NeuroRegulation

LORETA Neurofeedback at Precuneus in 3-year-old Female with Intrauterine Drug Exposure

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Abstract

This case study presents data for operant conditioning of alpha current source density (CSD) in a 3-year-old female that completed 20 sessions of EEG LORETA neurofeedback (LNFB) to address sequelae associated with intrauterine drug exposure (IUDE), including explosive reactions to unfavorable activities and siblings, deficits in self-care, self-direction, and social interaction. One of the more difficult processes is to assess children less than 6 years of age due to extreme variability in affect, interest, and focus. However, IUDE increases the range of potential problems and diagnostic confounds. This individual showed adaptive behavior improvements ratings by parents posttraining and was able to complete a measure of attention after training and at 30-day follow-up. Her data demonstrated a general increase in the trained CSD of the alpha frequency at precuneus across time. Additional changes were evident in the self-regulation network (SRN) posttraining with a significant decrease at follow-up suggesting a learning effect over time. This case study demonstrates that LNFB may produce positive effects in children under the age of 4.

Keywords: LORETA neurofeedback; intrauterine drug exposure; EEG; neuroimaging

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Introduction

This case study examines the effects of a standard procedure (Cannon, Congedo, Lubar, & Hutchens, 2009; Cannon et al., 2007; Cannon et al., 2014) of low-resolution electromagnetic brain tomographic neurofeedback (LNFB) in a 3-year-old female to aid in addressing sequelae associated with intrauterine drug exposure (IUDE). Differentiating IUDE and Neonatal Abstinence Syndrome (NAS) from other psychiatric symptoms is of growing concern due to the current opioid problem and its collateral damage. It is proposed that about 14–22% of pregnancies in the United States are complicated by exposure to opioid medications, and the trend is also shown in most European countries to a lesser degree (Huybrechts et al., 2017). However, establishing actual rates of illicit drug exposure during pregnancy are limited at best. NAS represents a cluster of problems and treatment for withdrawal symptoms when the infant is exposed to opiates and/or other drugs in utero. Currently, there are no diagnostic criteria to serve as a guide for treating problems that present in children suffering from IUDE. Intrauterine drug exposure and its potential long-term effects in the developing brain are of great concern for researchers and clinicians. The costs of treatment for NAS and IUDE are substantial for medical, social, educational, and support services to address this epidemic. It is also quite important that the foster care and adoption services for these children be informed of specific clusters of problems that occur to facilitate the proper care and adjustments for this growing population. Additionally, rates of diagnosis of Attention-Deficit/Hyperactivity Disorder (ADHD) in populations of children suffering from IUDE can be as high as approximately 36%, as contrasted to 2% in nonexposed children. In such cases there are currently no published data describing treatment efficacy with the use of stimulants or other medications to treat the clusters of symptoms that are present in these children.

There are relatively few data providing descriptive patterns of persistent cognitive, social, and executive function deficits in this population (Butz, Pulsifer, Leppert, Rimrodt, & Belcher, 2003; Franck, 1996; Freeman, 2000; Kelley, 1992; Kne, Shaw, Garfield, & Hicks, 1994; Mayes, Cicchetti, Acharyya, & Zhang, 2003; McNichol, 1999). The effects of IUDE can persist over the developmental continuum into adulthood, and the deficits seen across populations can vary (Bard, Coles, Platzman, & Lynch, 2000; Bhide & Kosofsky, 2009; Buckingham-Howes, Mazza, Wang, Granger, & Black, 2016; Derauf, Kekatpure, Neyzi, Lester, & Kosofsky, 2009; Jaeger, Suchan, Schölmerich, Schneider, & Gawehn, 2015; Nadebaum, Anderson, Vajda, Reutens, & Wood, 2012; Pulsifer, Radonovich, Belcher, & Butz, 2004; Robey, Buckingham-Howes, Salmeron, Black, & Riggins, 2014); however, executive functions, social and emotional delays, and integration of social cues and rules appear to be the most prevalent issues seen in the clinical experience of the current authors.

