Molecular Transducers of Regular Exercise Behavior

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Exercise is good for you, that much is known, but how does genomic variation contribute? And which molecular changes are induced?

Motivation

Regular physical activity is a key contributor to health (Shiroma et al. 2012). Even so, the majority of either Dutch or American population does not engage in regular physical activity at the recommended level. A growing literature illustrates that there is a substantial genetic contribution to the variation in regular exercise behavior between people, with heritability estimates increasing from childhood to late adolescence. In the latter over 80% heritability is reported (de Geus, et al. 2014). Several candidate genes have been suggested, such as *DRD1* and *DRD2*, but to date no genome-wide significant variants have been identified. Large literature exists on the impact of physical activity on physiological risk factors (such as inflammatory processes) for various chronic diseases. There is a paucity, however, of studies addressing low-level molecular pathways at the basis of the development of these risk factors.

This project will use a combination of highly standardized longitudinal assessment of survey-based exercise behavior, objectively measured exercise behavior (accelerometer data), genome-wide SNP data, IL450K array data, RNA-expression data, and metabolomics data that is currently available for participants of the Netherlands Twin Register (NTR).

	ExcQ	ExcA
ExcQ	66,114	1,031
ExcA	1,031	1,035
Genotype	11,371	616
IL450K	2,942	268
RNAseq	1,682	170
Metabolomics	5,658	365

***Table*.** Current number of participants in various combinations. (e.g. 66,114 subjects with only ExcQ (exercise from questionnaire) data, and 1,031 participants with ExcQ, and ExcA (exercise from accelerometry) data.

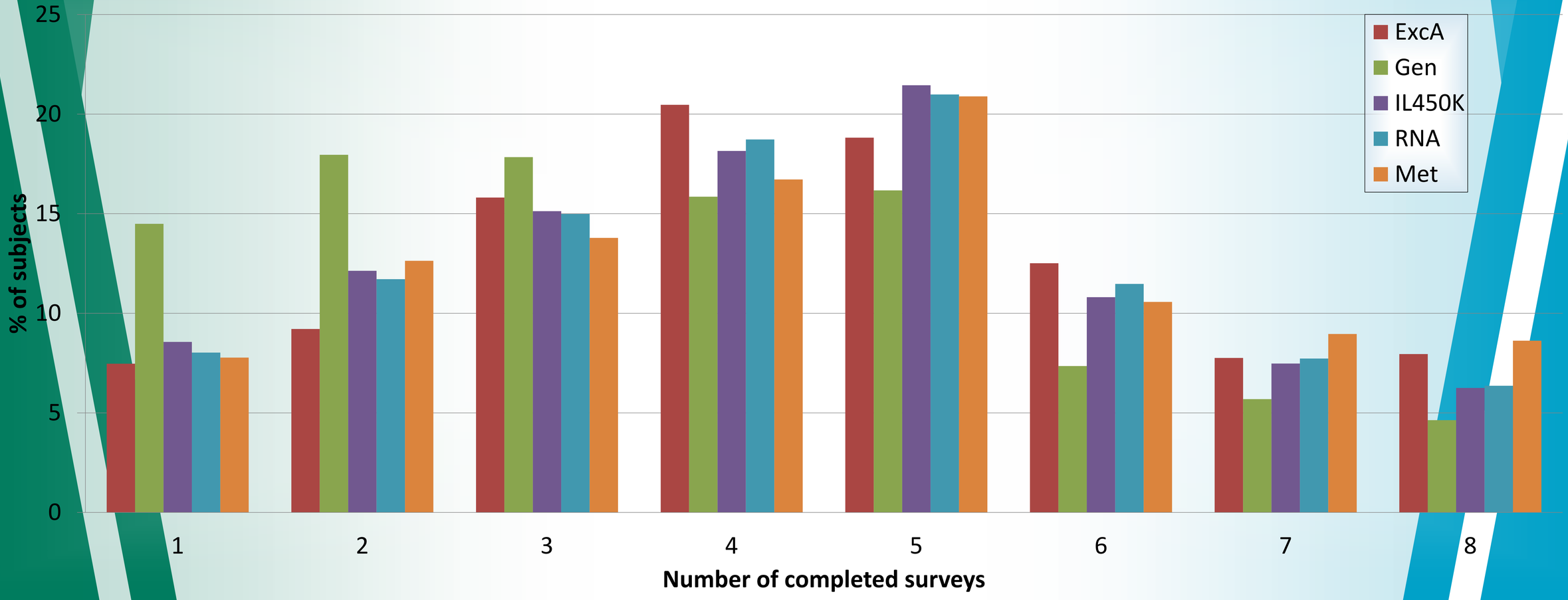

***Figure*.** Percentage of participants (*y*-axis) for whom *x* number of surveys are available, as well as either accelerometry data, genome-wide SNP data, IL450K aray data, RNA expression data, or metabolomics data.

Additional data collection

In addition to the data already available, the aim is to epigenotype an additional 150 individuals using the Illumina 850K array for whom accelerometry data is available.

Additionally data from the Avera Twin Register will be included in the analysis, once available, to test if the relationship between (epi)genetic variants and exercise behavior differs between populations (The Netherlands versus Midwest USA), which provides inside into gene-environment interaction.

Conclusive remarks

As is clear from above figure and tables, a lot of data is ready for use at the NTR. The majority of participants for whom either accelerometry, epigenetic, RNA, or metabolomics data is available have completed 3-5 questionnaires. This allows us to perform more in-depth analysis into longitudinal patterns of regular exercise behavior. When combined with the newly collected data at the Avera Twin Register, this project should have ample data to shed more light onto molecular mechanisms related to exercise behavior. The identification of molecular mechanisms that lead to differences in regular exercise behavior can help to identify specific biological or psychological determinants to prioritize as targets for intervention. Furthermore, this study may identify molecular effects of exercise behavior that could provide insight into the biological mechanisms underlying health benefits of exercise and may unravel how responsive these mechanisms are to frequency, intensity and longitudinal patterns of physical activity.

This project is a collaborative effort by the Avera Institute for Human Genetics, NTR, and Vrije Universiteit.
This work was supported by BBRMI-NL (NWO 184.021.007) and the Biobank-based Integrative Omics Study (BIOS) Consortium.
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