

mental illness. We aimed to develop a standardised assessment of need for pregnant women and mothers with severe mental illness.

**Methods:** Staff and service users identified relevant domains of need. Professional experts and service users were then surveyed and asked to rate the importance of the domains of the CAN-M (Camberwell Assessment of Need – Mothers). Reliability was established using 36 service user-staff pairs. Concurrent validity was assessed with the Global Assessment of Functioning.

**Results:** Inter-rater and test-retest reliability coefficients for unmet needs indicated excellent reliability. Relevant CAN-M domains correlated with the Global Assessment of Functioning symptom ( $p=0.05$ ) and disability ( $p < 0.01$ ) subscales.

**Conclusions:** The CAN-M is a reliable, valid instrument for assessing the needs of pregnant women and mothers with severe mental illness.

Nicotinic cholinergic mechanisms in the regulation of brain DNA-methyltransferase 1 (DNMT1) expression

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Perturbation of epigenetic mechanisms, which is likely associated with an overexpression of DNA-methyltransferase 1 (DNMT1) in telencephalic GABAergic neurons of schizophrenia (SZ) patients, participates in the pathophysiology of cognitive disorders.

We hypothesize that tobacco abuse, which is very frequent in SZ patients, may be an attempt to self-medicate cognitive dysfunction by reducing DNMT1 overexpression.

In mice treated with nicotine (4.5mg/kg/sc twice a day for 5 days) and decapitated 2,4,8,12 or 24 hrs after the last dose of nicotine, we counted the number of DNMT1 mRNA- and protein-positive neurons in various brain areas using a two-dimensional counting method.

Mice receiving nicotine exhibited a 30-40% decrease in the number of DNMT1 mRNA- and protein-positive neurons in layers I and II of cingulate, piriform, somatosensory cortices and caudate-putamen. A single dose of nicotine causes only marginal changes in DNMT1 mRNA expression.

The high affinity nicotinic receptor antagonist mecamylamine (2mg/kg/sc twice a day for 5 days) given along with nicotine attenuates the nicotine-induced decrease of DNMT1 mRNA-positive neurons in various brain areas.

We also found that cortical layer I and hippocampal GABAergic neurons include high levels of  $\alpha 4$  and  $\alpha 7$  nicotinic acetylcholine receptor (nAChR) subunits which can then mediate the action of nicotine on GABAergic interneurons. The observation that repeated injections of nicotine decrease the DNMT1 mRNA and protein expression in telencephalic layer I and II cortical GABAergic neurons suggests that in these neurons, nAChR may have an impact on the epigenetic modulation of chromatin remodeling.

Correlation between serum androgen levels and neuropsychological functions in schizophrenia

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**Background:** Older literature had repeatedly documented that physically frail male schizophrenics tended to be withdrawn with apathy, blunted affect and poor prognosis. However, in female

schizophrenics, signs of virilism portend poor prognosis and severe deterioration. Three published studies of 92 male schizophrenics, from India, Iran and Japan, showed negative correlations between testosterone (T) levels and negative symptoms.

**Methods:** Twenty-eight (18 male and 10 female) patients, aged 25-67 (mean=34.8) years, who fulfilled DSM-IV TR criteria for schizophrenia were selected, with the approval of local ethical committee. Serum levels of T, dihydrotestosterone and DHEA were estimated by radioimmunoassay. Neuropsychological tests were administered for each patient. Pearson correlation test, linear regression analysis and independent 't' test were used for statistical analysis.

**Results:** Mean PANSS score for all 28 patients was 82.3; 18 patients had predominantly positive symptoms and 10 had predominantly negative symptoms. Independent 't' test did not show any significant difference for any of the serum hormone levels between the groups of patients based on PANSS scores. However, when women were excluded, T levels were significantly lower in negative symptom dominant group ( $p=0.05$ ). A correlation between serum T levels, but not of other hormones, and the total scores on all neuropsychological test results was also noted ( $p=0.017$ ); verbal fluency showed the greatest correlation, followed by working memory. But when women were excluded, this significance disappeared.

**Conclusions:** Negative symptoms correlate negatively with T levels, but only in men. Neuropsychological findings correlate with T levels as well.

Functional dissection of SLITRK1 signaling

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**Background and aims:** Tourette syndrome (TS) is a neuropsychiatric disorder characterized by motor and vocal tics and associated complex behavioral abnormalities. There is strong support for a genetic basis to the disorder, however, the precise pattern of transmission and the identification of underlying genes has remained elusive. Recently, mutations in a gene termed SLIT- and NTRK-like family, member 1 (SLITRK1) have been shown to lead to rare forms of TS and associated disorders. The SLITRK family (SLITRK 1-6) includes neuronal transmembrane proteins that can control neurite outgrowth. Structurally, SLITRK family members are characterized by two leucine-rich repeat (LRR) domains located on the extracellular/intralumenal domain, a single transmembrane domain, and an intracellular/cytoplasmic domain that is of varying lengths. SLITRK1 has a cytoplasmic domain that is most different from the others, being both the shortest (53 amino acids), and lacking conserved potential sites of tyrosine phosphorylation. We are using molecular methods to dissect SLITRK1 signaling and metabolism.

**Methods:** We developed a bait from the human SLITRK1 protein and used it to screen libraries for SLITRK1-interacting proteins. In addition, we studied the metabolism of SLITRK1 in situ.

**Results:** We completed screens of both an adult and a fetal brain library and are characterizing the validated SLITRK1-interacting proteins. We have also characterized SLITRK1 metabolism and the effects of SLITRK1 mutations on its metabolism.

**Conclusions:** SLITRK1-interacting proteins may represent susceptibility loci for TS and related disorders, and are likely involved in the development of the central nervous system.