There are suggestions that network processes in the brain associated with these behaviors involve shifts in the default mode network (DMN) and its connectivity and overlap with other functional hubs and networks including task associated with social cognition (Mars et al., 2012; Sidlauskaite, Sonuga-Barke, Roeyers, & Wiersema, 2016). The EEG current source density (CSD) in ventromedial prefrontal cortex (PFC) and posterior cingulate were therefore targets for monitoring in this study with intent to understand behaviors as correlated with brain activity. In prior data with ADHD, a network associated with self-regulation (SRN) was put forth which demonstrated shifts in both amplitude and connectivity between these specific nodes relative to training one region and one frequency within it (Cannon, 2014). The client described in the present study completed a standard operant conditioning LNFB procedure with the aim of decreasing emotional reactivity to environmental cues (e.g., tantrums when not getting her way), and improving self-care, self-direction, social-executive and focused awareness (e.g., attention). Operant conditioning as defined in neurofeedback can be thought of in terms of pairing the alpha CSD at the region of training with a stimulus event (game or movie) in order to increase the likelihood of generating alpha CSD at certain levels across time. As this behavior is acquired and practiced then both regional and network changes should be evident with the added direction of psychometric data.

Methods

This case study is of a 3-year-old female presenting for LNFB to address issues associated with IUDE including difficulties with attention, focus, emotional regulation, and behavioral outbursts. The primary known intrauterine exposures were to cocaine and opioids; therefore, she would be better classified in the range of polydrug exposure. She lives in a supportive and nurturing environment with her adoptive parents and siblings, and because adoption occurred at an early age the problems of accompanying abuse and neglect often seen in these children were avoided. Upon her initial visit to the authors' clinic, a diagnostic interview was conducted, and the Adaptive Behavior Assessment System 3rd edition (ABAS-3) was provided to parents. The ABAS-3 is a rating scale useful for assessing skills of daily living in individuals with developmental delays, autism spectrum disorder, intellectual disability, learning disabilities, neuropsychological disorders, and sensory or physical impairments (Harrison & Oakland, 2015). We attempted to administer the Conners Kiddie Continuous Performance Test, Second Edition (K-CPT 2). The K-CPT 2 provides an objective measure of attention in children ages 4 to 7 years old. The 7.5-min performance-based assessment uses pictures of objects that are familiar to young children (Conners, 2015). It should be noted that the subject was under the minimum age for the K-CPT-2 test sample, but we sought a basal level on her ability to comply with task demands. However, at pretraining it was not possible to administer the K-CPT 2 due to the child's distractibility and random clicking behavior.

The client was prepared for EEG recording using a measure of the distance between the nasion and inion to determine the appropriate cap size for recording (Blom & Anneveldt, 1982). The head was measured and marked prior to each session to maintain consistency and for placement of frontal electrodes. The ears and forehead were cleaned for recording with a mild abrasive gel (NuPrep) to remove any oil and dirt from the skin. After fitting the caps, each electrode site was injected with electroconductive gel, and prepared so that impedances between individual electrodes and each ear were less than 10 KΩ. The LNFB training was conducted using the 19 leads of the standard international 10/20 system with linked ear reference. The center voxel for the region of training (i.e., left precuneus) was located at Talairach coordinates (x = -31, y = -81, z = 22). The data were collected and stored utilizing the Deymed TruScan Acquisition system with a band-pass set at 0.5–64 Hz at a rate of 256 samples per second. We used standard 6-mm tin cups ear electrodes. All recordings and sessions were carried out in a quiet, comfortably lit, clinical neurofeedback room at the authors' clinic. Lighting and temperature were held constant for the duration of the sessions.

LNFB training sessions were composed of six 5-min rounds and were conducted five times per week for 20 consecutive weekdays. Each session collected 3-min presession eyes-opened baselines (EOB). Each session required 48 minutes on average to complete. In the preliminary shaping session, the participant was introduced to the EEG on screen and educated on how to minimize artifact to get the optimal signal. She was instructed to control tongue and eye movements, blinks, and muscle activity in forehead, neck, and jaws. This helped to reduce the effects of extracranial artifacts from electromyographic (EMG) and electro-oculographic (EOG) signals during the sessions. During the preliminary session thresholds were set so that the participant met the reinforcement criteria (20%; e.g., generate the desired response at a minimal rate). The participant was informed of the inhibitory and reward aspects of the training. Thresholds were then set and maintained for the participant.

