0:00:05.8 Sarah Crespi: Welcome to the Science Podcast for May 21st, 2021. I'm Sarah Crespi. Each week we feature the most interesting news and research published in Science and its sister journals. First up, staff news writer, Kelly Servick. She talks about the specifics of using talk therapy alongside the drug MDMA, also known as ecstasy for treating PTSD. Next economist Pamela Jakiela discusses how it's important to keep tabs on mothers during early childhood development interventions like free day care or parenting classes, because what impacts kids can impact the parents too.

0:00:44.8 SC: Now we have staff writer and editor, Kelly Servick, she's here to talk about the future of MDMA. This is a controlled substance, sometimes called ecstasy or Molly, that has had some success in clinical trials for PTSD, alongside talk therapy. Okay, Kelly, how you doing?

0:01:04.5 Kelly Servick: I'm doing okay, how are you Sarah?

0:01:06.0 SC: Good, I'm good. Let's start with the recent clinical trial results, so this is of MDMA and therapy, and it was tested on PTSD patients. How did that go? How did that work?

0:01:19.0 KS: So there were 90 people in this study who were randomized to get kind of a unique course of psychotherapy, they had a series of preparatory sessions with a trained therapist, and then they got three eight-hour long experimental sessions, where they got either MDMA or a placebo, and then they got this series of integration sessions to process that experience, and the results were that two months after the last experimental session, the difference between the drug and the placebo groups was pretty clear, 67% of the participants who got MDMA no longer met the diagnostic criteria for PTSD at that point, compared with 32% of those who got a placebo, so this is sort of the biggest and most thorough study of its kind to really find potential benefits of this drug in PTSD.

0:02:10.5 SC: What are the effects of this drug on people? I think maybe from popular culture, people might think of it as something you take in a night club.

0:02:18.8 KS: Yeah, this has definitely a reputation of a club drug, that I think that these investigators are really trying to overcome, MDMA has a lot of complicated mechanisms and we don't understand all of them, but it's thought that many of its effects come from its ability to increase certain neurotransmitters in the brain, including dopamine and serotonin, and so people sometimes describe a euphoric experience, sometimes a sense of openness and a heightened ability for empathy, and you can imagine that's something that in the case of PTSD, therapists might aim to exploit if a trauma survivor is facing intrusive flashbacks and is really avoiding these disturbing memories of something that happened to them, this drug might give them sort of a less fearful, less judgmental state in which to reflect on and process what happened to them. That's the thinking.

0:03:10.0 SC: Well. So far, this clinical trial is a large clinical trial and it has some multi-month long results, what are the next steps for getting this approved by the FDA for treatment, for people that are not involved in a study.
0:03:23.1 KS: This study was sponsored by this non-profit organization called the Multidisciplinary Association for Psychedelic Studies MAPS, which does intend to seek formal FDA approval for the drug, and FDA has granted MDMA what's called a breakthrough designation, which would sort of expedite the agency's review of the data, so the next thing that needs to happen is a second phase three study with about a 100 participants to confirm the results that were published last week, and then MAPS would submit its data package to FDA for review. I think they're hoping by 2023.

0:03:55.8 SC: How does this treatment compare with other approved treatments for PTSD? Do we know if this approach, the results we've seen in these clinical trials so far are comparable.

0:04:05.2 KS: That's an important question. Researchers at MAPS pointed out that the placebo group here that just got the psychotherapy did see improvements, and that those are potentially comparable to what people see with other PTSD psychotherapies, but we really can't draw conclusions until these things go head-to-head in a clinical trial where we're comparing MDMA-assisted psychotherapy to some other type of psychotherapy or to the antidepressant drugs that are already approved for PTSD.

0:04:31.1 SC: Well, one tricky point here is that it's not just, here's a drug, now you feel better, there's actually this talk therapy component to the trial that we just talked about and the ones coming up, this is called drug-assisted therapy, is this a common approach for PTSD or other problems?

0:04:49.0 KS: It's a term that's been used before, but it's sort of what I wanted to dig into after I read these results because this is built as MDMA assisted psychotherapy, like what does that assisted mean? And I got different feedback about that. Medication-assisted therapy has been used to describe treatments for opioid addiction such as methadone, and some people have argued that that's not really an appropriate term, that it sort of downplays the value of the drug, and it's really a response to stigma around people seeking pharmacological treatment for their addiction. I think the situation here is a little bit different in that we know supervision is probably going to be important for psychedelic drugs, they've long had a reputation unfairly, I think a lot of researchers would suggest as being illicit substances with high potential for abuse, and then MDMA also does appear to sort of open people up to an experience, and there's this thought that then you need to sort of cultivate a particular experience for them, so the big question is just what are the essential parts of this psychotherapy and what does that need to look like?

