Summary of the IMpACT Nijmegen Spring Meeting 2009, May 5-6

- Please refer to the pdf files of the May 5 presentations by the participating countries for the adult ADHD programs at the different institutes.

- On the second day, the participants discussed their view on future directions in adult ADHD genetics research and/or potential collaboration projects for IMpACT. The following points were discussed:
  - Genotyping collaborations:
    - NOS1: (1) Eric will genotype the VNTR in the US sample.

      (2) Phil will look into possibilities in the UK.

      (3) We need to get into contact with IMAGINE, this might lead to interesting possibilities for further research.

      (4) In a bipolar child sample interesting pilot findings for this gene have been found.
    - SLC9A9: Eric suggests to perform analysis of this gene in IMpACT.
    - GLUT3, GLUT6: (1) SNP and CNV analysis could be combined in joined IMpACT publication.

      (2) These findings, together with additional findings on metabolism genes could be a new road/direction in ADHD etiology research.

      This could also relate to the neuronal energy metabolism theory (see papers Nora Volkow) that may underlay delayed sleep phase problems in ADHD.

      BMI and cardiovascular problems are also increased in (adult) ADHD patients.
    - KCNJ6, DIRAS2, BChE: Will be genotyped in the IMpACT sample by Germany.
    - Please comment on the Norwegian TPH1 and TPH2 paper. We may submit to Eur. J. Neuropsychopharmacology or the Int. J. Neuropsychopharmacology.
    - Spain wants to perform an IMpACT-wide analysis of SNPs/genes belonging to the SNaRE complex.
    - Another Spanish suggestion is to analyse selected miRNA genes, which they have already published a paper on this subject for anxiety disorders (see below). The Dutch group is also working on this, with a slightly different approach. Both groups will coordinate and see what would be useful for the entire IMpACT group.

      Muiños-Gimeno M, Guidi M, Kagerbauer B, Martín-Santos R, Navinés R, Alonso P, Menchón JM, Gratacòs M, Estivill X, Espinosa-Parrilla Y. Allele variants in functional MicroRNA target sites of the neurotrophin-3 receptor gene (NTRK3) as susceptibility factors for anxiety disorders. Hum Mutat. 2009 Mar 3. [Epub ahead of print]

- Germany is currently performing functional analyses at animal model and cellular level for NOS1, CDH13 and KCNJ6, i.e. knock-outs, gene expression assays and methylation assays.

- We decide to survey/harmonize within IMpACT the available imaging, neuropsychology and pharmacogenetics data in the future.

- We think it would be useful to perform comprehensive multilevel biobanking, including RNA (for transcriptome data), plasma (for proteome and metabolome data) and diurnal variation data (on metabolic parameters). The protocols for biobanking procedures will be put on the website by the different parties, as soon as we have one.

- Something that might be interesting for a EU project in one of the coming rounds may be an analysis of metabolic parameters (basal insulin, basal glucose, glucose tolerance, HbAIc, lipid profiles) and cardiovascular system parameters (blood pressure (24 h), ECG and blood pressure under (physical or social) stress, HRV.

- Norway is performing protein and gene expression analyses, that can also be used for interesting IMpACT genes.

- Norway also has access to a large (n=66.000) population sample, the HUNT study, which might come in handy for some of our ideas.

- In the UK, outbred mice have been phenotyped for activity phenotypes and these have been mapped to brain expression QTLs. In addition, rats have been given nicotine to drink during pregnancy and expression profiling in the brain (striatum) of the offspring has been monitored.

- For those of us who have IQ data and GWAS data, participation in the IQ GWAS consortium might be interesting, which we can take part through Phil.

- Phil brings up the point of self reports in adolescent and adult ADHD patients being not heritable. This is something we have to take into account when analyzing our patients. A twin-study on adult ADHD is currently missing from the literature to formally establish the extend of the heritability of adult ADHD.

- The Dutch group brings up the statistical analysis of GWAS data, which is using rather ‘simplistic’ models at the current time, not taking into account the complexity of the data. They suggest to use Bayesian Modelling to improve this.

- Epigenetics (DNA-methylation) is another interest in The Netherlands, but since this is highly tissue-specific and there is no real data on the comparability of brain- and peripheral methylation, yet, this would have to be a first step before this can be applied to (adult) patients. In Germany, this is also point of interest, there is already a paper on peripheral HTTLPR methylation and overlap with brain methylation; BDNF is currently being worked on.

From the discussions, the following conclusions and IMpACT goals were formulated:

A. Immediate goals

a. Genotyping: send info on gene names (SNaRE) and assays (GLUT3 CNV)
b. Analyse available genotyping results
c. Comment on TPH manuscript
d. Set up database
e. Establish website
f. Follow up the discussion about phenotype definition (see minutes of formal meeting)
g. Implement endophenotyping of 'easy' cardiovascular parameters, and BMI
h. Check if your sample includes any twins

B. Intermediate term goals

a. Survey/Categorize endophenotypes
b. Harmonize phenotyping instruments
c. Start extending endophenotyping
d. Collaborate on new initiatives/projects of IMpACT members (new genes/gene systems/approaches)
e. Prepare collaborative project proposals on GWAS
f. Finish DIVA translation
g. Exchange students between IMpACT sites

C. Longer term goals

a. Write collaborate projects implementing new (endo)phenotyping at the patient level and also the cell/tissue level

   → potential areas: Physiology-related ADHD phenotypes
   Neuroimaging
   Animal models

b. Establish twin registry (genetics and epigenetics)
c. Use each other's infrastructure and sampling sites