The participant was provided visual and auditory feedback with a game interface or children's videos, and points were achieved when able to simultaneously increase alpha current source density (CSD, 8–13 Hz) at the region of training (ROT), while minimizing EMG (35–55 Hz) and EOG (1–3 Hz) in linear combinations of channels (i.e., for EMG: T3, T4, T5, T6, O1, and O2; for EOG: FP1, FP2, F3, F4, F7, and F8). These criteria had to be maintained for .75 s to achieve 1 point. The auditory stimuli provided positive reinforcement with a pleasant tone when the criteria were met. Similarly, the visual stimuli were activated when the criteria were met (e.g., a car or a spaceship driving faster and straighter). Alternatively, slower speed of the car, driving in the wrong lane, or the spaceship flying slowly and crookedly were seen when the criteria were not met. The score for meeting the criteria was also seen by the participant in a small window of the game screen. Additionally, the visual stimuli contained a signal for reward and inhibits relative to a threshold level, and a bar graph illustrating reward, EOG, and EMG. When the children's video was used for feedback, the visual image remained clear and the sound remained on when criteria were met; otherwise the picture blurred, and sound was interrupted when criteria were not.

The regions within a theorized self-regulation network (SRN; Cannon, 2014) were identified as a focus of study based on their association with the precuneus and studies showing activation across attention, cognitive, and self-regulatory tasks. The center voxels for the regions of interest (ROIs) for this case study data are shown in Table 1. The mean CSD for the alpha 1 and alpha 2 frequencies were extrapolated from precuneus and network regions of interest for the EOB recordings at time 1, time 2 and time 3, in similar fashion the mean CSD for alpha for the LNFB training rounds were extrapolated and placed into SPSS 22 for analyses. We utilized paired comparisons to contrast pretraining and posttraining means for alpha CSD at left precuneus region of training (ROT), for associated network regions, as well as for psychometric data. We compared the mean score for the nine scales on the ABAS and K-CPT across all categories at each administration. We re-administered the ABAS-3 posttraining, and the K-CPT 2 posttraining and at 30-day follow-up.

Table 1
SRN Regions of interest for this study data.

Brodman Area (BA)	Hemisphere	x,y,z Coordinates	Neuro-anatomical	# Voxels
19	L	-31, -81, 22	Precuneus	3
13	R	39, -4, 8	Insula	6
23	R	4, -32, 29	Cingulate gyrus	5
25	L	-3, 10, -13	Subcallosal gyrus	6
29/30/31	L	-3, -46, 22	Posterior cingulate	6

From left to right are the Brodmann Area, Hemipshere, LORETA x,y,z coordinates, neuroanatomical label and number of voxels in the ROI.

Results

The results for the pre–post training paired comparisons for the ABAS-3 are shown in Table 3. In the figure from top to bottom are the domain measures and from left to right pre and post scaled scores for parents. Significant shifts did occur across time with the more interesting changes showing improvement in the social, self-direction, and leisure domains. Parents were provided summary of ABAS-3 recommendations and are continuing to address items as they arise. At a follow-up meeting 30 days after training, her mother reported continued reduction of problematic behaviors and more positive engagement in social and interpersonal domains. The client also recently started pre-Kindergarten and will continue to be monitored over time. In contrast to her inability to complete the K-CPT 2 during the pretraining assessment, she was able to complete this test posttraining and at the 30-day follow-up assessment. We contrasted the mean results for all scales of the K-CPT posttraining and at follow-up which showed statistically elevated errors relative to the 4-year-old normative group which had increased at follow-up with $t(9) = -3.12$, $p = .014$. These results must be interpreted cautiously due to her age being below that of the test's normative sample. Figure 1 and Table 2 show the results for alpha CSD contrasts for pre, post and follow-up EOB. The ROT (precuneus) did show significant increases at posttraining, and significant decrease at follow-up, which impacted the shifts in the remaining network nodes. In the figure are the CSD for 5 ROIs implicated in the SRN. The precuneus is shown in black to the left of each ROI. In general, there was a significant increase in mean alpha 1 CSD posttraining in all ROIs of the SRN, including the ROT, the precuneus. At 30-day follow-up there is a significant decrease in all network nodes. Alpha 2 shows a similar trend, although at posttraining the result was in the desired direction but did not reach significance. The same trend in alpha 2 CSD is present at follow-up with an interesting and significant decrease in CSD amplitude in 3 ROIS and relative higher amplitude in the right insula and orbital frontal cortex. Figure 4 shows the mean ROT alpha CSD levels for sessions 1, 5, 10, 15, and 20. The trend is in the desired direction $y = 14.112x + 59.199$; $R^2 = 0.8856$.

Table 2

Results for paired comparisons for combined ABAS-3 parent ratings were significant with t(18) = 2.86, p = .010.