0:05:48.4 SC: I mean, you just need guardrails to help make sure that you're not having a bad experience on the drug.

0:05:54.2 KS: Exactly, that's the question, how much guidance and what kind of guidance and how much should that look like the PTSD therapies that are already out there.

0:06:01.2 SC: They must have standardized it across the treatment in the study.

0:06:04.5 KS: They did. Yeah, this is a psychotherapy approach that was developed by MAPS, the
sponsor over many years, and it was specifically designed to support someone who has taken
MDMA, it's influenced by a bunch of different things, including controlled breathing techniques
and practices developed in the '60s for psychedelic therapy, and even indigenous rituals from
various places, it's pretty different from more mainstream, sort of evidence-based talk therapies for
PTSD.

0:06:32.0 SC: These are more confrontational in some ways.

0:06:34.5 KS: Yeah, the term they often use is directive, they're telling people say out loud in the
present tense what happened here, and recount this event in order to change your relationship to it
and learn not to avoid it, that's often the approach.

0:06:48.5 SC: Are the people who are on MDMA, in the talk therapy, are they told to revisit their
experiences?

0:06:55.0 KS: My understanding is that often they will get around to discussing those experiences,
that the therapists involved are encouraged not to push them too much in that direction, and they
don't have as much of a script of how a therapy session is supposed to go like, "Okay, now we're
gonna go back to the trauma, and now we're gonna do this." It's just a little bit more participant-
directed.

0:07:16.0 SC: We're getting closer to the FDA approving this in the next several years, are they
going to approve this specific therapy?

0:07:25.1 KS: That is a question I had going into this. And here's how much I understand now, we
don't know exactly what FDA is gonna stipulate about this drug when it decides. It usually doesn't
tell us those kinds of things in advance, but the MAPS team is anticipating based on their
conversations with the agency that the drug label will say, "This is for use alongside supportive
therapy," and there will be a FDA-mandated safety program that requires people who administer
MDMA to go through a special training, but FDA doesn't directly regulate psychotherapy, so it
likely wouldn't say "You have to give the MAPS therapy," or "You have to go through the MAPS
training." However, in practice, they might be the only game in town for a while, because a sort of a
subsidiary of MAPS would manufacture the drug and they intend to receive a five-year exclusivity
period on marketing the drug for PTSD, and they would also sell MDMA only to providers who are
in this database of people who have undergone their special 100-hour training program, so it seems
likely that that approach is gonna dominate at least at first, if this were to be approved.

0:08:30.0 SC: Just in 2020 psilocybin, which is a controlled substance and also a psychedelic drug,
has been approved for therapeutic use in the state of Oregon, will they be running into some similar
regulatory issues?

0:08:45.0 KS: It sounds like they will have to work through a lot of similar questions about what
kind of support and supervision needs to go along with psilocybin. So the measure that Oregon
voters approve describes a pretty controlled system, where are these state licensed providers, but
how those providers get qualified, what type of therapy they might get trained in, that still isn't
clear. So this is a bigger question for psychedelics, I think.

0:09:11.5 SC: We talked about MDMA and therapy and psilocybin and having a talk therapy component to that as well, is this gonna be more common going forward, not just for psychotropic drugs, but other kinds of drugs?

0:09:25.0 KS: One of the researchers I spoke to, described this idea of pairing a drug with psychotherapy as sort of a new zeitgeist in psychotherapy, I don't know how far that's going to extend, but it is clear that supportive therapy can be very beneficial to someone who's taking a drug for a psychiatric condition, so I think that's a possibility that this will open up more work on synergy between drugs and talk therapy, that has yet to be seen.

0:09:51.0 SC: Alright, thank you so much, Kelly.

0:09:52.2 KS: Thank you, Sarah.

0:09:53.5 SC: Kelly Servick is a staff writer for Science, you can find a link to the story we discussed at sciencemag.org/podcast. Stay tuned for my chat with Pamela Jakiela about why it's important to track effects on mothers when early childhood development intervention programs are underway.

