provides a mechanistic explanation for current, evidence-based treatments for PTSD and promises to facilitate developments of additional treatment approaches. Such somatic and psychotherapeutic modalities should be considered part of a balanced, biopsychosocial approach to recovery and rehabilitation for individuals with PTSD.

HOW PATHOGENIC BACTERIA PROFIT FROM YOUR STRESS

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Key words: Crohn's disease, inflammation, Escherichia coli, oligomannose glycans

Crohn's disease (CD) is a life-long chronic disorder characterized by intestinal inflammation. Current treatments for CD are directed towards abnormal immune responses rather than the intestinal bacteria that trigger intestinal inflammation.

Disease-molecular aspects: Adherent-Invasive Escherichia coli (AIEC) bacteria abnormally colonize the ileal mucosa in a subgroup of CD patients. Here we elucidate mechanisms by which clinical isolates of adherent-invasive *Escherichia coli* (AIEC) initially penetrate into the epithelial cell layer, replicate, and establish biofilms in Crohn's disease. AIEC utilises the type-1 fimbrial fimbrial FimH adhesin to bind to oligomannose glycans on the surface of host cells. Oligomannose glycans, exposed on early apoptotic cells, are the preferred binding targets of AIEC, so apoptotic cells serve as entry points for bacteria into the epithelial cell layer. Thereafter, the bacteria propagate laterally in the intercellular epithelial spaces. We demonstrate oligomannosylation at 2 distinct sites of a glycoprotein receptor for AIEC, the carcinoembryonic cell adhesion molecule 6 (CEACAM6 or CD66c) on human intestinal epithelia. The presence of the highest-affinity binding target of FimH (oligomannose-5 glycan) on CEACAM6 is demonstrated using LC-MS/MS. FimH interacts with CEACAM6, which then clusters. As mannose-dependence is omnipresent in microbial infections, this mechanism of colonization could also apply to other adherent-invasive pathogens.

Healing from the disease: AIEC can promote or perpetuate chronic inflammation and are therefore an interesting therapeutic target. Various strategies that target these *E. coli* strains have been developed to promote their intestinal clearance. Here, we review current AIEC-targeted strategies, especially anti-adhesive strategies that are based on the development of FimH antagonists. We discuss their potential as personalized microbiota-targeted treatments for CD patients abnormally colonized by AIEC.A large panel of mannose-derived FimH antagonists has been tested for their ability to inhibit E. coli adhesion to host cells. Documented reports suggest that monovalent mannosides are promising candidates