Skill Area	Mother Pre	Mother Post	Father Pre	Father Post
Communication	10	9	7	8
Community Use	6	5	4	6
Pre-Academics	6	5	6	8
Home Living	6	6	6	7
Health and Safety	8	8	5	7
Leisure	1	9	6	7
Self-care	8	9	7	8
Self-direction	5	8	4	5
Social	6	9	3	5
Motor	11	9	9	11

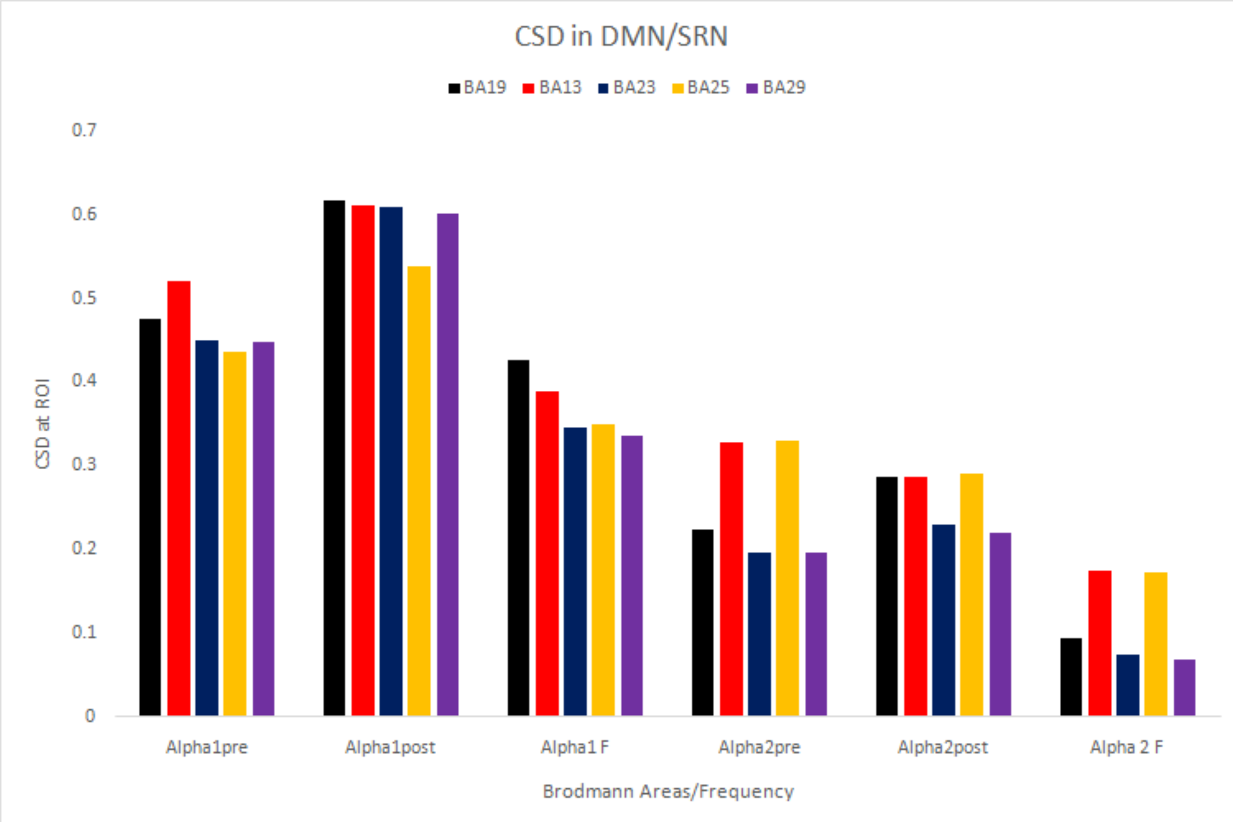

Figure 1. Results for paired *t*-test for pre/post pre/follow and post/follow alpha activity at specific SRN network ROIS corresponding to Table 2. In the figure from left to right are alpha 1 pre EOB, alpha 1 post EOB, alpha 1 follow EOB, alpha 2 pre EOB, alpha 2 post EOB and alpha 2 follow EOB.

Table 3
Paired sample results for region in SRN in alpha 1 and alpha 2 current source density.

