specifically responding to a certain drug. Despite decades of efforts though, pharmacogenetics appears to be still in its infancy.
Aim A clearer understanding of the pharmacodynamics and pharmacokinetics events in combination with the genetic and epigenetic controls of cells and molecular cascade must inform the future of personalised medicine.
Objectives To systematically review the current cutting edge knowledge about pharmacognetics in the search for the next groundbreaking biological key events that may provide the keys to future treatments.
Methods The major online databases are systematically searched with common keywords by two independent researchers and conflicting findings are solved during regular meetings dedicated to the topic in object. Manual searching of single bibliographies is also put in place.
Results Genes belonging to the serotoningeric, dopaminergic, glutamatergic and GABAergic systems are classic candidates for pharmacogenetics whose role was not confirmed by GWAS analyses, which, on the other hand, identified genes related to molecular pathways not associated with direct target of drugs used for the treatment of depression.
Conclusion Both hypothesis driven candidate genetic investigations and GWAS analyses have been conducted so far, leading to the identification of a handful of potential good candidates, but the replication rate of the positive association findings lags behind expectations. The current knowledge about the pharmacodyncamic and pharmacokinetic genetic determinants of antidepressant response is critically analysed and new candidates are presented discussed.
Disclosure of interest The authors have not supplied their declaration of competing interest.

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EW0176

A molecular pathway analysis informs the genetic risk for arrhythmia during antipsychotic treatment

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Background Arrhythmia is a potentially fatal side effect of antipsychotics. A biologic predictive tool to prevent it is missing.
Aim Identification of a genetic profile at risk for antipsychotic induced arrhythmia.
Objective Identifying a molecular pathway enriched for antipsychotic induced QT-modifications.
Methods Seven hundred and sixty-five SKZ individuals, $M = 556$, age = 40.93 ± 11.03 were included. QT-variation was a phase-specific created variable. A nested mixed regression served in R for clinical and molecular pathway analyses. Plink served for genetic analyses. Quality checking was standard, inflation factor was controlled by lambda values.
Results Quetiapine and Perphenazine were associated with QT variation ($P = 0.002$; Estimate = 5.79 and $P = 5.67e\text{-}06$; Estimate = 8.96 respectively). No other significant association was detected. No inflation was detected. Axon guidance and Collagen biosynthesis (Table 1) were associated with QT variation at a conservative (adjusted) P value < 0.01.
Conclusions Two molecular pathways were identified as possibly involved in QT modifications during antispsychotic treatment in SKZ patients. Previous evidence supports a role of the same pathways in cardiac disorders [1,2]. Interaction of specific SNPs with the drugs will be focus of further research.

Table 1 Molecular pathways enriched in association with QT modifications.

ID	Description	Gene Ratio	BgRatio	*P*-value	*P*.adjust	Qvalue
422475	Axon guidance	19/135	292/6750	4.6e–06	0.0022	0.0021
1650814	Collagen biosynthesis and modifying enzymes	8/135	59/6750	1.9e–05	0.0047	0.0044

Disclosure of interest The authors have not supplied their declaration of competing interest.
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EW0177

A molecular pathway analysis stresses the role of inflammation towards cognition in Schizophrenia

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Background Cognitive processes are impaired in Schizophrenia (SKZ). The nature of such impairment escapes definition.
Aim Identification of a genetic profile at risk of cognitive impairment.
Object Identifying a molecular pathways enriched for mutations associated with cognitive impairment.
Methods Seven hundred and sixty-five individuals from the CATIE, $M = 556$, mean age = 40.93 ± 11.03 were included. Verbal memory was outcome. R and Plink served for the analyses. Inflation factor was controlled by lambda values. Input for the pathway analysis were SNPs associated with outcome ($P < 0.05$) genomewide.
Results Gender (male, $P = 2.34e{-}05$; $t = -4.26$) and years of education ($P = 1.57e{-}03$; $t = 6.502$) were associated with verbal memory. Inflammation and oxidation were associated with outcome (Table 1, adj_$P < 0.01$).
Conclusions Being male and poorly educated were associated with poorer verbal memory. Inflammation and the arachidonic acid pathway were enriched in mutations associated with poorer verbal memory. This finding is in line with previous reports [1,2,3].

Table 1 Pathways enriched in association with verbal memory.

