

Digital Phenotyping, Genetic Subtypes, and Janssen
Autism Knowledge Engine (JAKE[®])

ISCTM Autism Working Group 2018 Autumn Meeting

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Digital Phenotyping

- ASD heterogeneity and complexity has led to desire for more objective clinical trial tools to measure ASD symptoms
- Digital phenotyping= use of web/mobile, sensor technologies to stratify, quantify, and track symptoms of ASD
- State of science is experimental
 - Large database is building with select measures
- Consortia and companies conducting large-scale studies



AIMS-2



ABC-CT

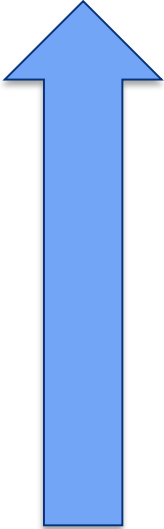


POND

- Common instrumentation, measures/stimuli, sensors can allow for cross-verification, validation of select markers

Digital Phenotyping

Examples of sensors, phenotypes, and evidence

Sensor / Technology	Clinical Phenotype Assessed (examples)	Progress in Biomarker Development
Mobile / Web Apps *	Digital phenotyping, behavior, remote video assess., etc.	 <p><i>More</i></p> <p><i>Less</i></p>
EEG *	Brain electrical activity/networks, spectral power, etc.	
Eye-tracking *	Attention, social gaze, visual tracking, pupillary response,	
Actigraphy (+)	Activity level, RRBs, sleep	
Face emotion proc.	Measures / quantifies affect, dynamic range /complexity	
Speech/Voice (+)	Speech duration/quality/turns, prosody, tone, vocabulary	
Skin Conductance	Emotional reactivity/dysregulation, anxiety, etc.	
Automated Beh. Ax.	Lab-based behavior pattern assessment	

- Multiple studies are increasing our understanding of the potential utility of measures as disease / stratification / change 'biomarkers'
- Confirmatory studies, analyses ongoing to confirm first candidate biomarkers to be used in clinical trials
- Continuing to link to theories, symptoms, known ASD causes

* denotes use across consortia/studies

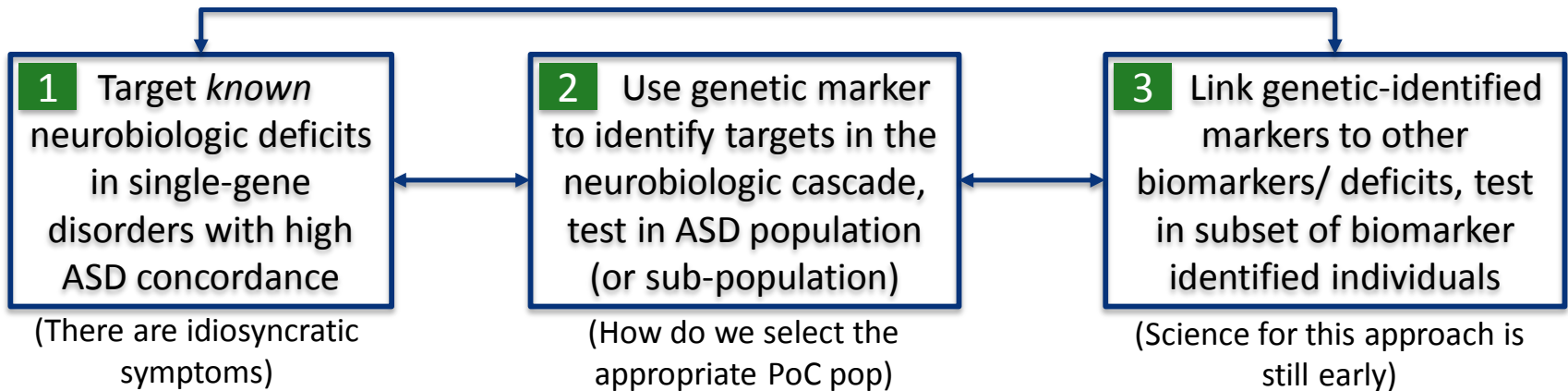
+ denotes also measured via smart phone

ASD Genetic Subtyping

- ASD highly heritable
 - 50-90% twin concordance¹
- De novo CNVs / whole exome sequencing
 - ~30% of ASD = single-gene disorders²

EHMT1 (<i>9q34.3</i>) Kleefstra Synd. 2	MAGEL2 (<i>15q11.2</i>) Prader-Willi Synd.	PTEN (<i>10q23.31</i>) Cowden Synd.	SHANK3 (<i>22q13.33</i>) Phelan-McDermid
FMR1 (<i>Xq27.3</i>) Fragile X Syndrome	MECP2 (<i>Xq28</i>) Rett Synd.	PTPN11 (<i>12q24.13</i>) Noonan Synd.	SYNGAP1 (<i>6p21.32</i>) SYNGAP1-rel. ID
FOXG1 (<i>14q12</i>) FOXG1 Synd.	NSD1 (<i>5q35.3</i>) Sotos Synd.	SCN1A (<i>2q24.3</i>) Dravet Synd.	TSC2 (<i>16p13.3</i>) Tuberous Sclerosis

Known genes enable multiple approaches for drug development:



Multiple approaches already leading to new discoveries in both idiopathic and single-gene forms of ASD

1 | My JAKE

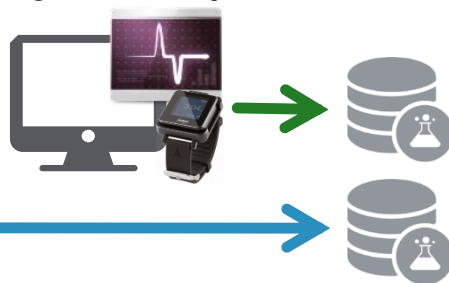
Web-and-mobile phenotyping portal that can organize & access data across providers



- 1st Study Endpoint
- Autism Behavior Inventory
- Multiple other caregiver- and site-reported outcomes

2 | JAKE Sense

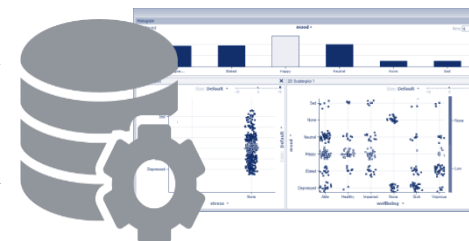
Experimental biosensor workbench creates sensitive, objective endpoints



- Lab-based sensors* across multiple experiments
- Home-based sensors*
- Explores ASD symptoms

3 | JAKE Stream

Data pipeline for more sensitive data to inform PoC subpopulation selection



- Complex data explores potential biomarkers
- Data mining has potential to advance the field

- Standardized across sites, integrated into clinical trials process
 - Data rapidly availability, dashboards for study adherence, data quality
- Multiple publications¹ on endpoints and potential biomarkers complement consortia data
 - JAKE system, ABI, facial affect recognition, eye-tracking, EEG, actigraphy

*sensors used for research only; not used to diagnose or treat any medical disease or disorder

Thank You!