Contrast	Mean	*SD*	*SE*	95% L	95% U	*t*	*df*	*p*
a1 pre – a1 post	-.1294	.03068	.01372	-.16757	-.09139	-9.438	4	.001
a1 pre – a1 follow	.09617	.03115	.01393	.05750	.13485	6.904	4	.002
a1 post – a1 follow	.2256	.03721	.01664	.17945	.27185	13.560	4	.000
a2 pre – a2 post	-.0083	.04589	.02052	-.06537	.04859	-.409	4	.704
a2 pre – a2 follow	.1377	.01592	.00712	.11796	.15749	19.347	4	.000
a2 post – a2 follow	.1461	.03224	.01442	.10608	.18615	10.133	4	.001

In the table from left to right are the mean, standard deviation, standard error, lower and upper 95%, *t*-value, degrees of freedom and *p*-value.

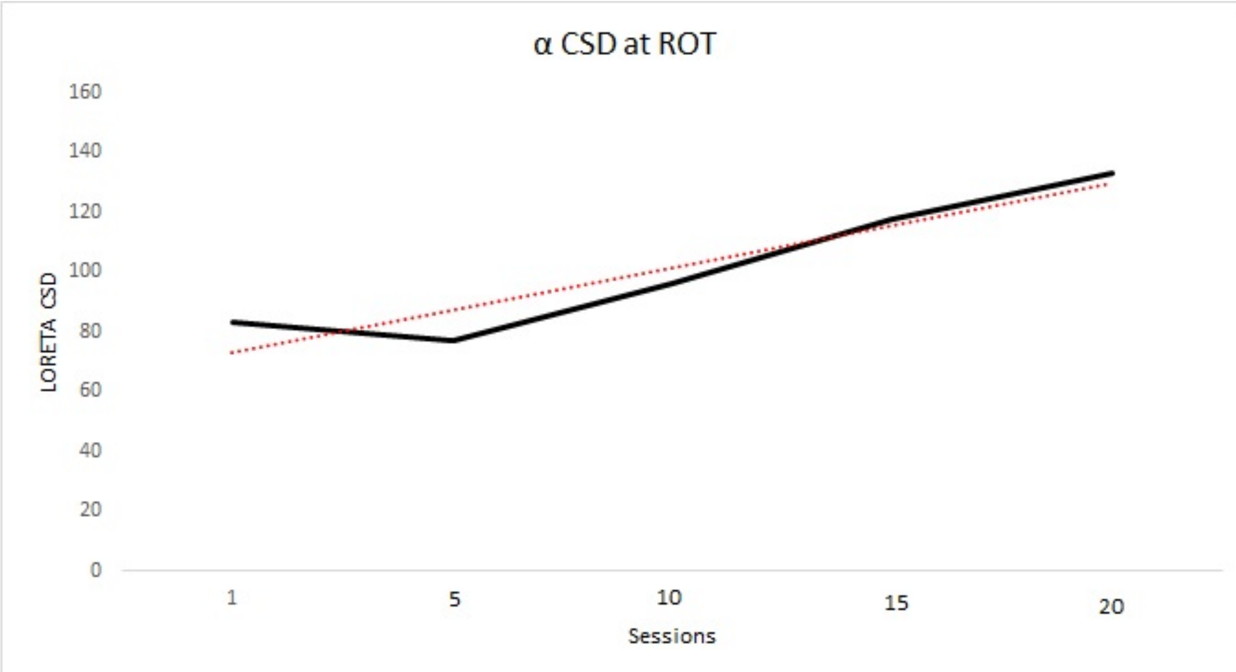

Figure 4. Learning trend for alpha CSD at region of training (ROT), y = 14.112x + 59.199; R^2 = 0.8856.

Discussion

The client was able to complete the 20 sessions of LNFB in the desired fashion. She improved across ABAS-3 ratings by parents and was able to complete an attention test posttraining and at follow-up. She generated a learning trend in the desired direction and shifted alpha CSD in a proposed self-regulation network. She was able to complete the K-CPT posttraining and, at 30-day follow-up with atypical scores in sustained attention and vigilance, there was a significant increase in atypical findings at follow-up. Prior research has noted the important relationship between this anterior insula region with DMN activity, in addition to attention, self-awareness, switching and socio-emotional functions (Menon & Uddin, 2010; Nomi et al., 2016; Odriozola et al., 2016; Uddin & Menon, 2009). Importantly the anterior insula is considered a core hub in the salience network (Goulden et al., 2014). In this respect children suffering from IUDE tend to have difficulties regulating emotionally charged reactions to the environment, including social and interpersonal aspects. In many cases they may be more aggressive and violent as contrasted with normative peers.

