Aggression

Overt behaviour with the intention of inflicting physical damage. Physiological trait with important roles throughout evolution (defence, predation). Can be impulsive (reactive, emotional) or instrumental (proactive, predatory).

In humans, maladaptive aggression leads to social maladjustment and crime. Aggression is also a symptom of Attention Deficit/Hyperactivity Disorder (ADHD), conduct disorder (CD) and schizophrenia.

Aggressotype

OBJECTIVES
To gain insight into the mechanisms underlying impulsive and instrumental aggression subtypes.

- Neural substrates: MRI analysis in ADHD patients.
- Genetic analysis in violent individuals.
- Functional molecular/cellular mechanisms: zebrafish and mouse models, human cell lines and epigenetic analysis.
- Functional brain circuits mechanisms.

To translate pre-clinical findings.

- Predictors of aggression/outcome.
- Non-pharmacological treatment: bio-feedback.
- Pharmacological treatment: stimulant treatment of ADHD prisoners, screening of novel treatments.

Neurobiological mechanisms of risk genes for aggression

Aggression linked genes (from genetic studies)

Development of zebrafish mutant lines.

Analyse neurochemical changes (gene expression)

Behavioural tests

Aggression

Mirror induced stimulation

Shoaling test

Anxiety

Open field test

Novel tank diving

Corrective/Screen

Novel treatment targets for pharmacological intervention

To identify novel pharmacological interventions that can be used to treat aggression.

- Screen for novel small molecules that modify aggression in one month-old larval fish.

Novel compounds (A, B, C, D…)

Screening

Behavioural tests, Neurochemical analyses

Database: promising therapeutic compounds/targets

University of Leicester

ZEBRASH WORK

Advantages of this model:

- Ease of maintaining and generating large numbers of zebrafish. Fast development.
- Ease of manipulating embryos.
- High-throughput screens (high cost efficiency).
- High genetic homology to mammals (neurotransmitters, hormones, disease linked genes, neural circuits…)
- Large number of mutant and transgenic lines.
- Genetic tools, techniques to monitor neural activity, optogenetics, genetic ablation.
- A battery of behavioural test (larval and adult zebrafish).
- Increasing number of human disorders modelled.