GAL is involved in mood regulation, including depression-related and anxiety-like behaviors. Activation of GALR1 and GALR3 receptors results in a depression-like behavior while stimulation of GALR2 receptor leads to anti-depressant-like effects. Moreover, GAL modulates 5-HT1A receptors (5-HT1AR), a key receptor in depression at autoreceptor and postsynaptic level in the brain. This interaction can in part be due to the existence of GALR1-5-HT1AR heteroreceptor complexes in discrete brain regions [5]. Not only GAL but also the N-terminal fragments like GAL(1–15) are active in the Central Nervous System [2, 3]. Recently, we described that GAL(1–15) induces strong depression-related and anxiogenic-like effects in rats, and these effects were significantly stronger than the ones induced by GAL [4]. The GALR1-GALR2 heteroreceptor complexes in the dorsal hippocampus and especially in the dorsal raphe (DR), areas rich in GAL(1–15) binding sites [5] were involved in these effects [4, 6] and demonstrated also in cellular models.

In the present study, we have analyzed the ability of GAL(1–15) to modulate 5-HT1AR located at postsynaptic sites and at the soma-dendritic level in rats. We have analyzed the effect of GAL(1–15) on the 5-HT1AR-mediated response in a behavioral test of depression and the involvement of the GALR2 in these effects. GAL(1–15) enhanced the antidepressant effects induced by the 5-HT1AR agonist 8-OH-DPAT in the forced swimming test [7]. These effects were stronger than the ones induced by GAL. The mechanism of this action involved interactions at the receptor level in the plasma membrane with changes also at the transcriptional level. Thus, GAL(1–15) affected the binding characteristics as well as the mRNA level of 5-HT1AR in the dorsal hippocampus and DR. GALR2 was involved in these effects, since the specific GALR2 antagonist M871 blocked GAL(1–15) mediated actions at the behavioral and receptor level [7].

Furthermore, the results on the proximity ligation assay (PLA) in this work suggest the existence of GALR1-GALR2-5-HT1AR heteroreceptor complexes since positive PLA were obtained for both GALR1-5-HT1AR and GALR2-5-HT1AR complexes in the DR and hippocampus. Moreover the studies on RN3B cells, where GALR1, GALR2 and 5-HT1AR exist [4], also showed PLA-positive clusters indicating the existence of GALR1-5-HT1AR and GALR2-5-HT1AR complexes in these cells [7].

In conclusion, our results indicate that GAL(1–15) enhances the antidepressant effects induced by the 5-HT1AR agonist 8-OH-DPAT probably acting on GALR1-GALR2-5-HT1AR heteroreceptor located at postsynaptic sites and at the soma-dendritic level. The development of new drugs specifically targeting these heteroreceptor complexes may offer a novel strategy for treatment of depression.

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S20: Finding Autism Before Diagnosis: identification of very early signs of autism spectrum disorders in human and mice

Chair: Noboru Hiroi, USA
Co-Chair: Jae Won Kim, Republic of Korea

Speaker 1: Katarzyna Chawarska, USA
Title: Attentional signatures of autism in infancy: Studies of siblings at risk for ASD
Abstract
Due to familial factors, younger siblings of children with Autism Spectrum Disorder (ASD) are at an increased risk for developing the disorder\(^1\). Although behavioral symptoms of ASD typically emerge during a child’s second year,\(^2\) recent work on younger siblings demonstrates that prodromal features of ASD are present already within the first months of life. These features include atypical attention toward stimuli relevant to social engagement, such as faces and speech sounds.\(^3\,4\) Similar deficits were observed in clinic-referred toddlers suggesting continuity of social attention impairments in ASD from prodromal to early syndromal stages.\(^5\,6\) This presentation will review: (1) the methodological underpinnings of prospective high-risk sibling studies and findings on patterns of autism onset in infancy, and (2) experimental studies on endo- and exogenous attention to multimodal social stimuli conducted during prodromal and early syndromal stages of the disorder.

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Speaker 2: Gianluca Esposito, Italy
Title: Atypical infant cries among incipient ASDs, developmentally delayed individuals, and language-impaired individuals

Abstract
To better understand social communication during early human development, a growing literature is assessing the vocal production of children with Autism Spectrum Disorders (ASD). Previous studies have provided preliminary evidence that disruptions in cry acoustics may be part of an atypical vocal signature of autism early in life.

In the current research we investigate the acoustic characteristics of cries elicited during real life events as well as cries elicited in experimentally standardized social interaction contexts (i.e. the Strange Situation Procedure - SSP).

Using these approaches, we found that 15-month-olds at high risk for ASD had atypical acoustical patterns of distress vocalization (e.g. shorter cry utterances, higher fundamental frequencies). Then, next step was to assess using multiple neuroimaging and electrophysiological techniques (EEG, EMG, GSR, etc) the effect on parental perception of ASD distress vocalizations. Perceived distress engendered by ASD cries related to increased activation in brain regions associated with emotional processing.

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Speaker 3: Elodie Ey, France
Title: Subtle abnormalities in the vocal behavior of mouse pups mutated in Shank2

Abstract
Mutations in genes coding for synaptic proteins were shown to increase susceptibility to autism spectrum disorders (ASD)\(^1\).\(^2\) Recently, the synaptic scaffolding protein PROSAP1/ShANK2 has been associated with ASD\(^3\)\(^–\)\(^6\). The mouse model lacking Shank2 displayed abnormal glutamatergic receptor expression and neurotransmission. Abnormalities in body weight as well as in vocal behavior emerged in the first two weeks of life of Shank2\(/-\) mice. We highlighted a different profile in the emission rate of pup isolation calls between Shank2\(/-\) mice and their wild-type littersmates. We did not highlight any significant genotype-related differences in the vocal repertoire used, in the organization of call types and in the acoustic structure. In this mouse model, subtle abnormalities in usage of ultrasonic vocalizations during development precede impairments in social communication in adulthood. Indeed, in adult Shank2\(/-\) mice, impairments in social interactions emerged together with abnormalities in usage and structure of ultrasonic vocalizations\(^4\). Together with other mouse models of ASD, the Shank2\(/-\) mice provide a comprehensive framework to identify new knowledge-based treatments.

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Speaker 4: Noboru Hiroi, USA
Title: Structure and function of neonatal social communication in a genetic mouse model of autism

Abstract
A critical step toward understanding autism spectrum disorder (ASD) is to identify both genetic and environmental risk factors. A number of rare copy number variants (CNVs) have emerged...