The medial parietal and posterior regions of the cortex play a significant role in self-regulation and learning; moreover, recent data suggest a high degree of overlap between DMN and regions activated in social cognitive tasks (Kuzmanovic et al., 2009; Schilbach, Eickhoff, Rotarska-Jagiela, Fink, & Vogeley, 2008). These overlapping regions include the ventromedial prefrontal, including orbital frontal cortex, posterior cingulate/retrosplenial cortices, and inferior parietal lobes. It is therefore relative that the proposed network and its functionality include regions associated with social cognition in addition to the affective and executive processes needed to perform in this domain. The default network has been investigated in 2-week-old to 2-year-old healthy subjects (Gao et al., 2009; Giovanello, Schnyer, & Verfaellie, 2009; Supekar et al., 2010), and is of particular interest concerning exposure to opioids and other drugs of abuse and their impact on the brain for all ages, but more importantly children.

Studies of the effects of opiates on the EEG typically show an increase in beta and higher alpha amplitude and also suggested a right hemisphere sensitivity to adverse opioid effects (Fingelkurts et al., 2008). The neural substrates impacted by IUDE remain unclear as does which neurometric and psychometric data best facilitate rigorous and accurate differential diagnosis. However, the risk of an ADHD diagnosis in these children is increased relative to the increase in DMN activity at rest (Sheinkopf et al., 2009), as well as the well described pronounced difficulties in sustained attention and impulse control across all prenatal substance exposure (Nygaard, Slinning, Moe, & Walhovd, 2016). The current data presents the effects of a standard operant conditioning model in which training produces effects in relative clusters of a network (SRN) that is shown to increase in CSD relative to training one node within it. Additionally, with specific practice of behavioral, social, and executive processes, the activity in this network decreased dramatically over time. This learning and neural efficiency result is important to understanding the effects of neurofeedback over time, in addition to the effects of practice.

The current case study does have limitations. Currently, there are few normative data to contrast children under the age of 4, especially concerning neurometric data. It is worthwhile to mention that younger children are excited and engaged by certain videos that attempt to engage them physically and verbally and patience on the part of the technician or provider is highly productive. Although there are limited data to evaluate normative DMN levels in children less than 6 years of age. She was able to generate a positive linear trend of alpha CSD in the ROT in the specific trained frequency. IUDE presents numerous challenges across all disciplines working with children and operant conditioning of the EEG and current sources within the brain may present the best first line approach to improving a multitude of symptoms and reducing the degree of medication in these children.

References

Bard, K. A., Coles, C. D., Platzman, K. A., & Lynch, M. E. (2000). The effects of prenatal drug exposure, term status, and caregiving on arousal and arousal modulation in 8-week-old infants. *Developmental Psychobiology*, *36*(3), 194–212.

Bhide, P. G., & Kosofsky, B. E. (2009). Neuro-developmental consequences of prenatal drug exposure. *Preface. Developmental Neuroscience*, *31*(1–2), 5. http://dx.doi.org/10.1159/000209397

Blom, J. L., & Anneveldt, M. (1982). An electrode cap tested. *Electroencephalography and Clinical Neurophysiology*, *54*(5), 591–594. http://dx.doi.org/10.1016/0013-4694(82)90046-3

Buckingham-Howes, S., Mazza, D., Wang, Y., Granger, D. A., & Black, M. M. (2016). Prenatal drug exposure and adolescent cortisol reactivity: Association with behavioral concerns. *Journal of Developmental & Behavioral Pediatrics*, *37*(7), 565–572. http://dx.doi.org/10.1097/DBP.0000000000000338

Butz, A. M., Pulsifer, M. B., Leppert, M., Rimrodt, S., & Belcher, H. (2003). Comparison of intelligence, school readiness skills, and attention in in-utero drug-exposed and nonexposed preschool children. *Clinical Pediatrics*, *42*(8), 727–739. http://dx.doi.org/10.1177/000992280304200809

Cannon, R. (2014). Parietal Foci for Attention/Deficit Hyperactivity Disorder: Targets for LORETA Neurofeedback with outcomes. *Biofeedback*, 42(2), 47–57. http://dx.doi.org/10.5298/1081-5937-42.2.01

Cannon, R., Congedo, M., Lubar, J., & Hutchens, T. (2009). Differentiating a network of executive attention: LORETA neurofeedback in anterior cingulate and dorsolateral prefrontal cortices. *International Journal of Neuroscience*, *119*(3), 404–441. http://dx.doi.org/10.1080/00207450802480325

