see attachment

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Cognitive deterioration is a major problem that can interfere with all areas of a person's life, including work, school and the social relationships. Moreover, it represents a symptom of different pathological conditions such as schizophrenia, depression but it is also associated with aging.

On these bases, it is important to characterize cognitive dysfunctions in order to identify the molecular mechanism underlying, which may represent an important target for drug intervention.

To this aim, adult male Wistar rats were exposed to chronic mild stress (CMS), a well-established model of depression, for 7 weeks before being tested in the novel object recognition (NOR). The animals were then sacrificed immediately after the end of the test session for the molecular analyses.

We found that, independently from the anhedonic phenotype, CMS rats showed a deficit in the NOR test, which is associated with an inability to phosphorylate GluN2B subunit on Ser1303 and to activate the mTOR pathway. In agreement with the role of these systems in the control of local protein synthesis, we observed an increase phosphorylated of the eukaryotic Elongation Factor 2 (eEF2) in the crude synaptosomal fraction after the NOR test specifically in control animals. Moreover, this activation is associated with a significant increase of oligophrenin-1 and of Bmal1 protein levels specifically in the control animals exposed to the NOR test.

In summary, our results suggest that the correct performance in a cognitive test is associated with the translation of specific mRNAs at synaptic levels and that the cognitive deficits due to chronic stress exposure are due to alterations of this mechanism. Moreover, we highlighted a fundamental role of the elongation step in the correct cognitive performance. It may be inferred that pharmacological intervention able to normalize these alterations might improve cognitive function in patients with major depression and stress-related disorders.