Description	GeneRatio	BgRatio	*P*value	*P*.adjust
Synthesis of Leukotrienes	5/105	17/6750	4.42E–06	0.0009
Arachidonic acid metabolism	7/105	45/6750	5.03E–06	0.0009
Glutathione synthesis and recycling	4/105	11/6750	1.68E–05	0.0021

Disclosure of interest The authors have not supplied their declaration of competing interest.
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EW0178

Psychiatric symptomatology as the initial presentation of brain cancer

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Glioblastoma multiforme is the most common primary adult brain tumor. Clinically, non-specific psychiatric symptoms may arise as their first and only manifestation, prior to any neurological deficits. The most form of psychiatric presentation of neurological diseases are depressive complaints, although these may also be accompanied by behavioral and/or cognitive, anxious and psychotic symptoms. By explaining this case report we aim to emphasize the importance of considering the diagnosis of an organic brain disease, even when only primary psychiatric symptoms are evident. The bibliographic research was made using PubMed and Scielo, and analysis of the electronic patient process. Man of 68 years with a history of hypertension, nephrectomy, splenectomy and left brachial plegia after a car accident. He had been previously seen by a psychiatrist for a 6-month history of depressive symptoms, which had been successfully treated. He later developed new behavioral changes such as heteroaggressiveness, social maladjustment and disfasia, for which he was sent to the emergency room. Brain-CT scan displayed a left front temporal expansive injury. Admitted to the Neurology Department for further diagnostic investigation. Subsequent MRI, detected massive infiltrative lesion with significant mass effect and cystic/necrotic area. The anatomopathology disclosed a glioblastoma grade IV. This case reinforces the importance of carrying a imagiologic workup in cases like this, especially on patients with atypical presentation of psychiatric symptoms.
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EW0179

Differential effects of MGluR5 receptor blockade on behavior, schizophrenia-relevant gene expression and neuronal activation patterns from development to aging mice

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Introduction The glutamate system is implicated both in mood disorders and schizophrenia. Mice lacking metabotropic mGlu5 receptors (mGluR5 KO) display schizophrenia-like abnormalities. Additionally, mGluR5 antagonists represent promising alternative anxiolytics/antidepressants. However, the underlying age-specific molecular/cellular mechanisms are only partially understood.
Objectives We aimed at identifying molecular alterations associated with a genetically induced mGluR5 deletion, which results in a schizophrenia-like phenotype. Additionally, we investigated age-specific effects of mGluR5 antagonists on emotional behaviour and c-fos activation.
Methods For analysis of mRNA and protein levels we performed Real-time RT-PCR and Western blot investigations of brains from mGluR5 KO and wild-type mice. Additionally we used classical behavioral tests for determining anxiety- and depression-like changes triggered by the mGluR5 antagonist 2-Methyl-6-(phenylethynyl)pyridine (MPEP). Finally, we used profiling of c-Fos expression, as marker of neuronal activity, induced by MPEP from postnatal day 16 (P16) to adulthood (P90).
Results We found reduced expression levels of reelin, GAD65, GAD67, parvalbumin, as well as NMDA and AMPA receptor subunits in mGluR5 KO mice, especially in the prefrontal cortex (PFC). We measured age-specific alterations in emotional behaviour of mGluR5 KO mice, with marked increase of anxiety during aging. There was a remarkably conserved activation of the paraventricular nucleus of the hypothalamus, implicated in stress regulation, by MPEP at all investigated ages, whereas the extended amygdala was specifically activated in adulthood only.
Conclusions Our animal data provide new insights into the potential role of mGluR5 in neurochemical and behavioural changes associated with schizophrenia and mood disorders during the lifespan.
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EW0180

Influence of personal meaning organization and 5-HTTLPR genotype on cortisol stress reactivity in healthy women

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Introduction Reactivity to acute psychosocial stress in the framework of a physiological multidimensional pattern affects several individual-level systems that include genetic factors and features related to personality development. The 5-HTTLPR genotype has been implicated in the modulation of susceptibility to environmental stimuli.
Objectives In the present study, 91 healthy young women were investigated (i) for their reactivity to a standardized psychosocial laboratory stressor (TSST), as measured by changes in salivary cortisol; (ii) in terms of 5-httlpr genotype and (iii) in terms of their personality profile according to the post-rationalist personal meaning organizations (PMOs), which are considered as adaptive modes of response to environmental stressors.
Methods Participants were divided into three 5-HTTLPR genotype groups (s/s; s/l, and l/s). The quantitative and qualitative variables that may affect circulating cortisol were compared among the three groups. A multiple linear quantile regression analysis was then performed to evaluate the effect of the personality profile, as Outward/Inward PMO, and 5-HTTLPR genotype on the median level of cortisol, considered as dependent variable.
Results Comparison of the variables that may affect circulating cortisol no significant differences. Salivary cortisol changed significantly in the course of the TSST. Reactivity to stress was affected by personality profile and the 5-HTTLPR genotype and also by body mass index and age.