[music]

0:10:17.5 SC: Early childhood development programs are at work around the world, but what does it mean for the mothers of children to suddenly get day care for their child or have a specialist visit to talk about parenting? The answer is, we don't know. Pamela Jakiela wrote a policy forum in this week's issue that focuses on this question and why the answer is important. Hi Pamela.

0:10:38.5 Pamela Jakiela: Hello.

0:10:39.0 SC: First, let's take early childhood development programs, what are the ultimate goals of these types of interventions?

0:10:46.2 PJ: Well, there are more than 250 million children around the world who are currently at risk of failing to meet their developmental potential because they are either not getting enough nutrition or not getting enough early childhood stimulation, and there are a lot of programs ranging from day care to early visits from child development specialists for children who are at risk, to support groups for mothers, to cash grant programs that are all intended to try to overcome these obstacles and help families and communities invest enough in young children so that they can get beyond the best possible developmental trajectories.

0:11:27.2 SC: As I said in my intro, this is something that we see around the world, organizations, governments, non-profits are interested in early childhood development goals. Can you talk about why that is?
0:11:39.0 PJ: Early childhood is an incredibly important stage in human development, and there is plenty of evidence showing that well-designed interventions, whether they're nutrition interventions or play-based stimulation interventions can have really long run impacts. They can improve health, they can improve adult incomes, and so increasingly, there is a recognition by governments in low and middle income countries, also in rich countries, and by donors and policy makers that it is important to try to build up the set of well-measured, well-studied policy tools we have, to try to improve outcomes in early childhood, because we've seen that there are policies that can have really big returns, and we worry that underinvestment in early childhood, because it has these feedback effects as you get older throughout childhood and into adulthood, if we don't invest enough in early childhood, you can get stuck in a cycle of poverty and low income, that investing enough in early childhood, we hope can help to break.

0:12:43.9 SC: So let's talk about mothers, what we know about the effects of early childhood development programs on them, this really hasn't been quantified, how are you able to look at this?

0:12:54.3 PJ: What we did in this piece, or for this piece, is we did a systematic review of a number of different literature, so I'm an economist, my co-author, Dr. Heather Knauer is a child development specialist, we did a review of the social science, the public health, the medical literature, trying to understand the set of impact evaluations of early childhood interventions in low and middle income countries over the last 15 years, and through those we identified about 500 studies, and we just went through them to look at which ones are measuring outcomes for children, which ones are measuring outcomes specifically about parenting, and which studies are measuring anything else about mothers or more generally other people in the household, and what we find is that a very small number of these studies, about 25 percent of all of the studies we found measure anything to do with the sort of well-being or activities beyond parenting of anyone else in the household.

0:13:51.0 SC: That's really surprising because there's also a lot of people interested in helping women, empowering women, getting women to the labor force or getting them more education, and those interventions would seem to overlap with the interventions that we're talking about here.

0:14:05.2 PJ: That's true. I think that part of what's going on is that you have people who maybe exist a little bit in their silo, so a lot out of early childhood interventions are being done by child development specialists, which is great, it is really important to carefully measure outcomes for children in these interventions, but I think that maybe working within that literature can lead people to be too laser-focused on the outcomes for children and to forget that when outcomes for children change through some of these interventions, that's because moms are doing different things and they likely are impacting mothers as well, and I think the flip side is that you do often see evaluations of empowerment programs or women's labor market programs that also don't necessarily focus particularly on what's happening for the children.

0:14:51.1 SC: Were you able to tell anything about the impact of these kinds of programs on women from the limited data that were available in the studies you looked across?

0:15:00.4 PJ: Yes, there are two areas in particular where it seems like even though the literature is
very sparse, we are able to say something. The first area is looking at day care and pre-school interventions. That's the category that is sort of relatively likely to report impacts on mothers and their labor force participation, but even so, it's only about less than a quarter of studies that report those outcomes, but we see when studies do report outcomes impacts on women's labor force participation, a number of these studies do increase women's labor supply, employment participation overall. So it is pretty clear among studies that are reporting these outcomes, which we don't know that that's a representative sample of all of the studies, but almost in all the studies that do report these outcomes find some positive impacts in the sense that access to day care, access to pre-school does increase women's labor force participation.

0:15:52.5 SC: Where else were you able to see impacts?