Cannon, R., Lubar, J., Congedo, M., Thornton, K., Towler, K., & Hutchens, T. (2007). The effects of neurofeedback training in the cognitive division of the anterior cingulate gyrus. *International Journal of Neuroscience*, *117*(3), 337–357. http://dx.doi.org/10.1080/00207450500514003

Cannon, R. L., Baldwin, D. R., Diloreto, D. J., Phillips, S. T., Shaw, T. L., & Levy, J. J. (2014). LORETA neurofeedback in the precuneus: Operant conditioning in basic mechanisms of self-regulation. *Clinical EEG and Neuroscience*, *45*(4), 238–248. http://dx.doi.org/10.1177/1550059413512796

Connors, C. (2015). Conners' Kiddie Continuous Performance Test. North Tonawanda, NY: Multi-Health Systems.

Derauf, C., Kekatpure, M., Neyzi, N., Lester, B., & Kosofsky, B. (2009). Neuroimaging of children following prenatal drug exposure. *Seminars in Cell & Developmental Biology*, *20*(4), 441–454. http://dx.doi.org/10.1016/j.semcdb.2009.03.001

Fingelkurts, A., Kähkönen, S., Fingelkurts, A., Kivisaari, R., Borisov, S., Puuskari, V., ... Autti, T. (2008). Reorganization of the composition of brain oscillations and their temporal characteristics during opioid withdrawal. *Journal of Psychopharmacology*, *22*(3), 270–284. http://dx.doi.org/10.1177/0269881108089810

Franck, E. J. (1996). Prenatally drug-exposed children in out-of-home care: Are we looking at the whole picture? *Child Welfare*, *75*(1), 19–34.

Freeman, J. (2000). Testing drug-exposed children. *Iowa Med*, *90*(6), 9.

Gao, W., Zhu, H., Giovanello, K. S., Smith, J. K., Shen, D., Gilmore, J. H., & Lin, W. (2009). Evidence on the emergence of the brain's default network from 2-week-old to 2-year-old healthy pediatric subjects. *Proceedings of the National Academy of Sciences of the United States of America*, *106*(16), 6790–6795. http://dx.doi.org/10.1073/pnas.0811221106

Giovanello, K. S., Schnyer, D., & Verfaellie, M. (2009). Distinct hippocampal regions make unique contributions to relational memory. *Hippocampus*, *19*(2), 111–117. http://dx.doi.org/10.1002/hipo.20491

Goulden, N., Khusnulina, A., Davis, N. J., Bracewell, R. M., Bokde, A. L., McNulty, J. P., & Mullins, P. G. (2014). The salience network is responsible for switching between the default mode network and the central executive network: Replication from DCM. *NeuroImage*, *99*, 180–190. http://dx.doi.org/10.1016/j.neuroimage.2014.05.052

Harrison, P. L., & Oakland, T. (2015). *Adaptive Behavior Assessment System*, *Third Edition (ABAS-3): Manual*. San Antonio, TX: Harcourt Assessment.

Huybrechts, K. F., Bateman, B. T., Desai, R. J., Hernandez-Diaz, S., Rough, K., Mogun, H., ... Patorno, E. (2017). Risk of neonatal drug withdrawal after intrauterine co-exposure to opioids and psychotropic medications: Cohort study. *BMJ*, *358*, j3326. http://dx.doi.org/10.1136/bmj.j3326

Jaeger, D. A., Suchan, B., Schölmerich, A., Schneider, D. T., & Gawehn, N. (2015). Attention functioning in children with prenatal drug exposure. *Infant Mental Health Journal*, *36*(5), 522–530. http://dx.doi.org/10.1002/imhj.21530

Kelley, S. J. (1992). Parenting stress and child maltreatment in drug-exposed children. *Child Abuse & Neglect*, *16*(3), 317–328.

Kne, T., Shaw, M. W., Garfield, E. F., & Hicks, J. (1994). A program to address the special needs of drug-exposed children. *Journal of School Health*, 64(6), 251–253. http://dx.doi.org/10.1111/j.1746-1561.1994.tb06197.x

Kuzmanovic, B., Georgescu, A. L., Eickhoff, S. B., Shah, N. J., Bente, G., Fink, G. R., & Vogeley, K. (2009). Duration matters: Dissociating neural correlates of detection and evaluation of social gaze. *NeuroImage*, *46*(4), 1154–1163. http://dx.doi.org/10.1016/j.neuroimage.2009.03.037

