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List of Instruments

Name of Instrument	Subdomain	Table Name
Endocannabinoid (eCB) Substudy	SU Consequence	ecb_y_ecb

General Information

An overview of the ABCD Study® can be found at abcdstudy.org and detailed descriptions of the assessment protocols are available at [ABCD Protocols](#). This page describes the contents of various instruments available for download. To understand the context of this information, refer to the release note [Start Page](#).

Endocannabinoid (eCB) Substudy

The ABCD Endocannabinoid (eCB) Substudy was developed by Krista Lisdahl and Cecilia Hillard along with collaborators across eight ABCD study sites (R21DA09109). The objective of this project is to examine the relationship between circulating endocannabinoid levels and neurocognitive, psychopathology, and substance use outcomes in a subsample of youth enrolled in the ABCD Study.

Instrument Descriptions

eCB Questionnaire

The eCB Questionnaire was designed in REDCap (by Krista Lisdahl and Cecilia Hillard) to measure state-based factors that have been previously shown to potentially impact circulating eCB levels (time of day the sample was collected, hours since last meal, drink and aerobic activity, last night's sleep duration, current pain and stress levels) (e.g., Cedernaes et al., 2016; Hanlon et al., 2015; Heyman et al., 2012; Monteleone et al., 2012) and were administered right before the blood draw. All data was quality control reviewed by the Substance Use workgroup and the eCB Substudy Coordinator (supervised by KL).

eCB Quantified Levels

Data were collected starting at the 2-year follow-up, with some samples to date collected at the 3-year and 4-year follow-ups. Data include 3ml blood samples. Dr. Hillard's laboratory extracted serum to measure (N-arachidonylethanolamine, **AEA**; 2-arachidonoylglycerol, **2-AG**), and endocannabinoid lipid mediators (2-oleoylglycerol, **2-OG**; oleoylethanolamide, **OAE**; palmitoylethanolamide, **PEA**). AEA, 2-AG, 2-OG, OAE, and PEA were quantified in lipids extracted from 0.4 ml of serum using isotope-dilution, mass spectrometry following the methods outlined in Spagnolo et al (2016). Briefly, solid phase extraction columns are used to separate lipids after the addition of deuterated standards (150 pg/μl AEA and 1800 pg/μl 2-AG). The LC-MS-MS analysis is conducted using an Agilent Technologies 6460 Triple Quad LC-MS with a Chromasil, 5 μ C18 column with dimensions of 250 × 2.00 mm. AEA, 2-AG, 2OG, OAE, and PEA amounts are determined using isotope dilution; standard curves are constructed from a set of 10 combos, each containing different AEA/2AG concentrations together with deuterated AEA and 2-AG at the same concentrations in the samples. The concentration ratios in the samples are calculated from area ratios using the slopes determined from the standard curves, and converted to concentrations using the amount of deuterated standard added and the original sample volume. Finalized AEA, 2-AG, PEA, OEA and 2-OG levels (pmol/mL) are provided and harmonized with the larger ABCD study dataset.

Notes and Special Considerations

The eCB Substudy was impacted by the COVID-19 pandemic, which resulted in shut-downs in blood sample collection at several sites at varying rates from 2020-2022, resulting in greater rates of missing blood draws. Four parents consented/youth participants assented to the eCB substudy blood draw, but did not provide data so their data is missing. A small subgroup of participants have longitudinal data; if scientists conduct cross-sectional analyses, this should be addressed. Longitudinal data at future time-points (4YR, 6YR, 8YR) are being collected.

References

- Cedernaes, J., Fanelli, F., Fazzini, A., Pagotto, U., Broman, J. E., Vogel, H., Dickson, S. L., Schiöth, H. B., & Benedict, C. (2016). Sleep restriction alters plasma endocannabinoids concentrations before but not after exercise in humans. *Psychoneuroendocrinology*, 74, 258–268. [Find here](#)
- Hanlon, E. C., Tasali, E., Leproult, R., Stuhr, K. L., Doncheck, E., de Wit, H., Hillard, C. J., & Van Cauter, E. (2015). Circadian rhythm of circulating levels of the endocannabinoid 2-

arachidonoylglycerol. *The Journal of clinical endocrinology and metabolism*, 100(1), 220–226. [Find here](#)

Heyman, E., Gamelin, F. X., Goekint, M., Piscitelli, F., Roelands, B., Leclair, E., Di Marzo, V., & Meeusen, R. (2012). Intense exercise increases circulating endocannabinoid and BDNF levels in humans—possible implications for reward and depression. *Psychoneuroendocrinology*, 37(6), 844–851. [Find here](#)

Monteleone, P., Piscitelli, F., Scognamiglio, P., Monteleone, A. M., Canestrelli, B., Di Marzo, V., & Maj, M. (2012). Hedonic eating is associated with increased peripheral levels of ghrelin and the endocannabinoid 2-arachidonoyl-glycerol in healthy humans: a pilot study. *The Journal of clinical endocrinology and metabolism*, 97(6), E917–E924. [Find here](#)

Spagnolo, P. A., Ramchandani, V. A., Schwandt, M. L., Kwako, L. E., George, D. T., Mayo, L. M., Hillard, C. J., & Heilig, M. (2016). FAAH Gene Variation Moderates Stress Response and Symptom Severity in Patients with Posttraumatic Stress Disorder and Comorbid Alcohol Dependence. *Alcoholism, clinical and experimental research*, 40(11), 2426–2434. [Find here](#)

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