1 Use of expression studies in deciphering NDDs and the brain in general

Although the genetic etiology of NDDs is far from being completely known, significant advances have been made in the last years in understanding specific biological pathways underlying the molecular mechanisms of these illnesses.

- What is single cell and how has it been used
- in this section I will describe several studies that utilised this single cell rna-seq approach

The advances in next generertion sequening technologies in recent years have provided many valuable insights into complex biological systems. NGS

1.1 Single-cell RNA-seq

Since the first paper showing the feasibility of characterizing expression profiles of individual cells using NGS technologies was demonstrated by Tang et al, single-cell RNA sequencing has been widely used to dissect the cellular heterogeneity within a population of cells. Additionally, this has generated an interest in obtaining high reseloution of single cells which can help identify rare populations that cannot be detected from bulk analysis. In this section, we will discuss the advances made in single-cell technologies in the recent years, and how these advances have helped our understaning in various aspects of neurodevelopmental disorders.

1.1.1 Application of scRNA-seq in the brain

The brain contains highly complex neural cell types and subtypes which are organized in specialised regions. Traditionally, neural cells were identified by morphology, excitability, connectivity and the location of the cell. However, with recent advamces, scRNA-seq approaches have become a common tool to assess and investigate the brains complexity and to identify

new subpopulations. From 2015 onwards over 80 papers have reported detailed characterization of brain cell types in different brain regions, and at developmental stages or disease status using scRNA-seq. In addition to the increasing number of publications, we have also observed an exponentially increasing number of sequenced cells per study in the last 5years. The technology is not only inspiring more studies in recent years, but also exponentially scaling up the number of single cells profiled in each study, which has empowered the construction of a comprehensive landscape of the cell types in the brain.

Table 1: Expression studies that utilised single-cell profiling technologies (Not ordered by any particular way)

Authors	**Year**	**Tissues**	**Method**	**No. of Cells/Nuclei**	**Age**	**No. of individuals**	**Data availability**
Velmeshev et al	2019	PFC and ACC	snRNA-seq	104,559	4-22 pm	15 ASD; 16 controls; total 31	
Late et al	2016	Brodmann's areas	snRNA-seq	4488	51 pm	1 healthy individual	
Nowakozski et al	2017	V1, PFC	scRNA-seq				

single-cell nuclei technique

Points to discuss: The first study that used it and why it was neccesary

The more recent study and hwo it used it in NDDs