Mars, R. B., Neubert, F.-X., Noonan, M. P., Sallet, J., Toni, I., & Rushworth, M. F. S. (2012). On the relationship between the "default mode network" and the "social brain." *Frontiers in Human Neuroscience*, *6*, 189. http://dx.doi.org/10.3389/fnhum.2012.00189

Mayes, L. C., Cicchetti, D., Acharyya, S., & Zhang, H. (2003). Developmental trajectories of cocaine-and-other-drug-exposed and non-cocaine-exposed children. *Journal of Developmental & Behavioral Pediatrics*, *24*(5), 323–335. http://dx.doi.org/10.1097/00004703-200310000-00003

McNichol, T. (1999). The impact of drug-exposed children on family foster care. *Child Welfare*, *78*(1), 184–196.

Menon, V., & Uddin, L. Q. (2010). Saliency, switching, attention and control: A network model of insula function. *Brain Structure and Function*, 214(5-6), 655–667. http://dx.doi.org/10.1007/s00429-010-0262-0

Nadebaum, C., Anderson, V., Vajda, F., Reutens, D., & Wood, A. (2012). Neurobehavioral consequences of prenatal antiepileptic drug exposure. *Developmental Neuropsychology*, *37*(1), 1–29. http://dx.doi.org/10.1080/87565641.2011.589483

Nomi, J. S., Farrant, K., Damaraju, E., Rachakonda, S., Calhoun, V. D., & Uddin, L. Q. (2016). Dynamic functional network connectivity reveals unique and overlapping profiles of insula subdivisions. *Human Brain Mapping*, *37*(5), 1770–1787. http://dx.doi.org/10.1002/hbm.23135

Nygaard, E., Slinning, K., Moe, V., & Walhovd, K. B. (2016). Behavior and attention problems in eight-year-old children with prenatal opiate and poly-substance exposure: A longitudinal study. *PLoS One*, *11*(6), e0158054. http://dx.doi.org/10.1371/journal.pone.0158054

Odriozola, P., Uddin, L. Q., Lynch, C. J., Kochalka, J., Chen, T., & Menon, V. (2016). Insula response and connectivity during social and non-social attention in children with autism. *Social Cognitive and Affective Neuroscience*, *11*(3), 433–444. http://dx.doi.org/10.1093/scan/nsv126

Pulsifer, M. B., Radonovich, K., Belcher, H. M. E., & Butz, A. M. (2004). Intelligence and school readiness in preschool children with prenatal drug exposure. *Child Neuropsychology*, *10*(2), 89–101. http://dx.doi.org/10.1080/09297040490911104

Robey, A., Buckingham-Howes, S., Salmeron, B. J., Black, M. M., & Riggins, T. (2014). Relations among prospective memory, cognitive abilities, and brain structure in adolescents who vary in prenatal drug exposure. *Journal of Experimental Child Psychology*, *127*, 144–162. http://dx.doi.org/10.1016/j.jecp.2014.01.008

Schilbach, L., Eickhoff, S. B., Rotarska-Jagiela, A., Fink, G. R., & Vogeley, K. (2008). Minds at rest? Social cognition as the default mode of cognizing and its putative relationship to the "default system" of the brain. *Consciousness and Cognition*, *17*(2), 457–467. http://dx.doi.org/10.1016/j.concog.2008.03.013

Sheinkopf, S. J., Lester, B. M., Sanes, J. N., Eliassen, J. C., Hutchison, E. R., Seifer, R., ... Casey, B. J. (2009). Functional MRI and response inhibition in children exposed to cocaine in utero. Preliminary findings. *Developmental Neuroscience*, *31*(1–2), 159–166. http://dx.doi.org/10.1159/000207503

Sidlauskaite, J., Sonuga-Barke, E., Roeyers, H., & Wiersema, J. R. (2016). Default mode network abnormalities during state switching in attention deficit hyperactivity disorder. *Psychological Medicine*, *46*(3), 519–528. http://dx.doi.org/10.1017/S0033291715002019

Supekar, K., Uddin, L. Q., Prater, K., Amin, H., Greicius, M. D., & Menon, V. (2010). Development of functional and structural connectivity within the default mode network in young children. *NeuroImage*, *52*(1), 290–301. http://dx.doi.org/10.1016/j.neuroimage.2010.04.009

Uddin, L. Q., & Menon, V. (2009). The anterior insula in autism: Under-connected and under-examined. *Neuroscience & Biobehavioral Reviews*, *33*(8), 1198–1203. http://dx.doi.org/10.1016/j.neubiorev.2009.06.002

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