bootstrap function in Haploview 3.2. Progranulin levels were compared by using the Kurskall-Wallis one way analysis of variance with Dunn's method for multiple comparisons.

Results: Five hundreds and 8 patients with BD (237 patients) and SKZ (271 patients) were included in the sample, with a mean age of 48.99±0.65 years and a mean age at onset of 28.30±047 years. The control group consisted of 567 German volunteers matched for ethnic background and age. Plasma samples were collected from 87 BD patients and 29 matched controls. A decreased allelic frequency of the minor versus the wild-type allele was observed for rs2879096 (23.2 versus 34.2%, $P < 0.001$, OR: 0.63, 95%CI: 0.49–0.80), rs4792938 (30.7 versus 39.7%, $P = 0.005$, OR: 0.70, 95%CI: 0.55–0.89) and rs5848 (30.3 versus 36.8, $P = 0.007$, OR: 0.71, 95%CI: 0.56–0.91). Progranulin plasma levels were significantly decreased in BD as compared with controls (89.69±3.97 ng/ml and 116.14±5.80 ng/ml, respectively, versus 180.81±18.39 ng/ml $P < 0.01$) and were not correlated with age.

Conclusions: Taken as a whole, GRN variability seems to decrease the risk to develop BD and SKZ, and progranulin plasma levels were significantly lower in patients vs controls. Nevertheless, a larger replication analysis is necessary to confirm these preliminary results.

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P.1.020 Forced swim stress enhances the survival of new dentate gyrus neurons in rat through a glucocorticoid receptor-dependent mechanism

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Adaptive and coping behaviours such as immobility in the forced swim (FS) retest are dependent on successful memory formation during initial training/tests. It has been suggested that stressful learning paradigms such as Morris water maze learning lead to enhanced survival of newly born neurons in the dentate gyrus (DG) and that these newly generated neurons may be involved in long-term memory formation. We have previously identified a signaling pathway, involving activation of ERK1/2 (extracellular signal-regulated kinase1/2), MSK1 (mitogen- and stress-activated kinase1), and Elk-1 (ets-domain-containing protein1) signaling molecules and activated within DG granule neurons following FS, which results in distinct epigenetic changes and induction of immediate early genes (IEGs; e.g. c-Fos/Egr-1) and the consolidation of the adaptive behavioural immobility response [1,2]. Glucocorticoid hormones, released as part of the stress response and acting via glucocorticoid receptors (GRs), enhance signaling through the ERK1/2/MSK1-Elk-1 pathway and thereby increase the impact on epigenetic and gene expression mechanisms. We aimed to determine if this signaling pathway leading to IEG induction is activated specifically in young adult-born dentate neurons following FS. Rats were injected twice daily for 5 days with BrdU to label new neurons. One, six or twelve weeks after BrdU treatment the rats were forced to swim (15 min, 25ºC-water), before being killed 1h later and tissue analyzed by immunofluorescence. FS-induced c-Fos was observed at all time points but there was no co-localization of the IEG with BrdU. Next, given that experiences during the first 1–2 weeks of a young adult-born DG neuron's life is important for its survival [3], we studied whether FS would promote neuronal survival. Rats were injected with BrdU for 5 days and split into groups: control and FS groups. The FS group underwent a 15-min FS challenge one week after the BrdU injections, whereas the control group remained in their home cages. Four weeks after the initial FS test both groups (i.e. control group and FS group) underwent another FS procedure and killed 1h later. The FS group, which had undergone a FS challenge four weeks previously, showed significantly more immobility

behavior compared with controls ($n = 8$, $p < 0.01$, Students t-test), indicating that they had remembered the initial FS test. No co-localization of c-Fos with BrdU was found in either group. The number of BrdU-positive neurons was higher in the dentate gyrus of the FS group (19.6 ± 2.1 neurons, $n = 8$) than in control animals (12.0 ± 1.1 neurons, $n = 4$) ($p < 0.03$, Student's t-test). To investigate a role of GRs in the survival-promoting effect of FS we pre-treated rats with the GR antagonist RU486 before the initial FS challenge. RU486 impaired the behavioural immobility response in the 4-week retest ($n = 7$/group; $p < 0.01$, post-hoc Bonferroni test) and abolished the FS-evoked increase in neuronal survival compared with the vehicle-pre-treated group ($n = 5$/control group, 7/FS group; $p < 0.001$, post-hoc Bonferroni test). Thus, a single FS challenge promotes the survival of new adult-born DG granule neurons, which requires GR activation at the time of the stressful challenge and which may contribute to the formation of long-term memories of the FS event.

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P.1.021 Longitudinal changes of N-acetyl-aspartate in early onset psychosis

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Background/Purpose of the study: Early-onset psychosis (EOP) is a severe condition which has been associated with a number of developmental disturbances and alterations of the brain. Low concentrations of N-Acetyl-Aspartate (NAA) are interpreted as a biological marker of changes in neural integrity. Studies using Proton Magnetic Resonance Spectroscopy (H-MRS) have shown reduced NAA levels in the Dorsolateral Prefrontal Cortex (DLPC) in both chronic and first-episode psychotic patients [1–2]. Reduction of frontal NAA levels has been described as a good predictor for poor outcome in psychosis [3]. However little is known about the course of these abnormalities as none of them where longitudinal studies or examine the changes of NAA levels over time in first episode early onset psychoses.

Hypothesis: NAA levels in the Dorsolateral Prefrontal Cortex will differ between patients with EOP and healthy controls at baseline and at two years follow-up. The objectives of the present study were: (1) To study the of n-acetyl-aspartate (NAA) levels in the Dorsolateral Prefrontal Cortex (DLPC) in child and