0:15:55.0 PJ: The other category that we really do feel like the literature is there enough to say something, is in terms of group parenting classes, there are now a number of studies of these interventions and quite a few that report improvements in women's mental health as a result, there's evidence from different studies that parent education, group parenting classes for mothers have reduced maternal depression in Bangladesh, in Guatemala, in Pakistan, in South Africa, in Uganda and in Zambia. So those are six different studies that all show the same pattern where well-structured parent education classes for moms can improve their mental health, and there are a number of other studies that show results that point in the same direction, maybe they're not quite statistically significant, or maybe they're looking at a slightly different mental health outcome, but overall, it does seem like group parenting classes, in particular, can improve women's mental health, which of course may be one of the ways that they then translate into impacts on early childhood development.

0:17:00.5 SC: Is this one of the recommendations that you would make then, based on what you've seen so far, is that researchers looking into this kind of thing should look at mental health of parents, look at whether or not they're re-entering the workforce, those kinds of questions?

0:17:12.4 PJ: In general, I think that's right. I think what's important to realize is that for many ECD interventions, though not necessarily all, you're trying to change not just outcomes for the children, but also behaviors of the parents, the other household members, and when that's the case, you can't necessarily get a well-rounded picture of the impacts of an intervention without measuring outcomes for other family members, it's not that you always need to measure these things, you might say, "Look, my vitamin A intervention is not really going to impact mothers," and you can make that case, you can discuss whether that's true based on your theory of change, but it's important to always think about, "Is this an intervention that is likely to impact other household members," and if so, it's important to measure those impacts to understand the full picture of effects of the program.

0:18:00.0 SC: When you look to see what the impact was of early childhood development interventions on parents, if there were any numbers, it was almost always mothers.

0:18:09.5 PJ: I think part of what you're asking is why not also look at fathers, they do something too, they're important too. And you're completely right, and I would say we did in this study also track impact on fathers, and out of 478 impact evaluations, there are only 12 that say anything about
the fathers, including just what they do as parents, partially, this is simply a recognition of the fact that in many societies, fathers do much less parenting than mothers, and honestly than grandmothers and sisters, but I think it's also a hole in the literature and a hole in the literature that is increasingly recognized that there are now a few interventions that have had success trying to get fathers more involved in parenting, and there's a greater recognition that these interventions that change labor supply or parenting behavior, they're likely going to have ramifications for the whole household.

0:19:06.0 SC: I guess someone could push-back on this and say, "This is still creep. We can't measure everything."

0:19:11.2 PJ: I think there's a recognition that measuring additional outcomes is costly, and so there are cases where it doesn't necessarily make sense to try to measure impacts that you are not going to have statistical power to pick up in your sample. We see this in the few evaluations that try to measure empowerment, often those estimates are extremely imprecise, and I think it's worth recognizing that many people who do studies, in fact, almost all of us don't have infinite budget to just measure everything we would want and things always will have to get cut.

0:19:42.9 SC: Right, and who is, is someone gonna make a decision based on the fact that this has a negative or positive impact on the parents.

0:19:49.0 PJ: Right, so one thing is that there are cases, and this is a little bit what I was getting to before, it seems important to at least discuss whether there are impacts that you are not measuring and picking up when we think about how do your results translate into implications for policy in that if you know you are not measuring something that is likely to change as a result of your intervention, then you should be explicit about the fact that you're likely missing part of the picture, and there are cases where if we think for instance, with these evaluations of group-based parenting, we find that many of them improve women's mental health. Now that's not necessarily a given, but if you think a program is already positive and it has additional positive impacts, it already is sort of cost-effective and that it has additional positive impact, then that may just make the case stronger, but it's important to recognize what you're measuring and what you're not measuring and what that means, and in particular with early childhood, it's really important that we don't have such a laser-focus on the welfare of children that we forget that women are also vulnerable, mothers in poor countries are a vulnerable group of people and their welfare matters too, and we really should be taking account of that in the design of these policies.

0:21:01.0 SC: Thank you so much, Pamela.

0:21:02.0 PJ: My pleasure.

0:21:03.0 SC: Pamela Jakiela, is an Associate Professor of Economics at Williams College in Massachusetts. You can find a link to the Policy Forum we discussed at sciencemag.org/podcast.

0:21:13.0 SC: And that concludes this edition of the Science Podcast. If you have any comments or suggestions for the show, write to us at sciencepodcast@aaas.org. You can listen to the show on the Science website at sciencemag.org/podcast. On the site, you'll find links to the research and news
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